e-ISSN:2602-2079

Volume 2
Issue 3
September - December 2018

JOURNAL of Surgery and Medicine

International Medical Journal

JOSAM

Volume: 2 - Issue: 3

Contents

Research article

Review of clinical and demographic features of frontal fibrosing alopecia (http://dergipark.gov.tr/josam/issue/36726/411086) / Pages: 197-200 PDF (/download/article-file/464137)
Güldehan Atış, Zeynep Altan Ferhatoğlu

Successful treatment of intussusception by hydrostatic reduction in pediatric patients: Is everything okay? (http://dergipark.gov.tr/josam/issue/36726/408972) / Pages: 201-204 PDF (/download/article-file/464143)
Burhan Beger

Comparison of three different sternal closure techniques after cardiac surgery in elderly patients (http://dergipark.gov.tr/josam/issue/36726/411872) / Pages: 205-209 PDF (/download/article-file/462209)
Mazlum Şahin, Helin El, Fatma Tuba İlal Mert

Determination of CYP2D6*3 and *4 allele frequency among Turkish population (http://dergipark.gov.tr/josam/issue/36726/416309) / Pages: 210-214 PDF (/download/article-file/463140)
Zehra Okat, Kübra Yaman, Kezban Uçar Çiftçi, Selina Toplayıcı, Elif Kurt, Yavuz Taga

Using multiplex PCR as a diagnostic tool to detect methicillin resistant Staphylococcus aureus (http://dergipark.gov.tr/josam/issue/36726/415215) / Pages: 215-217 PDF (/download/article-file/470714)
Sadık Akgün, Hakan Sezgin Sayiner

Positive association of neck circumference and cardio-metabolic risk factors in Ekiti, Nigeria (http://dergipark.gov.tr/josam/issue/36726/417473) / Pages: 218-222 PDF (/download/article-file/474354)
Dr. Taiwo Hussean Raimi, Dr. Samuel Ayokunle Dada, Abimbola Solanke

Comparative study of Mycobacterium tuberculosis and Mycobacterium bovis protein profiles (http://dergipark.gov.tr/josam/issue/36726/417158) / Pages: 223-227 PDF (/download/article-file/471639)

Mohammad Kazem Sharifi Yazdi, Amir Houshang Beheshtnejad, Azim Hedayatpour, Sara Sharifi-Yazdi, Fariborz Mehrani

Troponin I levels before bypass surgery after acute myocardial infarction; When to operate? (http://dergipark.gov.tr/josam/issue/36726/416286) / Pages: 228-232 PDF (/download/article-file/481718)
Mihriban Yalçın, Eda Gödekmerdan Katırcıoğlu, Serkan Yazman, Kaptanı Derya Tayfur, Melih Ürkmez

The demographic and clinical characteristics of patients with cerebral palsy: A retrospective, single center, observational study (http://dergipark.gov.tr/josam/issue/36726/418229) / Pages: 233-235
Yılmaz İnanç, Tuba Tülay Koca PDF (/download/article-file/484112)

General surgery service with limited feasibility in a rural hospital; Retrospective cohort study (http://dergipark.gov.tr/josam/issue/36726/422797) / Pages: 236-238 PDF (/download/article-file/489947)
Fatih Başak

Impact of a program of induced stress therapy on the motor and functional recovery of the upper limb of hemiplegic patients in Kinshasa, Democratic Republic of Congo (http://dergipark.gov.tr/josam/issue/36726/417843) / Pages: 239-243 PDF (/download/article-file/488348)
Teddy Bofosa, Eric Kam, François Njimbu, Ponce Mpefi, Tharcis Kayembe, Betty Miangindula

B-Mode ultrasound assessment of intima-media thickness of common carotid, internal carotid, brachial, femoral arteries and abdominal aorta in patients with cardiovascular risk factor (http://dergipark.gov.tr/josam/issue/36726/421768) / Pages: 244-248 PDF (/download/article-file/492855)
Ayşe Selcan Koç, Burçak Çakır Peköz

Effects of peri-operative administration of steroids on the blood glucose levels of patients with and without diabetes undergoing laparoscopic cholecystectomy (http://dergipark.gov.tr/josam/issue/36726/424450) / Pages: 249-252 PDF (/download/article-file/492857)
Duygu Demiriz Gülmez, Asu Özger Özgültekin, Osman Ekinci, Mehmet Gülmez

Can failure of choledochal cannulation in endoscopic retrograde cholangiopancreatography be prevented? (http://dergipark.gov.tr/josam/issue/36726/435834) / Pages: 253-256 PDF (/download/article-file/493353)
Yahya Kemal Çalışkan, Mustafa Uygar Kalaycı

Assessment of regional cerebral blood flow in patients with early and late onset alcohol dependence: SPECT study (http://dergipark.gov.tr/josam/issue/36726/420428) / Pages: 257-261 PDF (/download/article-file/497277)
Esin Erdoğan, Erdal Vardar, Gülay Durmuş Altun, Mehmet Fatih Fırat

An evaluation of the infection agents and the demographic characteristics of patients followed up on a mechanical ventilator in neurology intensive care: A retrospective, single center, observational study (http://dergipark.gov.tr/josam/issue/36726/427084) / Pages: 262-264 PDF (/download/article-file/499832)
Yılmaz İnanç, Yusuf İnanç

Evaluation of air pollution by PM10 and SO2 levels in Erzurum province, Turkey: Descriptive study (http://dergipark.gov.tr/josam/issue/36726/422921) / Pages: 265-268 PDF (/download/article-file/500269)
Zahide Koşan, Duygu Kavuncuoğlu, Elif Okşan Çalıkoğlu, Ezel Bilge Yerli

A case-control study on rosacea and vitamin D levels (http://dergipark.gov.tr/josam/issue/36726/428632) / Pages: 269-272 PDF (/download/article-file/500617)
Gülhan Gürel, Müjgan Karadöl, Emine Çölgeçen

The effect of osteoporosis on cochlear function in postmenopausal women: An observational study (http://dergipark.gov.tr/josam/issue/36726/429059) / Pages: 273-277 PDF (/download/article-file/500731)
Saime Sağıroğlu, Tuba Tülay Koca

Management of Bonsai intoxication at emergency service: A review of 61 cases (http://dergipark.gov.tr/josam/issue/36726/422416) / Pages: 278-282 PDF (/download/article-file/510722)
Nadiye Karabulut, Seda Demirel Dengi, Sündüs Görükmez, Seçil Arıca, Selman Yeniocak

The incidence of isthmocele may be higher than reported (http://dergipark.gov.tr/josam/issue/36726/424328) / Pages: 283-287 PDF (/download/article-file/503383)

Pervin Karlı, Banuhan Şahin, Fadıl Kara

Incidental findings at abdominal ultrasonography in health personnel working with radiation sources (http://dergipark.gov.tr/josam/issue/36726/430050) / Pages: 288-292 PDF (/download/article-file/506685)
Elif Gündoğdu, Mahmut Kebapçı

The relationship between dialysis adequacy and the rate of change in uric acid level by hemodialysis (http://dergipark.gov.tr/josam/issue/36726/433344) / Pages: 293-297 PDF (/download/article-file/510098)
Oktay Bozkurt, Cevat Topal, Mevlüde İnanç

The effects of perceived social support on postpartum depression (http://dergipark.gov.tr/josam/issue/36726/433898) / Pages: 298-302 PDF (/download/article-file/507346)
Kenan Taştan, Halime Pınar Demiröz

The effects of health warning labels on cigarette packages on patients who apply to cardiology clinic (http://dergipark.gov.tr/josam/issue/36726/435234) / Pages: 303-309 PDF (/download/article-file/510183)
Ercan Akşit, Çoşkun Bakar, Özgür Özerdoğan, Özge Turgay Yıldırım, Fatih Aydın, Ayşe Hüseyinoğlu Aydın, Bahadır Kırılmaz, Emine Gazi, Ali Duygu

The effect of CPAP during preoxygenation and PEEP during induction upon the duration of non-hypoxic apnea and hemodynamic parameters (http://dergipark.gov.tr/josam/issue/36726/436032) / Pages: 310-314
Havva Esra Uyar Türkyılmaz, Asutay Göktuğ, Selçuk Tur, Hülya Başar PDF (/download/article-file/510400)

Acute toxicities of three-dimensional conformal radiotherapy in the treatment of gynecological cancer, and retrospective dosimetric comparison of three dimensional conformal radiotherapy and invers intensity-modulated radiotherapy (http://dergipark.gov.tr/josam/issue/36726/421803) / Pages: 315-319
Halil Sağınç, Özgür Yıldırım, Bahar Baltalarlı PDF (/download/article-file/511331)

Rare and overlooked two diagnoses in low back pain: Osteitis condensans ilii and lumbosacral transitional vertebrae (http://dergipark.gov.tr/josam/issue/36726/429889) / Pages: 320-323
Elif Gündoğdu PDF (/download/article-file/513555)

Clinical outcome of stereotactic ablative radiotherapy with CyberKnife® for lung tumors: A single center experience (http://dergipark.gov.tr/josam/issue/36726/432680) / Pages: 324-329
Ebru Atasever Akkaş, Ebru Karakaya, Gonca Altınışık İnan, Yasemin Güzle PDF (/download/article-file/513982)
Adaş, Ömer Yazıcı, Esra Kekilli, Ferhat Kıran, Ferihan Ertan, Bülent Küçükpilakçı, Yıldız Güney

The clinic importance of bilirubin parameters in ankylosing spondylitis: Case control study (http://dergipark.gov.tr/josam/issue/36726/441711) / Pages: 330-333 PDF (/download/article-file/514753)
Tuba Tülay Koca, Gözde Yıldırım Çetin, Hasan Göğebakan, Vedat Nacitarhan

Review

Ethics education during medical residency training and biopsychosocial approach (http://dergipark.gov.tr/josam/issue/36726/429206) / Pages: 334-336 PDF (/download/article-file/513381)
Mehmet Ziya Gençer, Seçil Arıca, Ege Ağırman

Case report

Kounis syndrome as a result of anaphylactic reaction to diclofenac sodium: A case report (http://dergipark.gov.tr/josam/issue/36726/402775) / Pages: 337-338 PDF (/download/article-file/464155)
Abdullah İbrahim, Şahin Çolak, Mehmet Özgür Erdoğan, Mustafa Ahmet Afacan, Ayhan Sarıtaş, Hayati Kandiş

Oral hairy leukoplakia in the buccal mucosa of a healthy, HIV-negative patient (http://dergipark.gov.tr/josam/issue/36726/412354) / Pages: 339-341 PDF (/download/article-file/464133)
Gülhan Gürel, Sevinç Şahin, Betül Aytekin, Emine Çölgecen

Simultaneous dorsal dislocation of the proximal interphalangeal joints in two digits: A case report (http://dergipark.gov.tr/josam/issue/36726/409227) / Pages: 342-343 PDF (/download/article-file/461743)
Suavi Aydoğmuş, Can Emre Baş, Tahir Mutlu Duymuş, Adnan Behçet Kafadar

Rare and challenging two complications after prostate biopsy of an older man (http://dergipark.gov.tr/josam/issue/36726/410144) / Pages: 344-346 PDF (/download/article-file/464138)
Tuğba Turgut, Deniz Mut Sürmeli, Remzi Bahşi, Hande Selvi Öztorun, Murat Varlı

Cytomegalovirus myocarditis with rapid response to intravenous immunoglobulin therapy (http://dergipark.gov.tr/josam/issue/36726/413987) / Pages: 347-349 PDF (/download/article-file/463178)
Mehmet Türe, Hasan Balık, Meki Bilici, Alper Akın, Savaş Mert Darakci, Sercan Yücel Yanmaz

Mesenteric panniculitis: Case report (http://dergipark.gov.tr/josam/issue/36726/408634) / Pages: 350-352
Eddy Oleko Ekuke, Fatoumata Djouldé Diallo, El Bachir Benjelloun, Benajah Dafr-Allah PDF (/download/article-file/464102)

Syringomatous adenoma of the nipple: Case report (http://dergipark.gov.tr/josam/issue/36726/412609) / Pages: 353-355 PDF (/download/article-file/464320)
Şirin Yaşar, Nurhan Döner Aktaş, Ayşegül Sevim Keçici, Pembegül Güneş, Güldehan Atış

Klippel-Trenaunay syndrome in a patient presenting with venous stasis ulcer (http://dergipark.gov.tr/josam/issue/36726/415187) / Pages: 356-358 PDF (/download/article-file/471939)
Kevser Tural, Zeynep Bilgi, Ceyhun Coşkun

The rupture of the diaphragm: Case report (http://dergipark.gov.tr/josam/issue/36726/419440) / Pages: 359-360
Eddy Oleko Ekuke, Jamal Zhar, Hicham El Bouhaddouti PDF (/download/article-file/478913)

A case of langerhans cell histiocytosis associated with mantle cell lymphoma (http://dergipark.gov.tr/josam/issue/36726/403513) / Pages: 361-363 PDF (/download/article-file/480201)
Gülen Gül, Mehmet Ali Özcan, Fatih Demirkan, Sermin Özkal

Tuba-ovarian abscess in a sexually inactive teenager with Down syndrome: Case report and brief review of literature (http://dergipark.gov.tr/josam/issue/36726/417557) / Pages: 364-366 PDF (/download/article-file/483043)
Ramazan Cahit Temizkan, Muhammet Mesut Nezir Engin, Harun Güneş, Önder Kılıçaslan, Merve Aslantaş, Murat Kaya, Kenan Kocabay

Long term extracorporeal membrane oxygenation therapy for H1N1 influenza related acute respiratory distress syndrome and several complications (http://dergipark.gov.tr/josam/issue/36726/420716) / Pages: 367-369 PDF (/download/article-file/494481)
Behiye Deniz Kosovalı, Fatma İrem Yeşiler, Tülay Tunçer Peker, Mustafa Kemal Bayar

Life-threatening isosulfan blue induced anaphylaxis during laparoscopic hysterectomy (http://dergipark.gov.tr/josam/issue/36726/421505) / Pages: 370-373 PDF (/download/article-file/492856)
Melike Korkmaz Toker, Başak Altıparmak, Mustafa Turan, Bakiye Uğur, Semra Gümüş Demirbilek

A case of postmenopausal ovarian hyperandrogenemia diagnosed only by selective catheterization of ovarian vein (http://dergipark.gov.tr/josam/issue/36726/424326) / Pages: 374-376 PDF (/download/article-file/494478)
Vedat Uğurel, Mehmet Musa Aslan, Koray Elter

Cystic intestinal pneumatosis revealed by peritonitis in perforated peptic ulcer: A case report (http://dergipark.gov.tr/josam/issue/36726/426196) / Pages: 377-379 PDF (/download/article-file/497979)
Dandakoye Soumana Ismael, Anas Belhaj, Moussa Sylla, Somuah Tenkorang, Mouaqit Ouadii, Ibn Majdoub Hassani, Imane Toughrai, Hassan Moulay Farih, Khalid Mazaz, Ait taleb Khalid

Kidney clear cell sarcoma: About one case (http://dergipark.gov.tr/josam/issue/36726/426924) / Pages: 380-382 PDF (/download/article-file/499104)
Fadwa Allouche, Asmae Mazti, Fatima Zahra Terrab, Sanae Ghammad, Touria Bouhafa, Abderrahmane El Mazghi, Khalid Hassouni

A case report of gastrointestinal stromal tumor located in the jejunum (http://dergipark.gov.tr/josam/issue/36726/428003) / Pages: 383-384 PDF (/download/article-file/500339)
Belhaj Anas, Fatima Zahrae Terrab, Somuah Tenkorang, Karim Ibn Majdoub, Imane Toughrai, Moulay Hassan Farih, Khalid Hassouni, Khalid Mazaz

Ileal lipoma: A rare cause of ileo-colic intussusception in adult (http://dergipark.gov.tr/josam/issue/36726/428348) / Pages: 385-386 PDF (/download/article-file/500102)
Ahmed Zerhouni, Mourad Badri, Anas Belhaj, Karim Ibn Majdoub, Imane Toughrai, Khalid Mazaz

Avascular necrosis of lunate bone: Kienbock disease (http://dergipark.gov.tr/josam/issue/36726/423536) / Pages: 387-388 PDF (/download/article-file/503378)
Cihan Bedel, Göker Coşkun, Sefa Türkoğlu

Bilateral giant styloid process: Case report (http://dergipark.gov.tr/josam/issue/36726/426336) / Pages: 389-390
Burak Kersin, Ahmet Mahmut Tekin, Ahmet Keleş PDF (/download/article-file/525066)

Ocular retinoblastoma and neuroblastoma: A cytological impression (http://dergipark.gov.tr/josam/issue/36726/430299) / Pages: 391-395 PDF (/download/article-file/507233)
Kafil Akhtar, Binjul Juneja, Sadaf Haiyat, Abdul Waris

A case of pancreatic cyst hydatid misdiagnosed as pancreatic cancer (http://dergipark.gov.tr/josam/issue/36726/431576) / Pages: 396-398 PDF (/download/article-file/506926)
Belhaj Anas, Ouazzani Et-Tayeb, Zerhouni Ahmed, Souiki Tarik, Karim Ibn Majdoub Hassani, Imane Toughrai, Mazaz Khalid

Occlusion of the small bowel on a virgin abdomen: Case report (http://dergipark.gov.tr/josam/issue/36726/428890) / Pages: 399-400 PDF (/download/article-file/522112)
Eddy Oleko Ekuke, Meriem Lhaine, Hicham El Bouhadoutti

Spigelian hernia after laparoscopic hysterectomy: Case report (http://dergipark.gov.tr/josam/issue/36726/444053) / Pages: 401-402 PDF (/download/article-file/522654)
Zeynep Ozturk İnal, Hasan Ali Inal, Ender Alkan

Solitary involvement of multiple myeloma in the upper thoracic spine, and anterior approach to thoracic region without full sternotomy: A case report (http://dergipark.gov.tr/josam/issue/36726/437453) / Pages: 403-405
Mehmet Bülent Önal, Atilla Kırçelli, Erdinç Civelek PDF (/download/article-file/525806)

Achromobacter xylosoxidans infection in urinary tract in a secondary kidney stone patient: Case Report (http://dergipark.gov.tr/josam/issue/36726/437945) / Pages: 406-407 PDF (/download/article-file/528433)
Sercan Sarı, Emine Yeşilyurt, Neziha Yılmaz, Abdullah Gürel, Emin Gürtan, Laser Şanal

Case of an atypical located leiomyoma arising from rectus sheath (http://dergipark.gov.tr/josam/issue/36726/442268) / Pages: 408-409 PDF (/download/article-file/527506)
Görker Sel

A rare form of the lung cancer: Mucoepidermoid carcinoma: A case report (http://dergipark.gov.tr/josam/issue/36726/438745) / Pages: 410-412 PDF (/download/article-file/528572)
Göktan Temiz, Özgur Ömer Yıldız, Ömer Cenap Gülyüz, Nurettin Karaoğlanoğlu

(https://scholar.google.com/)

(https://orcid.org/register)

(https://www.medicres.org/turkey.html)

Best viewed in

J Surg Med. 2018;2(3):197-200.
DOI: 10.28982/josam.411086

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Review of clinical and demographic features of frontal fibrosing alopecia

Frontal fibrozing alopesi'nin klinik ve demografik özelliklerinin gözden geçirilmesi

Güldehan Atış [1], Zeynep Altan Ferhatoğlu [2]

[1] University of Health Sciences, Haydarpaşa Numune Training and Research Hospital, Department of Dermatology, Istanbul, Turkey
[2] University of Health Sciences, Istanbul Sultan Abdülhamid Han Training and Research Hospital, Department of Dermatology, Istanbul, Turkey

ORCID ID of the authors
GA: 0000-0001-5069-044X
ZAF: 0000-0003-3090-656X

Corresponding author / Sorumlu yazar:
Güldehan Atış
Address / Adres: Koşuyolu mah. Kalfaçeşme sok. Validebağ No:1, 34662, Üsküdar, İstanbul, Türkiye
E-mail: guldehan.atis@gmail.com

Ethics Committee Approval: Ethics committee approval was not received because of retrospective design of the study.
Etik Kurul Onayı: Etik kurul onayı çalışmanın retrospektif dizaynından dolayı alınmamıştır.

Informed Consent: The author stated that the written consent was obtained from the patients presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastalardan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Previous presentation: The manuscript was presented as oral presentation in IDEA Congress, March 8-11, 2018 in Ankara, Turkey.

Received / Geliş Tarihi: 30.03.2018
Accepted / Kabul Tarihi: 19.04.2018
Published / Yayın Tarihi: 19.04.2018

Abstract

Aim: Frontal fibrosing alopecia (FFA) is a progressive scarring alopecia that occurs on the frontotemporal area. The ethiopathogenesis of FFA is still unclear. Genetic predisposition, hormonal and environmental factors, and the use of personal care products have been put forward as etiological factors. Our aim was to evaluate the clinical and demographical features of FFA patients retrospectively during a two-year follow-up period.

Methods: Patients who admitted to our dermatology out-patient clinic between January 2016 and January 2018 were included in the study. Diagnosis was made histologically or based on the typical clinical presentation (ear to ear hair loss). Age at first presentation and onset of FFA, relevant medical comorbidities, family history, menopause status, clinical features, and medical therapies administered were recorded.

Results: All the patients were female and post-menopausal. Seven patients (87.75%) had hair loss on the eyebrows. Lonely hairs were observed in five patients (62.5%). Depression of frontal veins was observed in two patients (25%). Perifollicular erythema was observed in three patients (37.5%), and perifollicular scale was observed in four patients (50%). One of the patients (12.25%) exhibited a doll hair line. Two patients (25%) had early menopause history. The mean age of onset for graying hair was 30.87±11.39. Three patients (37.5%) had a history of premature hair graying. All the patients dyed their hair, and the mean age of hair dyeing was 31.5±10.50.

Conclusion: Perifollicular erythema and perifollicular scaling are important trichoscopic features of FFA. Environmental factors, autoimmune processes, and hormonal factors play a role in the development of FFA in genetically predisposed individuals. Premature hair graying and/or use of hair dyes (especially at early ages) can be a triggering or etiopathogenic factor for FFA.

Keywords: Cicatricial alopecia, Frontal fibrosing alopecia, Trichoscopy, Post menopause

Öz

Amaç: Frontal fibrozan alopesi (FFA) frontotemporal bölgede lokalize, ilerleyici bir sikatrisyel alopesidir. Etiyopatogenezi halen tam olarak bilinmemektedir. Genetik yatkınlık, hormonal ve çevresel faktörler, kişisel bakım ürünleri etyolojide suçlanmaktadır. Amacımız son 2 yıl içerisinde gözlenen FFA'lı olguların klinik ve demografik özelliklerinin incelenmesidir.

Yöntemler: Ocak 2016- Ocak 2018 tarihleri arasında dermatoloji polikliniğine FFA nedeniyle başvuran hastalar çalışmaya dahil edildi. Tanı histopatolojik olarak ya da tipik klinik bulgulara dayanılarak konuldu. Hastaların başvuru esnasındaki yaşı, hastalık başlangıç yaşı, ilişkili olabilecek tıbbi hastalıkları, aile öyküleri, menapoz durumları, klinik bulguları ve aldıkları tedaviler kaydedildi.

Bulgular: Hastaların hepsi kadın ve postmenapozal idi. Yedi hastanın (%87,75) kaşların da dökülme mevcuttu. Yalnız saçlar hastaların beşinde (%62,5) saptandı. Frontal venlerde çökme hastaların ikisinde (%25) gözlendi. Perifoliküler eritem üç hastada (%37,5), perifoliküler skuam dört hastada (%50) gözlenirken, bebek saçı şeklinde saç çizgisi bir hastada (%12,25) gözlendi. İki hastada (%25) erken menapoz öyküsü mevcuttu. Saçların beyazlama yaş ortalaması 30,87±11,39 idi. Üç hastada (%37,5) saçlarda erken beyazlama öyküsü mevcuttu. Tüm hastalar saçlarını boyatmıştı. İlk kez saç boyatlma yaş ortalaması 31,5±10,50 idi.

Sonuç: Perifoliküler eritem ve perifoliküler skuam FFA'nın önemli trikoskopik bulgularıdır. Çevresel faktörler, otoimmün proçesler, hormonlar genetik olarak yatkın bireylerde hastalığın ortaya çıkışını kolaylaştırmaktadır. Erken saç beyazlaması ve saç boyaları (özellikle erken yaşta maruz kalmak) FFA'da tetikleyici veya etyolojik faktör olabilir.

Anahtar kelimeler: Sikatrisyel alopesi, Frontal fibrozan alopesi, Trikoskopi, Post menapoz

How to cite / Atıf için: Atış G, Ferhatoğlu ZA. Review of clinical and demographic features of frontal fibrosing alopecia. J Surg Med. 2018;2(3):197-200.

Introduction

Frontal fibrosing alopecia (FFA) is a progressive scarring alopecia that occurs on the frontotemporal area [1]. Band-like scarring alopecia localized on the frontal, temporal, and parietal hairline and a partial or complete loss of eyebrows are often observed in FFA [2,3]. The incidence of the disease has been increased since it was first described 20 years ago. There are no epidemiological data about incidence and prevalence of FFA. It is a rare form of scarring alopecia [4]. It is considered a variant of lichen planopilaris and mainly affects postmenopausal women. FFA is rarely seen in men with an incidence of 3-5% among all patients. [1,5]. The ethiopathogenesis of FFA is still unclear. Genetic predisposition, hormonal and environmental factors, and use of personal care products have been put forward as etiological factors. Early menopause and history of hysterectomy are common in FFA patients. Treatment is usually disappointing, and management of the condition can be difficult [1].

Our aim was to evaluate the clinical and demographical features of FFA patients retrospectively during a two-year follow-up period.

Materials and methods

Patients who admitted to our dermatology out-patient clinic with FFA between January 2016 and January 2018 were included in the study. Diagnosis was made histologically or based on the typical clinical presentation. Age at first presentation and onset of FFA, relevant medical comorbidities, family history, and menopause status were recorded as demographic features. Patients who started menopause before 40 years of age were classified as early menopause patients [6]. Clinical features (such as lonely hairs, facial papules, depression of frontal veins, and eyebrow and eyelash involvement) and symptoms (such as pruritus, trichodynia, and trichoscopy findings such as perifollicular erythema and scale), and medical therapies administered were recorded. Photographs of patients were taken, and each patient gave written consent. In this study, the Helsinki Declaration principles were applied.

Results

During two year periods, 16350 patients admitted to our dermatology out-patient clinic. Eight (0.048%) of these patients were FFA. All the patients with FFA were female (100%). The mean age of the patients with FFA was 63±7.11 years. All the patients with FFA were post-menopausal (100%). The mean age of onset of disease was 54.87±10.06 years. Family history was unremarkable for all patients with FFA (100%). No patients had any symptoms such as pruritus, pain, or trichodynia. Seven patients (87.75%) had hair loss on the eyebrows, whereas one patient (12.25%) had no involvement of the eyebrows. None of the patients had eyelash involvement, facial papules, or accompanying lesions compatible with lichen planus. Lonely hairs (Figure 1) were observed in five patients (62.5%). Depression of the frontal veins (Figure 2) was observed in two patients (25%).

Figure 1: Lonely hairs on the atrophic background

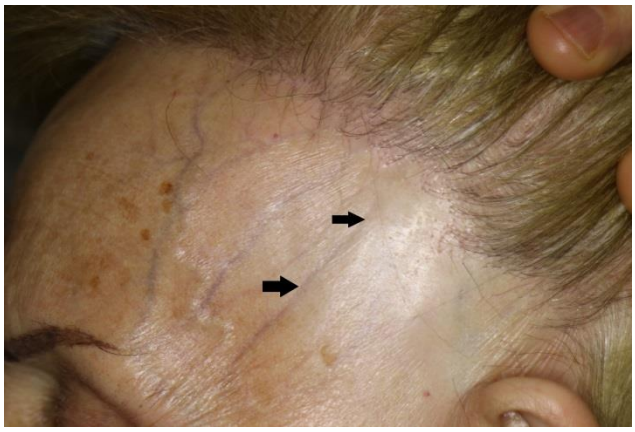


Figure 2: Depression of frontal veins on the atrophic background.

Figure 3: Perifollicular erythema (*) and perifollicular scale (arrow)

Figure 4: Doll hair line

Perifollicular erythema (Figure 3) was observed in three patients (37.5%), and perifollicular scale (Figure 3) was observed in four patients (50 %). Perifollicular hyperkeratosis was not observed in any patients upon trichoscopic investigation. One of the patients (12.25%) exhibited a doll hair line (Figure 4).

Six patients (75%) had loss of eyebrows as the initial symptom of the disease. Occipital region involvement was not observed in any patients. Two patients (25%) had thyroid disease, whereas six patients (75%) did not. The mean age at menopause was 42.25±6.60; in addition, none of the patients had a history of hysterectomy. Two patients (25%) had early menopause history. The mean age at onset of graying hair was 30.87±11.39. Three patients (37.5%) had a history of premature hair graying. All the patients dyed their hair, and the mean age of hair dyeing was 31.5±10.50. None of the patients had accompanying lichen planus lesions. The treatment methods used in our study are summarized in Table 1.

Table 1: Distribution of treatment methods in patient with FFA

Treatment methods	n (%)
Intralesional corticosteroids + topical corticosteroids + tacrolimus oinment	2 (25)
Intralesional corticosteroids + topical corticosteroids	1 (12.5)
Hyroxychloroquine + tacrolimus oinment	1 (12.5)
Topical corticosteroids	1 (12.5)
Intralesional corticosteroids + tacrolimus oinment +topical minoxidil	1 (12.5)
Topical minoxidil	1 (12.5)
No treatment	1 (12.5)

Discussion

Frontal fibrosing alopecia is a form of primary cicatricial alopecia that predominately affects women over the age of 50 and has a chronic course. In another study, the mean age of patients with FFA was 61.4, and the mean age of FFA onset was 59.8 [5]. In our study, the mean age of the patients with FFA was 63±7.11, and the mean age of FFA onset was 54.87 ±10.06 years. These results are consistent with those of other studies in the literature [7].

Trichoscopy is a non-invasive and effective technique used to distinguish FFA from other alopecias, such as alopecia areata, traction alopecia, and cicatricial margin alopecia. Absence of vellus hairs, absence of follicular openings, and presence of perifollicular scales and follicular hyperkeratosis are diagnostic features of FFA that are revealed in trichoscopic examination [8]. Especially during activation of the disease, local inflammation signs, such as perifollicular erythema and hyperkeratosis, can be observed via trichoscopic examination [7]. In our study, we detected perifollicular erythema in 37.5% of patients, and perifollicular scale was observed in 50% of patients, whereas perifollicular hyperkeratosis was not observed in any patients. This may be because the patients were under treatment. We think that trichoscopic examination is very useful for the diagnosis of FFA.

In a study, lonely hairs were found in 64% of patients, and depression of frontal veins was found in 8.7% of patients [7]. Eyebrow involvement is another common finding in FFA; the incidence of eyebrow involvement was 73–81% in the largest published series [9]. In our study, eyebrow involvement was found in 87.75% of FFA patients. In addition, lonely hairs were detected in 62.5% of patients, and depression of frontal veins was observed in 25% of patients. The incidences of lonely hairs and eyebrow involvement found in our study are similar to those in the literature, whereas the incidence of depression of frontal veins that we found was not consistent with the literature. This issue may be related to our small sample size.

Patient exhibition of a hairline reminiscent of that of a toy doll has been defined as a clinical sign of FFA. The doll hairline is highly suggestive of FFA. It is claimed that in the presence of this sign, further and more invasive investigations, such as videodermatoscopy and scalp biopsy, are unnecessary [2]. In our study, we found the doll hairline in one patient (12.5%) who had progressive FFA. We believe that the doll hair line can be a sign of progressive FFA and is not useful for early diagnosis.

A study suggested that incidences of early menopause and gynecologic surgery were higher in patients with FFA [8]. In Turkey, the average age of menopause onset is 47 years [10]. The incidence of early menopause is 1–4% in the normal population [11]. In our study, the incidence of early menopause was 25%, and the mean age at menopause onset was 42.25±6.60 in patients with FFA. FFA is not solely an immune-mediated disease. It is known that unknown hormonal mechanisms play a role in the etiopathogenesis of FFA. We found that early menopause is common in patients with FFA, which is consistent with the literature.

Environmental factors, such as the use of certain facial moisturizers, have also been put forward as triggering factors for FFA in the literature. The incidence of facial product usage, including usage of moisturizers and sunscreens, was higher in women with FFA [12].

Strazzulla et al. found that the incidence of facial moisturizer usage was 94% in male FFA patients. In the same study, the incidence of facial moisturizer usage was high in patients with FFA. They also found that the incidence of sunscreen usage was higher in the FFA group than in the control group (p=0.0012). They hypothesized that certain components of cosmetics may contribute to the development of FFA. In addition, chemical ultraviolet filters, including benzophenone-3, may have an endocrine disrupting effect, which has been shown in some animal studies [13].

In our study, we investigated the incidence of hair dyeing. The relationship between hair dyeing and FFA has never been investigated before. All our patients had a history of hair dyeing, and three patients (37.5%) had a history of hair dyeing at early ages because of premature hair graying. Hair dyes include many kinds of chemical agents. We suggest that exposure to certain chemical agents in hair dyes, like exposure to certain agents in facial moisturizers and sunscreens, could lead to the development of FFA.

Graying of the hair before the age of 20 in whites is referred to as “premature hair graying” (PGH). PGH could be associated with early exhaustion of melanocyte reservoirs due to genetic factors. This issue could be related to environmental factors, inflammation, or to psychological stress. The incidence of PGH is 26.4% in our country [14]. In our study, we found that the incidence of PHG was 37.5% in patients with FFA, which is higher than that of the normal population. In the literature, an association between FFA and PGH has not been identified. It is known that autoimmune disorders could be associated with PHG [15]. A T-cell mediated autoimmune reaction against hair follicles has been detected in FFA patients. In addition, FFA could be accompanied by autoimmune disorders like autoimmune thyroid disease [16]. We believe that PHG and FFA

could have the same pathogenetic mechanisms associated with autoimmunity.

This study has some limitations, including its retrospective design and lack of a control group. Another limitation is its small sample size.

In conclusion, FFA is a type of cicatricial alopecia that commonly affects post-menopausal women. Trichoscopic examination is a non-invasive and effective technique for the diagnosis of FFA. Perifollicular erythema and perifollicular scaling are important trichoscopic features of FFA. The etiopathogenesis of FFA is still unclear, although environmental factors, autoimmune processes, and hormonal factors appear to play a role in the development of FFA in genetically predisposed individuals. PHG and/or hair dyeing (especially at early ages) can be a triggering or etiopathogenic factor for FFA. Further studies are needed to evaluate the role of PHG and hair dyeing in the pathogenesis of FFA.

References

1. To D, Beecker J. Frontal fibrosing alopecia: Update and review of challanges and success. J Cutan Med Surg. 2017;1:1-8.
2. Brandi N, Starace M, Alessandrini A, Bruni F, Piraccini BM. The doll hairline: A clue for the diagnosis of frontal fibrosing alopecia. J Am Acad Dermatol. 2017;77:127-8.
3. Kumbasar E, Gökdemir G, Köşlü A. Postmenopozal frontal fibrozan alopesi: olgu sunumu. Türkderm. 2006;40:29-30.
4. Rudnicka L, Rakowska A. The increasing incidence of frontal fibrosing alopecia. In search of trigerring factor. JEADV. 2017;31:1579-80.
5. Heppt MV, Letule V, Laniauskaite L, Reinholz M, Tietze JK, Wollf H, et al. Frontal fibrosing alopecia: a retrospective analysis of 72 patients from a German Academic Center. Facial Plast Surg. 2018;34(1):88-94.
6. Santoro N, Mechanism s of prematüre ovarian failure. Ann Endocrinol (Paris). 2003;64(2):87-92.
7. Moreno-Arrones OM, Saceda-Corralo D, Fonda-Pascual P, Rodrigues-Barata AR, Buendia-Castano D, Alegra-Sanchez A, et al. Frontal fibrosing alopecia: clinical and prognostic classification. J Eur Acad Dermatol Venereol. 2017;31(10):1739-45.
8. Sidharth S, Jha AK, Tiwary PK. A dermoscopic diagnosis and activity evaluation of frontal fibrosing alopecia in a Indian lady. İndian Dermatol Online J. 2017;8(2):162-3.
9. Vano-Galvan S, Saceda-Corralo D, Moreno-Arrones OM, Camacho-Martinez FM. Updated diagnostic criteria for frontal fibrosing alopecia. J Am Acad Dermatol. 2018;78(1):21-2.
10. Özcan H, Oskay Ü. Menopoz döneminde semptom yönetiminde kanıta dayalı uygulamalar. Göztepe Tıp Dergisi. 2013;28(4):157-163.
11. Görgel EB, Çakıroğlu FP. Menopoz döneminde kadın. Ankara Üniversitesi Basımevi. Ankara 2007 p:5
12. Kidambi AD, Dobson K, Holmes S, Carauna D, Marmol VD, Vujovic A, et al. Frontal fibrosing alopecia in men: an association with facial moisturizers and sunscreens. Br J Dermatol. 2017;177:260-1.
13. Strazzulla LC, Avila L, Lo Sicco K, Shapiro J. Response to "frontal fibrosing alopecia in men- an association with facial moisturisers and sunscreen". Br J Dermatol. 2017;177(1):323.
14. Belli AA, Etgu F, Gök SÖ, Kara B, Doğan G. Risk factors for premature hair graying in young turkish adults. Pediatr Dermatol. 2016;33(4):438-42.
15. Sonthalia S, Sarkar R. Premature graying of hair: The voids and tiffs. Pigment Int. 2015;2:73-5.
16. Akbaş A, Kılınç F. Examination of clinical and demographic characteristics of 14 cases with frontal fibrosing alopecia. Medical Science and Discovery. 2018;5(1):110-5.

J Surg Med. 2018;2(3):201-204.
DOI: 10.28982/josam.408972

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Successful treatment of intussusception by hydrostatic reduction in pediatric patients: Is everything okay?

Pediatrik hastalarda hidrostatik redüksiyon ile başarılı intususepsiyon tedavisi: Her şey tamam mı?

Burhan Beger [1]

[1] **Van Yuzuncu Yil University, Department of Pediatric Surgery, Van, Turkey**

ORCID ID of the authors
BB: 0000-0002-1565-8062

Abstract

Aim: Intussusception, which is defined as telescopic insertion of proximal bowel segment into distal bowel segment, can be cured completely with surgical intervention. Intussusception can be successfully treated by ultrasound guided hydrostatic reduction (USGHR) if there is no necrosis or perforations of intestines. However, misdiagnosing or omitting secondary conditions which can be seen together with intussusception leads to an inevitable rise in morbidity. In this study, we would like to present a retrospective review of the intussusception patients which developed complications due to misdiagnosis within a pediatric surgery clinic in terms of diagnosis and treatment.

Methods: 12 patients who were treated for intussusception using USGHR between May 2014 and September 2017 in Van Yuzuncu Yil University Faculty of Medicine Pediatric Surgery Department were retrospectively reviewed for missed conditions and coincidental pathologies. The data about these case series such as age, sex, patient symptoms, diagnosis and treatment methods, complications and hospitalization periods were evaluated.

Results: 12 (5 Female – 7 Male) patients, who were diagnosed with invagination with complaints of abdominal pain, refractory emesis, crying attacks, bloody stool and abdominal distension that treated with USGHR with a mean age of 34 (Range 6 – 98) months, showed a worse clinical prognosis due to missed secondary conditions. Missed secondary pathologies included appendicitis (3 cases), lymphoma (1 case), Meckel diverticulitis (1 case), appendiceal intussusception (3 cases), acute gastroenteritis (3 cases) and Henoch-Schonlein Purpura (1 case). The patient with Henoch-Schonlein purpura diagnosis was treated with USGHR in combination with corticosteroids and all the other cases required open surgery. Follow-up of the patient with Henoch-Schonlein purpura is ongoing whereas all the other cases were treated successfully.

Conclusion: Although most intussusception cases are successfully treated with non-surgical USGHR treatments in our pediatric surgery clinic, missing the conditions that are seen with invagination causes an increase in surgical intervention rates, morbidity rates and medical costs. The main challenge for pediatric surgeons in invagination cases caused by pathological leading point conditions is the possibility of missing the actual underlying disease which caused the invagination following a successful USGHR after target-sign is detected. Although ultrasound and computed tomography studies might be helpful in preliminary diagnosis, it must be kept in mind that an actual diagnosis can only be done with surgery in some cases.

Keywords: Misdiagnosis, Intussusception, Ultrasound guided hydrostatic reduction

Öz

Amaç: İntussusepsiyon, proksimal bağırsak segmentinin distal bağırsak segmentinin içine teleskopik olarak girmesi olarak tanımlanır, kesin tedavisi cerrahidir. Bağırsaklarda nekroz veya perforasyon yoksa Ultrason eşliğinde Hidrostatik redüksiyon (USGHR) ile başarılı bir şekilde tedavi edilebilir. Bununla birlikte, intussusepsiyon ile görülebilen ikincil anomalilerin yanlış tanı alması veya atlanması morbiditede kaçınılmaz bir artışa yol açar. Bu çalışmada, bir çocuk cerrahisi kliniğinde tanı ve tedavi açısından yanlış tanıya bağlı komplikasyonlar gelişen intussusepsiyon hastalarının retrospektif olarak gözden geçirilmesini sunmak istedik.

Yöntemler: Mayıs 2014 ve Eylül 2017 arasında Yüzüncü Yıl Üniversitesi Çocuk Cerrahi Kliniği'nde intussusepsiyon tanısı alan ve USGHR ile tedavi edilen 12 hasta ıskalanmış tanılar ve ek patolojiler açısından retrospektif olarak değerlendirildi. Bu olgu serisindeki hastaların yaşı, cinsiyeti, semptomları, uygulanan tanı ve tedavi yöntemleri, komplikasyonlar ve hastanede kalış süreleri değerlendirildi.

Bulgular: Ağrı, kusma, ağlama atakları, dışkıda kan ve abdominal distansiyon şikayetleri ile başvuran ve USGHR ile tedavi edilen ve ortalama yaşları 34 (Aralık 6 - 98) ay olan 12 (5 kadın - 7 erkek) hasta, atlanmış sekonder durumlar nedeniyle daha kötü bir klinik prognoz gösterdi. apandisit (3 olgu), lenfoma (1 olgu), Meckel divertikülit (1 olgu), apendikal intussusepsiyon (3 olgu), akut gastroenterit (3 olgu) ve Henoch-Schonlein Purpura (1 olgu) atlanmış sekonder patolojilerdi. Henoch-Schonlein purpura tanısı olan hasta USGHR ve kortikosteroidler ile birlikte tedavi edildi ancak diğer tüm olgular açık cerrahi gerektirdi. Henoch-Schonlein purpurası olan hastanın takibi devam ederken, diğer tüm olgular başarıyla tedavi edildi.

Sonuç: Çocuk cerrahisi kliniğimizdeki invajinasyon hastalarının çoğu USGHR ile cerrahi yapılmadan başarılı bir şekilde tedavi edilmesine rağmen, sekonder patolojiler gözden kaçırıldığında cerrahi girişim endikasyonu, artan morbidite ve medikal maliyetler kaçınılmazdır. Lead point'in mevcut olduğu invajinasyon vakalarında, bu hastalar için en önemli dezavantaj, ultrasonografide target sign görüntüsünün saptanmasını takiben yapılan başarılı bir USGHR ye rağmen altta yatan patolojinin ıskalanmasıdır. Ultrasonografi ve bilgisayarlı tomografi çalışmaları ön tanı için yararlı olsa da, gerçek bir teşhisin sadece bazı durumlarda cerrahi ile yapılabileceği akılda tutulmalıdır.

Anahtar kelimeler: Yanlış teşhis, İntussusepsiyon, Ultrason eşliğinde hidrostatik redüksiyon

Corresponding author / Sorumlu yazar:
Burhan Beger
Address / Adres: Van Yüzüncü Yıl Üniversitesi, Akademisyen Kampüsü, K2-17/4, Van, Türkiye
E-mail: burhanbeger@hotmail.com

Ethics Committee Approval: Ethics committee approval was not received because of retrospective design of the study.
Etik Kurul Onayı: Etik kurul onayı çalışmanın retrospektif dizaynından dolayı alınmamıştır.

Informed Consent: The author stated that the written consent was obtained from the patients presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastalardan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 22.03.2018
Accepted / Kabul Tarihi: 19.04.2018
Published / Yayın Tarihi: 19.04.2018

How to cite / Atıf için: Beger B. Successful treatment of intussusception by hydrostatic reduction in pediatric patients: Is everything okay? J Surg Med. 2018;2(3):201-204.

Introduction

Intussusception, which is the most common cause of intestinal obstructions seen in children between 4-10 months of age, can either be idiopathic or caused by a variety of conditions such as Meckel diverticulum, intestinal duplication, benign polyps, malignant lymphoma, Peuts-Jeghers syndrome, mesenteric cysts, intestinal wall hematoma of hemophilia, allergic purpura or hamartoma [1-3]. In idiopathic intussusception, the first line of non-surgical treatments are the pneumatic or hydrostatic reduction when there is no intestinal necrosis or perforations are present [1]. As the incidence rate of intussusception with a secondary condition is around 6%, surgical treatment is indicated in most of those cases [2,4]. In those cases, severe or even fatal complications such as bowel perforations or peritonitis can be seen due to the difficulties in the treatment of the conditions [2,5]. In intussusception diagnosis, ultrasonography (USG) has an almost 100% sensitivity and specificity. However, in complicated intussusception cases with various pathological anomalies ultrasonography or computed tomography (CT) does not show the similar success rates [2,3,6]. In those cases, secondary anomalies which can be seen with intussusception due to wrong or incomplete diagnosis can easily be missed.

In patients with intussusception, when the reduction treatment whether using gas or liquid enemas is unsuccessful, the patients can be taken into emergency surgery [2]. This study's main objective is to assess the patients who developed complications due to missed additional conditions with intussusception in terms of diagnosis and treatment.

Materials and methods

In our clinic, ultrasound guided hydrostatic reduction (USGHR) is routinely used for treatment of intussusception with exception of these conditions such as leading point, bowel necrosis and peritonitis. All patients received intravenous 0.9% Normal Saline 20 mg/kg/hour and midazolam was given as a premedication. Due to perforation risks, antibiotic prophylaxis was given in a single dosage of 50 mg/kg cephazolin and 30mg/kg metronidazole. With the patient laying in right lateral position a 14–18 Fr Foley's catheter was introduced into the anal canal and the balloon was inflated with 15-25 ml of saline. Foley's catheter size was chosen according to patient body size. Then the balloon of the catheter was placed in anal seal to avoid leaking back of the fluid. The on call radiologist used high resolution ultrasound IU22 (Philips, Netherlands) to image the intussusception. A clinician from Pediatric Surgery department remained in attendance in the suite.

Normally USGHR is ineffective in existence of leading point. Uncommonly in the proper use of USGHR can solve invaginated segment while there is leading point or additional pathologies. In this retrospective study; twelve patients that treated with USGHR with misdiagnose conditions and coincidental pathologies in Van Yuzuncu Yil University Faculty of Medicine Pediatric Surgery Department from May 2014 and September 2017.

Patients' age, gender, symptoms, treatment techniques, complications and hospitalization periods were retrospectively noted.

Results

The study included 12 patients (5 female, 7 male) with a mean age of 34 (Range: 6-84) months. The patients all presented to the clinic in 72 hours right after the first symptoms are seen. Patients had at least one of the following symptoms which are abdominal pain (12 cases), emesis (9 cases), crying jags (8 cases), blood in the stool (4 cases) and abdominal distension (2 cases). In total abdominal x-rays, it was seen that the colonic gases built up in the upper left quadrant of the abdomen in 6 patients. Following the detection of target-sign in USG, all patients had a pre-diagnosis of intussusception. The patients were treated by using USGHR. After the confirmation of the successful treatment with USG, the patients were discharged.

During post-op follow-up period, a number of patients presented to the clinic again after 2 to 32 days following discharge with complaints of loss of appetite, emesis, acute abdominal pain, abdominal distension and bloody stools. 3 patients with repeated complaints of loss of appetite, emesis and abdominal distension following 2-5 days after discharge were taken into emergency open surgery and perforated appendicitis was diagnosed. In 2 patients who presented to the clinic on 16th and 32nd days of successful USGHR treatment with acute abdomen were diagnosed with Meckel diverticulitis (1 case) and Burkitt lymphoma (1 case) (Figure 1, 2) during surgery.

Figure 1: Invaginated ileo-ileal segment

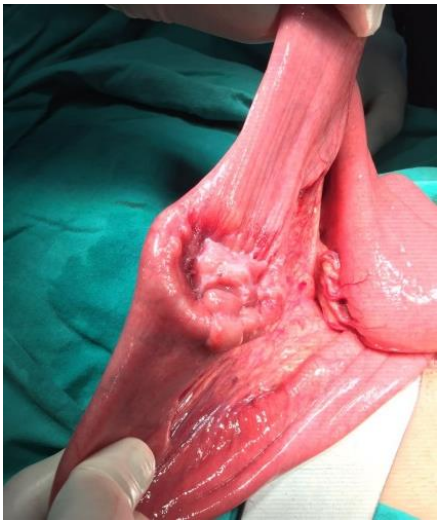


Figure 2: Burkitt Lymphoma as a leading point

In 3 patients with continued complaints of intermittent abdominal pain and emesis were successfully treated with incidental appendectomy although repeated intussusception or leading points were not detected. In three patients with suspected leading point following a repeated invagination were taken into surgery and the patients were diagnosed with acute gastroenteritis instead of leading point. A patient who presented to the clinic with rectal bleeding, palpable purpura in lower extremity and repeated intussusception was treated with USGHR in combination with corticosteroids and target-sign appearance disappeared after the treatment in follow-up USG. This patient was taken into follow-up for Henoch-Schonlein purpura. And all other patients made a successful recovery. The patients were briefly documented on the table 1.

Table 1: Demographic data of patients with misdiagnose conditions, treatment method and second application time to hospital after discharge

Age(months) / Gender	Misdiagnose Conditions	Treatment	Second admission to the hospital after discharge
24/F	Acute Appendicitis	Laparotomy	2 Days
36/M	Acute Appendicitis	Laparotomy	2 Days
24/M	Acute Appendicitis	Laparotomy	3 Days
38/M	Meckel Diverticulum	Laparotomy	16 Days
70/M	Henoch-Schonlein Purpura	Steroid	3 Days
10/F	Acute Gastroenteritis	USGHR	2 Days
14/M	Acute Gastroenteritis	USGHR	1 Day
13/F	Acute Gastroenteritis	USGHR	2 Days
40/M	Appendiceal Intussusception ?	Appendectomy	3 Days
58/F	Appendiceal Intussusception ?	Appendectomy	1 Day
19/F	Appendiceal Intussusception ?	Appendectomy	3 Days
62/M	Burkitt's Lymphoma	Excision of the mass	32 Days

F: Female, Male: Male

Discussion

Additional conditions such as appendicitis, lymphoma, Meckel diverticulitis, appendiceal intussusception, acute gastroenteritis or Henoch-Schonlein purpura can be missed during non-surgical treatment of invagination patients with or without leading points. Those missed cases due to wrong or incomplete diagnosis causes an increase in morbidity, medical costs and hospitalization periods of the patients. This study gives out a guideline on the diagnosis and treatment for the pediatric surgeons who come across with such cases.

Intussusception is second most common reason for emergency intervention following acute appendicitis in pediatric surgery clinics and is the most common cause for intestinal obstructions seen in children between 4-10 months [1,7]. Intussusception in seen in 1-4 in every 1000 live births in developed countries whereas the incidence rate is slightly higher in developing countries [1,7]. The most common symptoms include refractory emesis, intermittent abdominal cramps and pain with varying degrees of severity and bloody stools [1,8]. Intussusception usually has an idiopathic nature but in about 6% of the cases, an underlying pathological leading point is present [1,2]. In idiopathic intussusception diagnosis, ultrasonography has an almost 100% sensitivity and specificity rate [6]. Non-surgical interventions such as hydrostatic, pneumatic or external manual reduction techniques are the first line of choice in treatment in cases without bowel necrosis or perforation [6]. In the event of complication development following an unsuccessful non-surgical procedure, surgical interventions are indicated as the most reliable method [6].

The main challenge for pediatric surgeons in intussusception is the diagnosis and treatment of invaginations caused by pathological leading points [1,2,5,10]. In those patients, USG has a 75% sensitivity and specificity rate whereas CT has 50% [2]. This situation is the main reason of missing the underlying anomaly which causes invagination in the first place or additional anomalies which can be seen with invagination. Chang's [11] study reported a non-surgically treated case diagnosed with intussusception. The patient's condition got worse and patient was taken into surgery. While the surgeons were expecting to find intussusception-related complications, they detected a missed diagnosis of perforated appendicitis. Another study done by Newman [12] on 6 cases reported that ultrasound images of a perforated appendicitis can mimic intussusception. An interesting point we found out was the absence of gas build-up in upper left quadrant and crying attacks in invagination cases with appendicitis. The most important disadvantage in those conditions for pediatric surgeons is the possibility of missing an underlying acute appendicitis diagnosis following a successful reduction of invagination, which the appendicitis is the leading point. Good USG results following USGHR for both clinical and control purposes can be deceiving for the surgeon. Another possible misdiagnosis is appendiceal intussusception which has the common clinical and radiological findings of both appendicitis and intussusception [13,14]. Target sign, which is typical in USG of intussusception, can be detected in this condition. They are usually spontaneously resolved or USGHR is used to reduce it easily. Due to the possibility of frequent recurrences, we suggest appendectomy in cases which require surgery for intussusception.

Intussusception rates peak during summer and winter months when respiratory and gastrointestinal infections are frequent [15]. Acute gastroenteritis following a successful reduction can cause recurrent intussusception. For this reason, we suggest a repeated USGHR in recurrent intussusception when there is no clear surgical indication and suspicion about leading points. In the literature, there are intussusception cases that are reported to have leading points of Henoch-Schonlein purpura and Burkitt lymphoma [16-18]. Especially in our patient with Burkitt lymphoma, we find it really interesting that the patient showed both good clinical and ultrasonography results following a successful USGHR. In intussusception cases with Henoch-Schonlein purpura, adding steroids to USGHR treatment can prevent recurrences.

Limitations of our study are its retrospective design, the low number of patients and the short follow-up period after USGHR treatment of intussusception. A prospective study involving a large number of patients may provide early detection of misdiagnosis and coincidental pathologies.

Conclusion

Although most intussusception cases are successfully treated with non-surgical USGHR treatments in our pediatric surgery clinic, missing the conditions that are seen with intussusception causes an increase in surgical intervention rates, morbidity rates and medical costs. The main challenge for

pediatric surgeons in intussusception caused by pathological leading point conditions is the possibility of missing the actual underlying disease which caused the intussusception following a successful USGHR after target-sign is detected. Although USG and CT studies might be helpful in preliminary diagnosis, it must be kept in mind that an actual diagnosis can only be done with surgery in some cases.

References

1. Chua JHY, Chui CH, Jacobsen AS. Role of surgery in the era of highly successful air enema reduction of intussusception. Asian Journal of Surgery. 2006;29(4):267-73.
2. Lin XK, Xia QZ, Huang XZ, Han YJ, He GR, Zheng N. Clinical characteristics of intussusception secondary to pathologic lead points in children: a single-center experience with 65 cases, Pediatr Surg Int. 2017;33(7):793-7.
3. Yao XM, Chen ZL, Shen DL. Risk factors for pediatric intussusception complicated by loss of intestine viability in China from June 2009 to May 2014: a retrospective study, Pediatr Surg Int. 2015; 31(2):163–6.
4. Wang Z, He Q, Zhang H, Zhong W, Xiao W, Lu L. Intussusception patients older than 1 year tend to have early recurrence after pneumatic enema reduction. Pediatr Surg Int. 2015;31(9):855–8.
5. Kee HM, Park DM, Lim JY, Yi DY, Lim IS. A Case of Intussusception with Acute Appendicitis. Pediatr Gastroenterol Hepatol Nutr. 2015;18(2):134-7.
6. Mensah Y, Glover Addy H, Etwire V, Appeadu Mensah W, Twum M. Ultrasound guided hydrostatic reduction of intussusception in children at Korle Bu Teaching Hospital: An initial experience. Ghana Med J. 2011;45(3):128–31.
7. Morsi AH, Ahmed O, Ahmed RK. Adding a custom made pressure release valve during air enema for intussusception: A new technique. African Journal of Paediatric Surgery. 2015;12(4):232.
8. Esposito F, Ambrosio C, DeFronzo S, Panico MR. Fluoroscopy-guided hydrostatic reduction of intussusception in infancy: role of pharmacological premedication. La Radiologia Medica. 2015;120(6):549-56.
9. Vazquez JL, Ortiz M, Doniz MC, Montero M, Del Campo VM. External manual reduction of paediatric idiopathic ileocolic intussusception with US assistance: a new, standardised, effective and safe manoeuvre. Pediatr Radiol. 2012;42(10):1197–204.
10. Hagan I, Con C, Shepher N, McGann G. Acute suppurative appendicitis complicating ileocolic intussusception due to a caecal lipoma. European Journal of Radiology Extra. 2006;60(3):113-5.
11. Chang TP, Russell SA. Perforated appendicitis and appendicolith in a child presenting as intussusception: a case report. Pediatr Emerg Care. 2011;27(7):635-8.
12. Newman B, Schmitz M, Gawande R, Vasanawala S, Barth R. Perforated appendicitis: an underappreciated mimic of intussusception on ultrasound. Pediatr Radiol. 2014;44(5):535–41.
13. Jonah L, Verhey P, Dobos N. Preoperative CT diagnosis of appendiceal intussusception. American Journal of Roentgenology. 2006;187(3):325-6.
14. Tavakkoli H, Sadrkabir SM, Mahzouni P. Colonoscopic diagnosis of appendiceal intussusception in a patient with intermittent abdominal pain: a case report. World Journal of Gastroenterology. 2007;13(31):4274.
15. Ocal S, Cevik M, Boleken ME. A comparison of manual versus hydrostatic reduction in children with intussusception: Single-center experience. African Journal of Paediatric Surgery. 2014;11(2):184.
16. England RJ, Pillay K, Davidson A, Numanoglu A. Intussusception as a presenting feature of Burkitt lymphoma: implications for management and outcome. Pediatric Surgery International. 2012;28(3):267-70.
17. Cull DL, Rosario V, Lally KP, Ratner I, Mahour GH. Surgical implications of Henoch. Schönlein purpura. J Pediatr Surg. 1990;25(7):741-3.
18. Peru H, Soylemezoglu O, Bakkaloglu SA, Peru H, Elmas S. Henoch Schonlein purpura in childhood: clinical analysis of 254 cases over a 3-year period. Clin Rheumatol. 2008;27(9):1087-92.

J Surg Med. 2018;2(3):205-209.
DOI: 10.28982/josam.411872

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Comparison of three different sternal closure techniques after cardiac surgery in elderly patients

Yaşlı hastalarda kardiyak cerrahisi sonrası üç farklı sternum kapatma tekniğinin karşılaştırılması

Mazlum Şahin [1], Helin El [2], Fatma Tuba İlal Mert [2]

[1] Department of Cardiovascular Surgery, Haseki Teaching and Research Hospital, Istanbul, Turkey
[2] Department of Cardiovascular Surgery, Şişli Teaching and Research Hospital, Istanbul, Turkey

ORCID ID of the authors
MŞ: 0000-0001-9630-6634
HE: 0000-0001-5233-6057
FTİM: 0000-0003-4987-8837

Corresponding author / Sorumlu yazar:
Mazlum Şahin
Address / Adres: Kardiyovasküler Cerrahi Bölümü, Haseki Eğitim ve Araştırma Hastanesi, Millet Cad. No: 11, 34096, Fatih, İstanbul, Türkiye
Tel: +90212 5294400
E-mail: mzlmshn@gmail.com

Ethics Committee Approval: Ethics committee approval was received from Haseki Teaching and Research Hospital regional ethical committee with the study ID number 498 in 2017.
Etik Kurul Onayı: Etik kurul onayı Haseki Eğitim ve Araştırma Hastanesi Etik Kurulundan 2017 yılında 498 kayıt numarası ile alınmıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 02.04.2018
Accepted / Kabul Tarihi: 23.04.2018
Published / Yayın Tarihi: 23.04.2018

Abstract

Aim: To identify the effectivity of stainless steel wires (SSW), Robicsek technique (RT) and thermoreactive nitinol clips (TNC) for sternal closure in elderly patients.

Methods: We conducted a prospective randomized study to compare SSW, RT and TNC in the sternal closure between January 2015 and January 2017. Patients over 60 years old who required sternal closure following cardiac surgery were enrolled into the study. Preoperative characteristics, operative parameters and EuroSCORE were recorded for each patient. In postoperative period, duration of intensive care unit stay and hospitalization, complications and mortality rates were analyzed. All patients evaluated according to the Visual analogue scale score (VAS) on 1st, 3rd and 5th day after the operation.

Results: 96 patients (32 patients with SSW, 32 patients with RT and 32 patients with TNC) required sternal closure. Patients in which sternal closure was performed with TNC, achieved significantly shorter hospitalization period ($p=0.014$) and no any dehiscence ($p=0.014$). We achieved significantly better VAS scores in patients with TNC ($p<0.001$, $p<0.001$ and $p<0.001$, respectively). In multivariate regression analysis, superficial sternal wound infection (SSWI) and DSWI were the only predictive factors for sternal dehiscence ($p=0.029$ and $p=0.015$, respectively).

Conclusion: Our study showed that using TNC decreased the hospitalization duration, DSWI, sternal dehiscence development and postoperative pain intensity. SSWI and DSWI were found to be the only predictive factors for sternal dehiscence in multivariate regression analysis..

Keywords: Sternotomy, Sternal closure, Stainless steel wires, Nitinol clips, Robicsek technique

Öz

Amaç: Yaşlı hastalarda sternal kapanma için paslanmaz çelik tellerin (PÇT), Robicsek tekniğinin (RT) ve termoreaktif nitinol klipslerinin (TNK) etkinliğini saptamak.

Yöntemler: Ocak 2015 ile Ocak 2017 yılları arasındaki sternal kapamada PÇT, RT ve TNK'yi karşılaştırmak için prospektif randomize çalışma yaptık. Ameliyat öncesi veriler, operasyon parametreleri ve EuroSCORE değerleri her hasta için kaydedildi. Ameliyat sonrası dönemde yoğun bakım ünitesinde kalış süresi, hastanede yatış günü, komplikasyonlar ve mortalite oranları analiz edildi. Tüm hastalara operasyondan 1., 3. ve 5. günden sonra vizuel analog skala (VAS) ile skorlama yapıldı.

Bulgular: Çalışma protokolü sırasında 96 hastaya (PÇT'li 32 hasta, RT'li 32 hasta ve TNK'li 32 hasta) sternal kapama uygulandı. TNK ile sternal kapatma yapılan hastalarda hastanede yatış süresi önemli ölçüde kısaydı ($p=0.014$). Sternum ayrılması PÇT uygulanan hastalardan altısında, RT uygulanan hastaların dördünde gelişirken, TNK ile sternal kapama yapılan hastalarda açılma gelişmedi ($p=0.014$). TNK'li hastalarda anlamlı olarak daha iyi VAS skorları elde edildi (sırasıyla $p<0.001$, $p<0.001$ ve $p<0.001$). Çok değişkenli regresyon analizinde derin sternal yara enfeksiyonu (DSYE) ve yüzeyel sternal yara enfeksiyonu (YSYE) sternal dehisens için tek prediktif faktör olarak saptandı (sırasıyla $p=0.029$ ve $p=0.015$).

Sonuç: Çalışmamız TNK'nin sternal kapanış sonrasında hastaneye yatma süresi, DSYE, sternal ayrılma gelişimi ve postoperatif ağrı stresini azalttığını göstermiştir. Çok değişkenli regresyon analizinde YSYE ve DSYE sternal ayrılma için tek prediktif faktör olarak bulunmuştur.

Anahtar kelimeler: Sternotomi, Sternal kapatma, Paslanmaz çelik tel, Nitinol klipsler, Robicsek tekniği

How to cite / Atıf için: Şahin M, El H, Mert FTİ. Comparison of three different sternal closure techniques after cardiac surgery in elderly patients. J Surg Med. 2018;(3):205-209.

Introduction

In cardiovascular operations, median sternotomy (MS) is one of the most preferred technique to access the heart, aorta and pulmonary vessels [1]. The MS ensures wide mediastinal view for cardiovascular surgeons and also provides shorter operation time. Moreover, patients experience less pain and faster recovery time in postoperative period [2]. However, besides its advantages, MS includes some potential complications like; sternal wound infections, mediastinitis and sternal dehiscence, especially in patients with obesity, chronic obstructive pulmonary disease and in elderly patients [3].

Previous reports have stated that sternal closure techniques have an important role in operation success and prevention of operative and postoperative complications after MS [4,5]. Recently, stainless steel wires (SSW) are accepted as standard method for closure of sternum with acceptable complication rates [6]. However, to achieve superior sternum resistance to tension, cardiovascular surgeons developed new techniques and fixation materials for sternum closure. Robicsek et al. [7] have stated that bilateral and longitudinal parasternal fixation with SSW is associated with lesser sternal dehiscence. On the other hand, Sarıkaya et al. [8] have demonstrated that thermoreactive nitinol clips (TNC) were safe and effective for sternal closure with shorter operation time and lower costs.

Although previous studies evaluated the role of SSW, Robicsek technique (RT) and TNC, there is no prospective study in the literature which compared the efficiency of three different sternal closure techniques in patients older than 60 years of age. In present study, we for the first time, aimed to identify the efficiency of SSW, RT and TNC in the sternal closure in elderly patients.

Materials and methods

After obtaining ethical approval from the Haseki Teaching and Research Hospital regional ethical committee with the study ID number 498, we conducted a prospective randomized study to compare SSW, RT and TNC in the sternal closure. Patients >60 years old who required sternal closure following cardiac surgery were enrolled into the study. The study was held between January 2015 and January 2017, and all operations were performed by a single experienced surgeon. The randomization was done by a computer based random number sequencing program and the surgeon was informed from the result of the randomization in the morning of surgery with a non-transparent envelope. Operations under emergency conditions, patient with a history of sternotomy, patients with a body mass index >40 and patients in which internal mammillary artery could not be used were excluded from the study. Also, patients which have a severe chronic obstructive pulmonary disease and a history of opioid use were excluded from the study. Written consent was obtained from patients and/or relatives one day before surgery.

In our clinic protocol, all patients were showered with 4% chlorhexidine scrub the evening before surgery. After general anesthesia induction, skin surface of operation area was shaved and skin was scrubbed with alcoholic iodine. Antibiotic prophylaxis was begun 30 minutes before the surgery and continued for at least 24 hours with 4x1 gr cefazolin sodium. At the end of the operation, sternum closure technique was performed according to the randomization result. In first group, sternal closure was done with six to eight stainless steel wires which pass through sternum (Figure 1a). In group 2, RT which can be defined as application of appropriate two circumferential wires on each side of the sternum (Figure 1b). In third group, an electrocautery and scalpel was used in presternal layers. After sufficient intercostal groove distance was obtained, sternum was measured for adequate clip size. Then, the cooled clips were applied around sternum in the previously created area. At the temperature of body, clips regained their original shape and strength (Figure 1c). After sternotomy closure, the deep fascia and skin was closed with 0 PDS and 3-0 monocryl intradermal sutures.

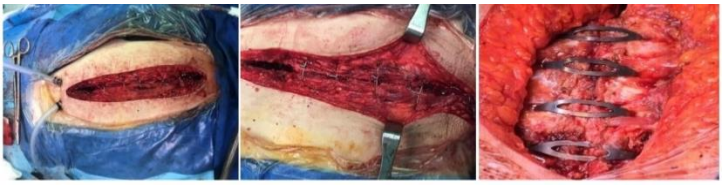


Figure 1: Sternal closure techniques; stainless steel wire (a: left), Robicsek technique (b: middle) and thermoreactive nitinol clips (c: right), respectively

EuroSCORE

European System for Cardiac Operative Risk Evaluation (EuroSCORE) is a relatively new nomogram which was developed in 1999 to assess the surgical risk of patients who have underwent cardiac surgery [9]. The scoring system aims to predict patient mortality in the first 30 days following cardiac surgery by using patient related factors including age, sex, presence of obstructive pulmonary disease, extracardiac arteriopathy, neurological dysfunction disease, previous cardiac surgery, serum creatinine level, presence of active endocarditis and presence of critical preoperative state. Also, EuroSCORE evaluates cardiac related factors including unstable angina, left ventricular dysfunction, presence of myocardial infarct, pulmonary hypertension and operation related factors such as operations in emergency conditions, procedures other than cardiopulmonary arterial bypass graft, surgery on thoracic aorta and post-infarct septal rupture.

Visual analogue scale (VAS) score

The VAS score is the assessment method for evaluating subjective pain intensity [10]. For evaluation of VAS pain score, usually 10 centimeter continuous scale with horizontal and vertical line is used. In this scale, score of zero means ‘no pain’, higher VAS scores show increment in pain intensity and score of 10 means ‘the worst imaginable pain’ or/and ‘pain as bad as it could be’.

Medical history of patients was obtained and detailed physical examination was performed for all patients. Preoperative characteristics and operative parameters were recorded. Also, EuroSCORE was calculated for each patient. In postoperative period, duration of intensive care unit stay, hospitalization duration, complications and mortality rates were analyzed. Mild sternal wound erythema without clinical symptoms was regarded as superficial sternal wound infection (SSWI). Purulent exudates discharge from wound, sternal osteomyelitis, lack of sternal stability with elevated inflammatory parameters was accepted as deep sternal wound

infection (DSWI). Also, presence of mediastinitis and sternal dehiscence were noted. Postoperative analgesia was managed with non-steroidal anti-inflammatory agents (twice a day routinely and extra dose given if patients require more analgesia and had a VAS score under six) and tramadol (dose given if patients had a VAS score above six). All patients VAS scores were noted in 1st, 3rd and 5th day after the operation. Preoperative, intraoperative and postoperative variables were compared between three groups according to sternal closure method, as mentioned above. Additionally, patients were compared according to the presence of sternal dehiscence.

Statistical analysis

The Statistical Package of Social Sciences for Windows (SPSS) version 20 was used for statistical analysis. We divided patients into three groups based on sternal closure method. Categorical variables were presented as numbers and percentages and compared with Chi Square test. Continuous variables were presented as means and standard deviations and compared with independent sample t test. Correlation analyses were evaluated using Pearson's correlation coefficient. Statistical significance was considered when two-tailed p value <0.05.

Results

During study protocol, 96 patients (32 patients with SSW, 32 patients with RT and 32 patients with TNC) underwent sternal closure. The gender distribution and mean age of patients between groups did not differ significantly (p=0.194 and p=0518, respectively). Diabetes mellitus and hypertension were the most common comorbidities in each group. The EuroSCORE was 3.6±0.9 in SSW group, 3.8±0.9 in RT group and 3.7±0.8 in TNC group (p=0.660). Preoperative characteristics of patients were summarized in Table 1.

Table 1: Preoperative characteristics of patients

	Groups			
	SSW (n=32)	Robicsek (n=32)	TNC (n=32)	p value
Gender (male/female)	23/9	29/3	27/5	0.194
Age (year)*	70.5±4.3	70.8±4.2	71.3±5.3	0.518
Body Mass Index (kg/m2)*	28.7±3.7	29.3±4.2	29.3±3.4	0.490
Comorbidity				
Diabetes mellitus	8	15	12	0.304
Hypertension	13	17	12	0.804
Chronic Renal Failure	1	2	3	0.307
Chronic Obstructive Pulmonary Disease	2	4	6	0.133
Cancer	2	2	1	0.578
Smoking History	16	14	13	0.456
EUROSCORE*	3.6±0.9	3.8±0.9	3.7±0.8	0.660
Cardiac Ejection Fraction*	50.3±8.7	51.3±9.2	47.0±8.1	0.135

*: Mean ± standard deviation, SSW: Stainless steel wire, TNC: Thermoreactive nitinol clips

Coronary Artery Bypass Grafting was the most common operation type in each group (p= 0.529). The mean duration of cardiopulmonary bypass was 104.5±36.8, 112.8±36.9 and 105.6±46.2 minutes in SSW, RT and TNC groups, respectively (p= 0.924) Cross time was the longest in RT group (p= 0.153). The operative parameters listed in Table 2.

Intensive care unit stay did not show significant difference according to sternal closure technique (p=0.532). However, hospitalization period was 7.5±2.3 days in SSW group, 7.5±2.5 days in RT group and 6.3±0.5 days in TNC group and these results demonstrated that patients in which sternal closure was performed by TNC achieved significantly shorter hospitalization period (p=0.014). Hemorrhage and SSWI development were comparable between groups (p=0.610 and p=0.224, respectively). However, DSWI was significantly less common after sternal closure with TNC. DSWI was detected in five patients in SSW group, in four patients in RT group and none of the patients in TNC group (p=0.032). We also faced mediastinitis in two patients (one patient's sternal closure was performed by SSW and another's was performed by RT). Dehiscence was observed in six cases in which sternal closure was performed with SSW and in four cases in which sternal closure was performed with RT. We did not face any dehiscence in patients in which TNC was used for sternal closure (p=0.014). The TNC was the common technique to manage sternal dehiscence (five cases after SSW and four cases after RT). Dehiscence time was significantly longer in patients with SSW than in patients with RT (p=0.009). According to the VAS score, we have seen a trend in pain reduction following days after operation. The VAS score of patients in which TNC used was 5.2±0.6 in 1st postoperative day, 3.6±0.8 in 3rd postoperative day, 3.3±0.6 in 5th postoperative day and we have achieved significantly better VAS scores in patients with TNC (p<0.001, p<0.001 and p<0.001, respectively). The death occurred in two patients (Table 3).

Table 2: Operative parameters between groups

	Groups			
	SSW (n=32)	Robicsek (n=32)	TNC (n=32)	p value
Operation type				0.529
CABG	23	24	25	
Mitral valve replacement	3	2	1	
Aortic valve replacement	3	1	1	
Cardiac tumor	0	2	0	
Bentall procedure	2	1	2	
Ascending aorta replacement	0	2	0	
CABG + Mitral valve replacement	1	0	1	
CABG + Ascending aorta replacement	0	0	2	
CABG*	2.5±1.6	2.4±1.6	2.7±1.3	0.504
Off Pump technique	3	4	4	0.698
Single IMA	29	25	21	0.133
CPB Time (minute)*	104.5±36.8	112.8±36.9	105.6±46.2	0.924
Cross Time (minute)*	51.5±26.7	67.3±35.1	63.5±32.5	0.153
Hemorrhage (cc)*	562.5±336.5	485.9±340.4	489.1±236.1	0.341
Post extubation time (hour)*	5.8±2.5	9.1±4.8	6.5±3.6	0.540
Atrial fibrillation	11	11	14	0.444
IABP	2	2	2	1.000

*: Mean ± standard deviation, SSW: Stainless steel wire, TNC: Thermoreactive nitinol clips, CABG: Coronary artery bypass graft, IMA: Internal mammillary artery, CPB: Cardiopulmonary bypass, IABP: Intra-aortic balloon pump

Table 3: Post-operative values of patients who underwent sternal closure

	Groups			
	SSW (n=32)	Robicsek (n=32)	TNC (n=32)	p value
Intensive Care Unit Stay (day)*	2.5±0.9	2.6±1.0	2.3±0.5	0.532
Hospitalization Time (day)*	7.5±2.2	7.5±2.5	6.3±0.5	0.014
Complications				
Hemorrhage	2	3	1	0.610
Superficial Sternal Wound Infection	5	3	2	0.224
Deep Sternal Wound Infection	5	4	0	0.032
Mediastinitis	1	1	0	0.387
Reproduction in Wound Culture	4	5	3	0.709
Dehiscence	6	4	0	0.014
Time of Dehiscence (day)*	3.2±7.2	1.5±4.2	N/A	0.009**
Sternum Revision Method				0.017
SSW	0	0	0	
Robicsek	1	0	0	
TNC	5	4	0	
Second Revision Requirement	0	0	0	
Visual Pain Score*				
Post-op first day	6.8±1.2	7.4±0.8	5.2±0.6	<0.001
Post-op third day	5.5±1.4	5.4±1.1	3.6±0.8	<0.001
Post-op fifth day	4.6±1.0	4.7±1.1	3.3±0.6	<0.001
Mortality	1	1	0	0.387

*: mean ± standard deviation, **: SSW vs Robicsek technique, SSW: Stainless steel wire, TNC: Thermoreactive nitinol clips

When we divided the patients according to the presence of dehiscence, all preoperative and operative parameters were similar between groups. We detected infectious complications in

all patients with sternal dehiscence including SSWI in 3/10 patients (30%), DSWI in 5/10 patients (50%) and mediastinitis in 2/10 patients (20%). However, we only faced SSWI in 7/86 patients (8.1%) and DSWI in 4/86 (4.7%) patients in which dehiscence did not occur. The VAS scores were significantly higher in patients with sternal dehiscence. Moreover, sternal closure with SSW and RT was more common in patients with dehiscence (p=0.014) (Table 4). In multivariate regression analysis, SSWI and DSWI were the only predictive factors for sternal dehiscence (p=0.029 and p=0.015, respectively) (Table 5).

Table 4: Comparison of patients with and without dehiscence occurrence

	Dehiscence (n=10)	Non-dehiscence (n=86)	p value
Gender (male/female)	8/2	71/15	0.843
Age (year)*	68.9±2.2	71.1±4.8	0.162
Body Mass Index (kg/m2)*	28.8±4.6	29.2±3.7	0.799
Comorbidity			
Diabetes mellitus	3 (30%)	32 (37.2%)	0.658
Hypertension	4 (40%)	38 (44.2%)	0.803
Chronic Renal Failure	0	6 (7%)	0.394
Chronic Obstructive Pulmonary Disease	0	12 (14%)	0.211
Cancer	1 (10%)	4 (4.7%)	0.476
Smoking History	3 (30%)	40 (46.5%)	0.325
EUROSCORE*	4.0±0.9	3.7±0.8	0.251
Cardiac Ejection Fraction*	52.0±9.2	49.2±8.7	0.350
Operation			0.271
CABG	8 (80%)	64 (74.4%)	
Mitral valve replacement	1 (10%)	5 (5.8%)	
Aortic valve replacement	1 (10%)	4 (4.7%)	
Cardiac tumor	0	2 (2.3%)	
Bentall procedure	0	5 (5.8)	
Ascending aorta replacement	0	2 (2.3%)	
CABG + Mitral valve replacement	0	2 (2.3%)	
CABG + Ascending aorta replacement	0	2 (2.3%)	
CABG*	2.8±1.6	2.5±1.5	0.533
Off Pump technique	2 (20%)	9 (10.5%)	0.376
Single IMA	8 (80%)	67 (70.9%)	0.881
CPB Time (minute)*	89.8±18.8	109.4±41.2	0.188
Cross Time (minute)*	43.5±11.1	62.4±32.9	0.110
Hemorrhage (cc)*	530.0±310.9	510.5±308.1	0.850
Post extubation time (hour)*	4.7±1.1	7.4±4.1	0.135
Atrial fibrillation	5 (50%)	31 (36%)	0.394
IABP	0	6 (7%)	0.394
Superficial Sternal Wound Infection	3 (30%)	7 (8.1%)	0.032
Deep Sternal Wound Infection	7 (70%)	2 (2.3%)	<0.001
Mediastinitis	2 (20%)	0	<0.001
Sternal Closure Method			0.014
SSW	6 (60%)	26 (30.2%)	
Robicsek	4 (40%)	28 (32.6%)	
TNC	0	32 (37.2%)	
Reproduction in Wound Culture	6 (60%)	6 (7%)	<0.001
Visual Pain Score*			
Post-op first day	8.0±0.9	6.3±1.2	<0.001
Post-op third day	6.3±1.3	4.7±1.3	<0.001
Post-op fifth day	5.2±0. 9	4.1±1.1	0.002
Mortality	2 (20%)	0	<0.001

*: Mean ± standard deviation, SSW: Stainless steel wire, TNC: Thermoreactive nitinol clips, CABG: Coronary artery bypass graft, IMA: Internal mammillary artery, CPB: Cardiopulmonary bypass, IABP: Intraaortic balloon pump

Table 5: Multivariate regression analysis for dehiscence occurrence

	Odds Ratio*	p value
Deep Sternal Wound Infection	15.3 (1.7-169.1)	0.015
Superficial Sternal Wound Infection	11.7 (1.3-107.1)	0.029
Reproduction in Wound Culture	0.5 (0.1-12.9)	0.676
Mediastinitis	2.4 (0.1-68.2)	0.998
Sternal Closure Method	0.4 (0.1-2.9)	0.999

*: 95% confidence interval

Discussion

Although, many different definition of elderly population is available, there is no standard numerical criterion on the age at which a person becomes old. Recently, United Nation accepted the cutoff value as 60+ years of age to refer to the older population [11]. With developments in the field of health, life expectancy has become longer in the last century, thus, the number of elderly people who require treatment for cardiac surgery with sternotomy has increased. However, elderly patients carry additional risk factors such as; immobilization, vitamin D deficiency, chronic renal failure for sternum fragility [12]. Also, decrease in osteoblastic activity delays the bone healing in elderly patients, thus, technique of sternal closure require special attention in elderly patients.

Numerous papers have investigated the best technique for sternal closure following cardiac surgery. Dunne et al. [13] reported both SSW and cabling systems are safe options for sternal closure and one technique is not superior to another (0.7% and 3.7% rewiring rate for SSW and cabling system, respectively, p=0.12). In another study, Sarıkaya et al. [14] compared RT and TNC. They stated that the dehiscence rate was similar between groups (6.3% for RT and 7.7% for TNC with p value >0.005). In contrast, Bejko et al. [15] achieved significantly better dehiscence rates with using TNC than SSW (0% and 1.6% rewiring requirement following TNC and SSW respectively, p=0.003). In present study, we did not face any sternal dehiscence in patients in which sternal closure was performed with TNC when compared with other patients in which sternal closure was performed with SSW or RT (p=0.017). However, multivariate regression analysis showed that sternal closure technique was not a predictive factor for sternal dehiscence in present study (p=0.999).

Sternal wound infections are one of the most serious conditions after sternotomy and occurred between 0.5% and 6.8% according to the literature [16]. It's well known that being elderly is a risk factor for sternal wound infections and also, presence of diabetes mellitus, kidney dysfunction, chronic obstructive pulmonary disease and peripheral vascular disease, which are more common in elderly population, contribute to infectious complications following sternotomy. The classification of sternal wound infections and mediastinitis enables a better comparison of researches. The infection of surgical wounds of sternotomies should be considered as (A) SSWI if only the skin and subcutaneous tissue are involved, (B) DSWI ıf wound infection associated with sternal osteomyelitis without infected retrosternal space, and (C) Mediastinitis when infected retrosternal space occurs with sternal osteomyelitis [17]. Nikolaidis et al. [18] stated that incidence of DSWI was lower with TNC than SSW after sternal closure (1.7% vs 2.3%). Additionally, they claimed that infectious complications were associated with mortality. In another study, Sarıkaya et al. [8] suggested the use of TNC for the management of sternal dehiscence and they claimed that TNC breaks infection-dehiscence circle and decreases the risk of mediastinitis. Similarly, Bejko et al. [15] faced significantly less DSWI in cases in which TNC was used when compared with the cases in which SSW was used (0.2% vs 1.6%, p=0.02). In present study, we did not face any DSWI following TNC (in five cases after SSW and in four cases after RT, p=0.032) and our study demonstrated that the use of TNC for sternal closure significantly decreases sternal infectious complications.

Superior stability of sternal closure may reduce the mediastinitis incidence. Borger et al. [19] reviewed the data of 12,267 consecutive cardiac surgical patients who had undergone sternotomy and stated that TNC had superior results for the prevention of mediastinitis when compared with SSW. Also, Bejko et al. [20] compared 1702 patients with SSW and 572 patients received TNC. They found that the use of the TNC was

a better sternal closure technique in prevention of mediastinitis. In present study, we did not face any mediastinitis cases following TNC and only faced two mediastinitis cases (one case with SSW and one case with RT). However, we could not show the importance of sternal closure technique on mediastinitis. We believe that our relatively small study sample led to this outcome.

Postoperative pain deteriorates patients comfort, breathing movements and is associated with delay in patient mobilization. Previous reports about effect of sternal closure technique on postoperative period pain had controversial results. Hashim et al. [21] showed superiority of biological bone adhesive molecule on VAS score after sternal closure, over SSW. In contrast, Dunne et al. [13] found statically significant difference in VAS score in favor of sternal closure with SSW over sternal cables. In another study, Elghonemy et al. [22] found that sternal plating procedure had a benefit of lesser postoperative pain and reduced narcotic use. In present study, we achieved significantly better VAS scores after sternal closure with TNC. We think that with the TNC there will be less sternal dehiscence, infection and pain.

Although, this paper is the first prospective randomized study that investigated effectivity and safety of SSW, RT and TNC for sternal closure in elderly patients, our study has some limitations. First of all, our study sample included relatively small number of patients. Secondly, we did not analyze the cost of these three sternal closure techniques, which may be the possible subject of another investigation. Lastly, present study only analyzed the short-term outcomes and we consider future researches with long-term follow-up results will clarify the superiority of these techniques to one another.

In conclusion, our study, for the first time, showed that use of TNC decreases the hospitalization duration, DSWI and sternal dehiscence development and postoperative pain intensity following sternal closure due to cardiac surgeries. Moreover, SSWI and DSWI were found as the only predictive factors for sternal dehiscence in multivariate regression analysis. The present study findings must be supported by further prospective, randomized studies with a higher patient volume.

References

1. Murray KD, Pasque MK. Routine sternal closure using six overlapping figure of 8 wires. Ann Thorac Surg. 1997;64:1852-4.
2. Plass A, Grünenfelder J, Reuthebuch O, Vachenauer R, Gauer JM, Zünd G, et al. New transverse plate fixation system for complicated sternal wound infection after median sternotomy. Ann Thorac Surg. 2007;83:1210-2.
3. Liu JY, Birkmeyer NJ, Sanders JH, et al. Risks of morbidity and mortality in dialysis patients undergoing coronary artery bypass surgery. Northern New England Cardiovascular Disease Study Group. Circulation. 2000;102:2973–7.
4. Levin LS, Miller AS, Gajjar AH, Bremer KD, Spann J, Milano CA, et al. An innovative approach for sternal closure. Ann Thorac Surg. 2010;89:1995-9.
5. Negri A, Manfredi J, Terrini A, Rodella G, Bisleri G, El Quarra S, et al. Prospective evaluation of a new sternal closure method with thermoreactive clips. Eur J Cardiothorac Surg. 2002;22:571-5.
6. Sharma R, Puri D, Panigrahi BP, Virdi IS. A modified parasternal wire technique for prevention and treatment of sternal dehiscence. Ann Thorac Surg. 2004;77:210-3.
7. Robicsek F, Daugherty HK, Cook JW. The prevention and treatment of sternum separation following open-heart surgery. J Thorac Cardiovasc Surg. 1977;73:267-8.
8. Sarıkaya S, Büyükbayrak F, Altaş Ö, Yerlikhan O, Fedakar A, Rabuş M, Kırali K. Thermoreactive nitinol clips for re-sternotomy in cases of sternal dehiscence. Türk Göğüs Kalp Damar Cerrahisi Dergisi. 2013;21:669-75.
9. Roques F, Nashef SA, Michel P, Gauducheau E, De Vincentiis C, Baudet E, Cortina J, David M, Faichney A, Gavrielle F, Gams E. Risk factors and outcome in European cardiac surgery: analysis of the EuroSCORE multinational database of 19030 patients. European Journal of Cardio-thoracic Surgery. 1999;15:816-23.
10. Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: what is moderate pain in millimetres? Pain. 1997;72:95-7.
11. Freund AM, Smith J. Self-definition in old age. Zeitschrift fur Sozialpsychologieç 1997;28:44-59.
12. McCarthy JP, Skinner TA, Norman RW. Urolithiasis in the elderly. Can J Urologyç 2011;18:5717–20.
13. Dunne B, Murphy M, Skiba R, Wang X, Ho K, Larbalestier R, Merry C. Sternal cables are not superior to traditional sternal wiring for preventing deep sternal wound infection. Interact Cardiovasc Thorac Surg. 2016 May;22(5):594-8.
14. Sarıkaya S, Aksoy E, Özen Y, Dedemoğlu M, Özgür MM, Büyükbayrak F, Kırali K. Thermoreactive nitinol clips: propensity score comparison with Robicsek technique. Asian Cardiovascular and Thoracic Annals. 2015;23:399-405.
15. Bejko J, Bottio T, Tarzia V, De Franceschi M, Bianco R, Gallo M, Castoro M, Bortolussi G, Gerosa G. Nitinol flexigrip sternal closure system and standard sternal steel wiring: insight from a matched comparative analysis. Journal of Cardiovascular Medicine. 2015;16:134-8.
16. Cotogni P, Barbero C, Rinaldi M. Deep sternal wound infection after cardiac surgery: evidences and controversies. World Journal of Critical Care Medicine. 2015;4:265-72.
17. El Oakley RM, Wright JE. Postoperative mediastinitis: classification and management. Ann Thorac Surg. 1996;61:1030–6.
18. Nikolaidis N, Karangelis D, Mattam K, Tsang G, Ohri S. The use of Nitinol clips for primary sternal closure in cardiac surgery. Annals of Thoracic and Cardiovascular Surgery. 2013;19:330-4.
19. Borger MA, Rao V, Weisel RD, Ivanov J, Cohen G, Scully HE, David TE. Deep sternal wound infection: risk factors and outcomes. The Annals of Thoracic Surgery. 1998;65:1050-6.
20. Bejko J, Tarzia V, De Franceschi M, Bianco R, Castoro M, Bottio T, Gerosa G. Nitinol flexigrip sternal closure system and chest wound infections: insight from a comparative analysis of complications and costs. The Annals of Thoracic Surgery. 2012;94:1848-53.
21. Hashim S, Chin LY, Krishnasamy S, Sthaneswar P, Mokhtar RA. Effect of sternal closure with biological bone adhesive on pain visual analogue score and serum cytokine. Journal of Cardiothoracic Surgery. 2015;10:32-8.
22. Elghonemy YF, Hussein MA. Titanium plate fixation versus wire sternal closure in coronary artery bypass graft patients: Need for rigid sternal fixation. Journal of the Egyptian Society of Cardio-Thoracic Surgery. 2016;24:150-8.

J Surg Med. 2018;2(3):210-214.
DOI: 10.28982/josam.416309

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Determination of CYP2D6*3 and *4 allele frequency among Turkish population

Türk popülasyonunda CYP2D6*3 ve *4 allel frekansının saptanması

Zehra Okat [1,2], Kübra Yaman [1,2], Kezban Uçar Çiftçi [1,2], Selina Toplayıcı [1,2], Elif Kurt [1,2], Yavuz Taga [1,2]

[1] Department of Biochemistry, School of Medicine, Marmara University, Maltepe, Istanbul, Turkey
[2] Genetic and Metabolic Diseases Research and Implementation Centre, Marmara University, Maltepe, Istanbul, Turkey

ORCID ID of the authors
ZO: 0000-0002-9966-9884
KY: 0000-0002-4318-0529
KUÇ: 0000-0003-2448-6538
ST: 0000-0003-4221-7219
EK: 0000-0003-1956-575X
YT: 0000-0001-9450-5031

Corresponding author / Sorumlu yazar:
Zehra Okat
Address / Adres: Marmara Üniversitesi, Tıp Fakültesi, Biyokimya Anabilim Dalı, Maltepe, 34854, İstanbul, Türkiye
E-mail: zehraokat1980@gmail.com

Ethics Committee Approval: This project was approved by the Medical Faculty Ethics Committee of Marmara University (Number: B.30.2.MAR.0.01.02/AEK/207; Date: 01/03/2012).
Etik Kurul Onayı: Bu proje Marmara Üniversitesi Tıp Fakültesi Etik Kurulu tarafından onaylandı (Sayı: B.30.2.MAR.0.01.02 / AEK / 207; Tarih: 01.03.2012).

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 17.04.2018
Accepted / Kabul Tarihi: 25.04.2018
Published / Yayın Tarihi: 25.04.2018

Abstract

Aim: CYP2D6 takes part in the family of cytochrome P450 enzymes, which is account for the detoxification of multifarious xenobiotics and various drug commonly used in medicine. CYP2D6 is a polymorphic gene encompassing more than 80 known polymorphism within the coding and promoter regions. The mutant CYP2D6*3 allele revealed with the deletion of A2637 found in exon 5 region. The other common mutant allele is CYP2D6*4 and this allele stem from a splice site defect of G1934A can be classified as the most typical mutations. The present study primarily aims to determine the CYP2D6*3 and *4 frequency defects among Turkish population.

Methods: Within the framework of the study, two critical alleles of CYP2D6 wild type allele, and CYP2D6*3 -CYP2D6*4 mutated alleles are genotyped on eighty healthy volunteers, who are unrelated, by the method of polymerase chain reaction (PCR)-restriction fragment length polymorphism (RFLP).

Results: CYP2D6*4 allele frequency, which was identified as the loss of BstNI site, was determined as 13.16% on the examined reference group. Besides, the CYP2D6*4/CYP2D6*4 genotype ratio for the searched reference group was observed in only 2.63%. The heterozygous CYP2D6*3 allele frequency was determined as 1.32% on the examined reference group. Finally, CYP2D6*3/CYP2D6*3 genotype was not encountered in that searched reference group.

Conclusion: In the light of those findings, it can be clearly stated that the prevalence of CYP2D6*3 and *4 allelic variants in the Turkish population is the same with the other demographic groups in Turkey.

Keywords: CYP2D6 polymorphism, Xenobiotics, Turkish population, PCR-RFLP

Öz

Amaç: CYP2D6, çeşitli ksenobiyotiklerin ve ilaçların detoksifikasyonundan sorumlu sitokrom P450 enzim ailesi içerisinde yer almaktadır. CYP2D6, kodlama ve promotör bölgelerinde 80'den fazla bilinen polimorfizm içeren bir polimorfik gendir. En tipik mutasyonlar olarak sınıflandırılan, CYP2D6*3 mutant alleli, ekson 5'de A2637'nin delesyonuyla, CYP2D6*4 mutant alleli ise G1934A'nın splice site defektiyle meydana gelmiştir. Bu çalışmada öncelikle Türk toplumunda CYP2D6*3 ve *4 frekans defektlerinin belirlenmesi amaçlanmıştır.

Yöntemler: Çalışma çerçevesinde; CYP2D6'nın iki kritik alleli olan wild tip ve mutant CYP2D6*3-*4 allelleri, birbirleriyle ilişkisiz 80 sağlıklı kontrol üzerinde, Polimeraz Zincir Reaksiyonu (PZR) ve Restriksiyon Fragment Uzunluk Polimorfizmi yoluyla genotiplendirilmiştir (RFLP).

Bulgular: BstNI bölgesinin kaybı olarak tanımlanan CYP2D6*4 allel frekansı, incelenen referans grupta %13.16 olarak belirlenmiştir. Ayrıca; referans grupta araştırılan CYP2D6*4/CYP2D6*4 genotip oranının sadece %2.63 olduğu gözlemlenmiştir. Analiz edilen referans grupta; heterozigot CYP2D6*3 allel frekansı % 1.32 olarak tespit edilmiştir. Son olarak, CYP2D6*3/CYP2D6*3 genotipine araştırılan referans grubunda rastlanılmamıştır.

Sonuç: Bu bulgular ışığında, Türk populasyonunda CYP2D6*3 ve *4 allelik varyant prevalanslarının diğer demografik gruplarla aynı olduğu açıkça belirtilebilir.

Anahtar kelimeler: CYP2D6 polimorfizmi, Zenobiyotik, Türk popülasyonu, PZR-RFLP

How to cite / Atıf için: Okat Z, Yaman K, Çiftçi KU, Toplayıcı S, Kurt E, Taga Y. Determination of CYP2D6*3 and *4 allele frequency among Turkish population. J Surg Med. 2018;2(3):210-214.

Introduction

CYP2D6 enzyme is associated with the metabolism of currently used drugs, including antidepressants, antipsychotics, antiarryhythmics, anti-cancer, beta blockers, and beta-adrenoceptor [1,2]. In this respect, CYP2D6 locus is fairly polymorphic and recently, around 120 variant CYP2D6 alleles are included in that category (www.cypalleles.ki.se/CYP2D6.htm).

CYP2D6 alleles may be divided into these sub-items: alleles causing non-functional products refer as poor metabolizers (PMs); alleles induce a reduction at - metabolism ratio to be known as heterozygote extensive metabolizers (HEMs); alleles resulting in ultra-rapid metabolism ultra-rapid metabolizers (UMs) means individuals with genetically raised CYP2D6 activity and finally alleles who have minor functional effects called extensive metabolizers (EMs) [3]. In this respect, CYP2D6 gene is located in chromosome 22q13.1. CYP2D6*4 allele which is known as splice site G1934A transition induce truncated protein creation among Caucasians. And also, this mutation is one of the most prevalent mutations for this population group. Similarly, the transition from G to A at the intron 3/exon 4 boundary in CYP2D6 gene region accompanies inappropriate mRNA splicing. This defect leads to a frame shift and immature termination. In the same way, the transition from G to A was defined as a key defect at CYP2D6 locus, and it was presumed to represent 80-90% of the mutant alleles in PM [4]. Allele CYP2D6*3 is a frameshift mutation generated by a 1-bp deletion (2637delA) in exon 5. Those mutations result in the reduction of CYP2D6 isoenzyme activity or non-activity of CYP2D6 isoenzyme, which is finally sourced PM phenotype [5], hydroxylation deficiency of various classes of mostly used drugs, endogenous substances and environmental toxic chemicals [6,7] escalated risk of therapeutic failure or adverse side effects following a drug treatment [6]. Individuals who have two null CYP2D6 alleles are named as poor metabolizers (PMs) and researchers have found that PMs are seen in 5-10% of the Caucasians [8]. The CYP2D6*4 allele, subsequent to CYP2D6*5 and CYP2D6*3, is the most effective null allele in CYP2D6 allele group, resulting PM phenotype augmentation among Europeans (12-22%) [9].

Materials and methods

Study population

Eighty healthy donor volunteers, 54 males (72%) (Mean age=35.88 years SD± 12.78) and 22 females (28%) (Mean age=34.00 years SD=±11.66), four volunteers excluded who have participated in genotype study. They were referred from Haydarpaşa Numune Training and Research Hospital (Turkey). Healthy volunteers who are not related any disorder and have no medical history created the control group. This project was approved by the Medical Faculty Ethics Committee of Marmara University (Number: B.30.2.MAR.0.01.02/AEK/207; Date: 01/03/2012). All controls approvals were obtained after fully described the nature of the procedures to be applied in the investigation.

Molecular analysis

A total of eighty Genomic DNA were extracted using commercial kit for the genomic DNA extraction procedure using the salting out method from 200 µl of whole blood. Four samples could not be realized due to the inadequate amount of DNA. At the examination of the intron 3 polymorphism, 355 bp region of the CYP2D6 (CYP2D6*4) gene was amplified using primers PF: 5'-GCC TTC GCC AAC CAC TCC G-3', and PR: 5' AAA TCC TGC TCT TCC GAG GC-3'). PCR was conducted with a master mix (a total volume of 25 µl). PCR program requires the following conditions: first of all initial denaturation at 94 °C for 5-minutes, 30 cycles of denaturation at 94 °C for 1 minute, annealing at 60 °C for 1 minute, extension at 72 °C for 1.5 minutes, and final extension at 72°C for 10 minutes [10]. Amplified product which made up of PCR method was digested during overnight with 10 U of the restriction endonuclease *Bst* NI (*Mva* I) at 60 °C. Figure 1 illustrates the restriction patterns and classification of the genotypes.

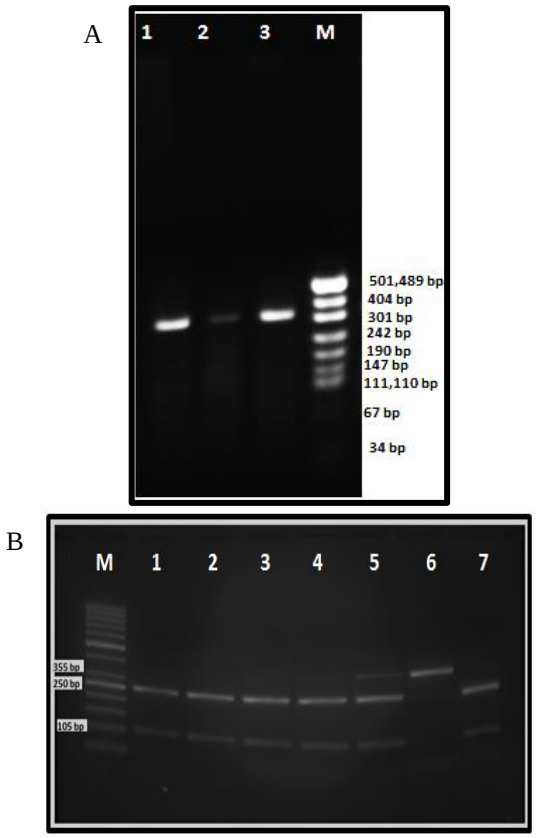


Figure 1: PCR products and RFLP Pattern of CYP2D6 Intron 3 Polymorphism.
A: PCR products of CYP2D6 Intron 3 Polymorphism, 355 bp (Line 1, 2, 3), Marker: pUC19/Msp I DNA ladder (Base pair ranges involve; 501, 489, 404, 331, 242, 190, 147, 111, 110, 67, 34 bp)
B: RFLP Pattern of CYP2D6 Intron 3 Polymorphism. Marker: 50 bp DNA Ladder (Base pair ranges involve; 1000, 900, 800, 700, 600, 500, 400, 300, 250, 200, 150, 100, 50 bp)

- CYP2D6*4/*4 genotype; Poor metabolizer (PM); it carries inactive in two alleles; 355 bp (Line 6)
- CYP2D6 wt/*4 genotype; Heterozygote extensive metabolizer (HEM); carries one functional allele; 355, 250,105 bp (Line 5)
- CYP2D6 wt/wt genotype; Homozygote extensive metabolizer (EM); carries two functional alleles; 250,105 bp (Line 1,2,3,4 and 7)

270 bp region of the (CYP2D6*3) gene was amplified using primers PF: 5'-GAT GAG CTG CTA ACT GAG CCC-3', PR: 5'-CCG AGA GCA TAC TCG GGA C-3' for the examination of the exon 5 polymorphism. PCR was conducted via master mix. PCR program requires the following conditions: firstly initial denaturation at 94 °C for 5 minutes, 40 cycles of denaturation at 94 °C for 1 minute, annealing at 62 °C for 1

minute, extension at 72°C for 1.5 minutes, and the final extension at 72 °C for 10 minutes [10]. Amplified PCR product was digested during overnight with 10 U of the restriction endonuclease Hpa II (Msp I) at 37 °C. Figure 2 indicates the restriction patterns and classification of the genotypes.

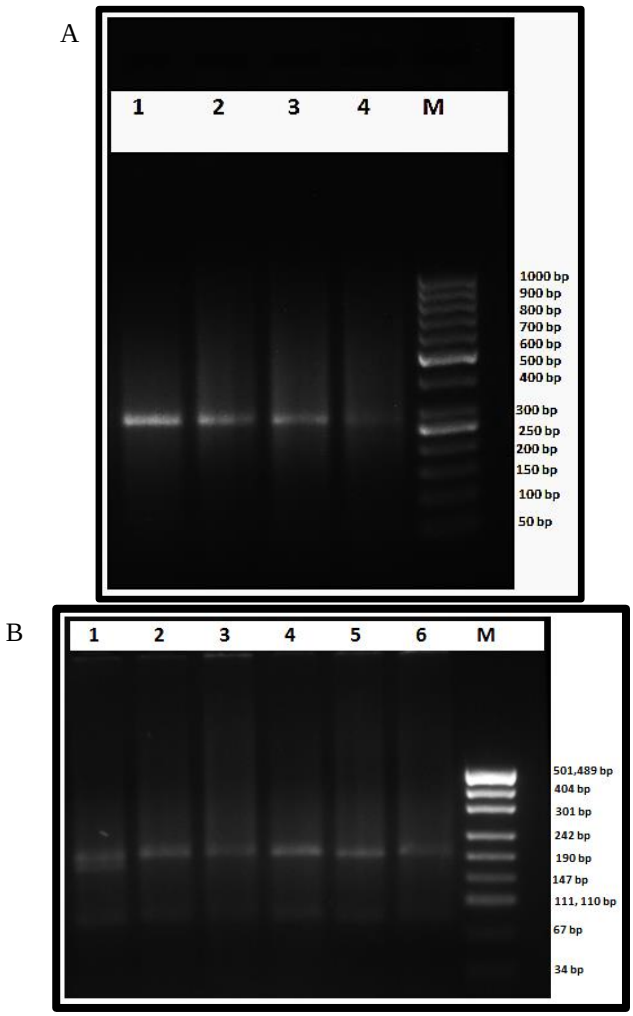


Figure 2: PCR products and RFLP Pattern of CYP2D6 Exon 5 Polymorphism.
A: PCR products of CYP2D6 Exon 5 Polymorphism, 270 bp (Line 1, 2, 3, 4)
Marker: 50 bp DNA Ladder (Base pair ranges involve; 1000, 900, 800, 700, 600, 500, 400, 300, 250, 200, 150, 100, 50 bp)
B: RFLP Pattern of CYP2D6 Exon 5 Polymorphism
Marker: pUC19/Msp I DNA ladder (Base pair ranges involve; 501, 489, 404, 331, 242, 190, 147, 111, 110, 67, 34 bp)

- CYP2D6 wt/ wt genotype; Homozygote extensive metabolizer (EM); carries two functional alleles; 188,82 bp (Line 2,3,4,5,6)
- CYP2D6 wt/*3 genotype; Heterozygote extensive metabolizer (HEM); carries one functional allele; 188, 168, 82, 20 bp (Line 1)
- ***In this study CYP2D6*3/*3 genotype (PM) was not present; it carries inactive in two alleles; 168, 82, 20 bp.

Statistical Analysis

Our data were collected from the standpoint of range, frequencies (number of controls), mean± standard deviation ± SD and relative frequencies (percentages) where applicable. In these analyses, SPSS Version 14 was employed. Online Encyclopedia for Genetic Epidemiology (OEGE) software (2006) was used for calculating chi-square Hardy-Weinberg equilibrium test. In order to contrast the main categorical variables this test was used. In chi-squared test, the probability value (*p*- value) below 0.05 was accepted as statistically significant.

Results

Chi-square Hardy-Weinberg equilibrium was calculated for CYP2D6*3 and CYP2D6*4 (CYP2D6*3 $\chi 2$: 0.0135, P value: 0.9075, CYP2D6*4 $\chi 2$: 0.4718, P value: 0.4922). For CYP2D6*4 allele, individuals with one normal (250, 105 bp) and one mutated allele (355 bp) named as heterozygous. But homozygous individuals express 355 bp band while normal individuals show only 250, 105 bp fragments. When the results were evaluated, 76.32 % of the volunteers (n=58) had wild-type 'WT' allele. And also, 2.63 % of the cases (n=2) had two *4 (mutated) alleles, and they were homozygous for CYP2D6. 21.05% of the subjects (n=16) had one *4 allele, and they were heterozygous for CYP2D6*4. CYP2D6*4 mutant (MUT) allele frequency was 13.16%, wild-type 'WT' allele frequency was 86.84% in this group (Table 1).

For CYP2D6*3 allele, heterozygous individuals indicate 188, 168, 82 and 20 bands, homozygous individuals show 168, 82, 20 bp bands, while normal individuals demonstrate only 182, 82 bp fragments. 97.37% of the volunteers (n=74) had WT allele. 0% of cases (n=0) had two *3 (mutated) alleles, and they were homozygous for CYP2D6. 2.63% of the subjects (n=2) had one *3 allele, and they were heterozygous for CYP2D6*3. CYP2D6*3 MUT allele frequency was 1.32 %, wild-type 'WT' allele frequency was 98.68% in this group (Table 1).

Table 1: Genotype and allele frequency of CYP2D6*4 and CYP2D6*3 among Turkish population.

	Genotype Frequency (n=76)			Allele Frequency (n=152)	
	PM (%)	EM (%)	HEM (%)	WT (%)	MUT (%)
CYP2D6*4	2 (2.63%)	16 (21.05%)	58 (76.32%)	86.84%	13.16%
CYP2D6*3	0 (0%)	2 (2.63%)	74 (97.37%)	98.68%	1.32%

N: total number, MUT: mutant allele, WT: wild type allele, PM: homozygous mutant status, EM: homozygous normal status, HEM: heterozygote

Discussion

CYP2D6 polymorphism's susceptibility to different diseases had been inspected, including certain cancers, systematic pituitary adenomas, lupus erythematosus, Parkinson's disease, Balkon nephropathy and ankylosing spondylitis [11,12]. In cancer supportive treatment, 25% of all medicines is metabolized by CYP2D6 enzyme, involving tamoxifen, cytotoxic drugs and other drugs used [1,2]. Furthermore, CYP2D6 gene is liable for the detoxification of various carcinogens including polycyclic aromatic hydrocarbons (PAHs), and nitrosamines [2]. Therefore, CYP2D6 expression variation may have a role in drug-drug interaction and the susceptibility of cancers. However, in the various types of cancer, the significance of CYP2D6 allelic variants stays as a challenging and controversial issue. In that scope, some of the researches proposed CYP2D6 to have a role in cancer development; but some of the studies did not support this suggestion.

In some studies, it is stated that EM genotype may cause the tendency to various cancers whereas in other researches it is claimed that PM genotype may lead to the same tendency. The relationship between PM and EM genotypes, and tendency to cancer is still not explicit. It is considered that the individuals with PM genotype are less exposed to carcinogenic and genotoxic xenobiotic metabolites in comparison to those with EM genotype, but they are exposed to unmetabolized xenobiotics and toxic effects, which are stemmed from undetermined countless factors [13]. It is thought that mentioned toxic effects might promote to the development of carcinogenesis in PMs

[14]. Most of the variant alleles comprising of CYP2D6*3,*4, and *5 led to the production of the nonfunctional enzyme and those related variants were mostly evaluated as the PM phenotype [15]. Among European Caucasians, the PM is predicted among 7 to 10 % [16-20]. In that framework, CYP2D6*4 is a well- known defective allele among 21 % of the Caucasian population. In a different analyses it was shown that, CYP2D6*4 mutant allele frequency was rare in the Chinese, Japanese, Korean, and its deficiency or incidence had been reported about 1-3% [15, 18]. CYP2D6*4 allele frequencies in various populations were indicated as follows, 21% in Germans, 18% in Americans, and 8% in African Americans [19]. In a study which was performed in Turkey, CYP2D6*4 homozygote mutation rate was found as 4%, and allele frequency was 21% [20]. In addition to these analyses, Aydın et al. reported the CYP2D6*4 allele frequency as 15.4% in Turkey [19]. In the present study, the number of volunteers carrying CYP2D6*4 mutation turned out to be 18 (23.68%): 16 (21.05%) were heterozygous, and 2 (2.63%) were homozygous. Within the entire of control group, CYP2D6*4 allele frequency was measured as 0.13 (13.16%). As we compared our results with the study of Aynacıoğlu et al. [21], Aydın et al. [19], Sahin et al. [22], we determined that the frequencies of allele and homozygous mutations were nearly close.

If we talk about the inability of this study, in our analyses the main failure is to determine the other nonfunctional defective alleles (3*) in Turkish population. But this mutant allele is rare in most of white populations and also in Turkish populations: the detected allele frequency for *3 is 0.00 [21] or 0.025 [19]. In this study, the number of volunteers with CYP2D6*3 mutation was 2 (2.63%): 2 (2.63%) were heterozygous and 0 (0%) were homozygous. In all volunteers, CYP2D6*3 MUT allele frequency was 0.01(1.32%). In a different study, Antunes et al. [23], investigated the association between phenotypes and genotypes in patients with breast cancer in Brazil. They found the allelic frequencies as 2%, 18.1%, and 1% for the mutated alleles *3,*4, and *10, respectively. Another study which was performed by Jardim et al. [24] studied the presence of polymorphic alleles of CYP2D6*3,*4,*5,*6 and *10 in southern and southeastern regions of Brazil. Moreover, they also reported the allelic frequencies as 33%, and 38% for the polymorphic alleles *4 and*10, respectively. The polymorphic alleles *5 and *6 turned out to be heterozygous in one patient, and allele *3 was not observed in the reference population. The results of this study resemble to those reported by Antunes et al. [23] and Jardim et al. [24]. When they are compared to the results of Aynacıoğlu et al. [21], allele frequencies and homozygous mutations turns out to be similar. This study's results were close to the ones found in previous studies in Asia, Sweden, Denmark, India, Malaysia, China, Japan, Europe [25-28].

As a result, the present study shown that 2.63% of the Turkish individuals who are living in the city of İstanbul are the carriers of two nonfunctional mutated alleles, *4 being homozygous for CYP2D6*4 but there were no 0 (0%) homozygous for CYP2D6*3 in volunteer group. It is clinically crucial to be able to define those individuals who have altered pharmacokinetics for CYP2D6 substrates for preventing adverse drug reactions. Because CYP2D6 is capable of metabolize 25% of commonly prescribed drugs.

Although the population of this study is not broad as to be capable to reflect whole Turkish population, we believe that if the results to be obtained from here are evaluated with the results of other studies to be conducted in different regions of Turkey in this field, they may contribute to the determination of frequency of CYP2D6 gene variants in Turkish population. Consequently, the results obtained from different populations would contribute to the area of pharmacogenetics applications in medicine.

References

1. Brosen K, Gram LF. Clinical significance of the sparteine/debrisoquine oxidation polymorphism. Eur J Clin Pharmacol. 1989;36(6):537-47. PMID: 2570698.
2. Dahl ML, Bertisson L. Genetically variable metabolism of antidepressants and neuroleptic drugs in man. Pharmacogenetics. 1993;3(2):61-70. PMID: 8100166.
3. Cascorbi I. Pharmacogeneticist's of cytochrome P4502D6: genetic background and clinical implication. Eur J Cln Invest. 2003; 33(2):17-22. PMID: 14641552.
4. Gough AC, Miles JS, Spurr NK, Moss JE, Gaedigk A, Eichelbaum M, et al.. Identification of the primary gene defect at the cytochrome P450 CYP2D locus. Nature. 1990;347(6295):773-6. DOI: 10.1038/347773a0.
5. Van Der Weide J, Steinjns L. Cytochrome P450 enzyme system: genetic polymorphisms and impact o clinical pharmacology. Ann Clin Biochem. 1999;36(6):722-9. DOI: 10.1177/000456329903600604.
6. Lavandera JV, Parera VE, Batlle A, Buzaleh AM. CYP2D6 polymorphisms in patients with porphyrias. Mol Med. 2006;12(9-10):259-63. DOI: 10.2119/2005-00047.Lavandera.
7. Stamer UM, Bayerer B, Wolf S, Hoeft A, Stüber F. Rapid and reliable method for cytochrome P450 2D6 genotyping. Clin Chem. 2002;48(9):1412-7. PMID: 12194916.
8. Sistonen J, Sajantila A, Lao O, Corander J, Barbujani G, et al. CYP2D6 worldwide genetic variation shows high frequency of altered activity variants and no continental structure. Pharmacogenet Genomics. 2007;17(2):93-101. DOI: 10.1097/01.fpc.0000239974.69464.f2 .
9. Fernandez-Santander A, del Saz M, Tejerina A, Bandres F. CYP2D6*4 allele and breast cancer risk: is there any association? Clin Transl Oncol. 2012;14(2):157-9. DOI: 10.1007/s12094-012-0776-4.
10. Schur BC, Bjerke J, Nuwayhid N, Wong SH. Genotyping of cytochrome P450 2D6*3 and *4 mutations using conventional PCR*. Clinica Chimica Acta. 2001;308(1-2):25-31. PMID: 11412814.
11. Lennard MS. Genetic polymorphism of sparteine/debrisoquine oxidation: a reappraisal. Pharmacology and Toxicology. 1990;67(4):273-83. PMID: 2077517.
12. Mayer UA. Pharmacogenetics- five decades of therapeutic lessons from genetic diversity. Nat Rev Genet. 2004;5(9):669-76. DOI: 10.1038/nrg1428.
13. Taninghera M, Malacarnea D, Ugolinia A, Parodia S. Drug metabolism polymorphisms as modulators of cancer susceptibility. Mutat Res. 1999 May;436(3):227-61. PMID: 10354524.
14. Preston-Martin S, Pike MC, Ross RK, Jones PA, Henderson BE. Increased cell division as a cause of human cancer. Cancer Res. 1990;50(23):7415-21. PMID: 2174724.
15. Zanger UM, Raimundo S, Eichelbaum M. Cytochrome P450 2D6: overview and update on pharmacology, genetics, biochemisry. Naunyn Schmiedebergs Arch Pharmacol. 2004;369(1):23-37. DOI: 10.1007/s00210-003-0832-2.
16. Alvan G, Bechtel P, Iselius L, Gundert-Remy U. Hydroxylation polymorphisms of debrisoquine and mephenytoin in European populations. Eur J Clin Pharmacol. 1990;39(6):533-7. PMID: 2151318.
17. Bradford LD. CYP2D6 allele frequency in European Caucasions, Asians, Africans and their descendants.Pharmacogenomics. 2002;3(2):229-43. DOI: 10.1517/14622416.3.2.229.
18. Bertilsson L, Dahl ML, Dalen P, Al-Shurbajı A. Molecular genetics of CYP2D6: clinical relevance with focus om psychotropic drugs. Br J Clin Pharmacol. 2002;3(2):111-22. DOI: 10.1046/j.0306-5251.2001.01548.x.
19. Aydin M, Hatirnaz O, Erensoy N and Ozbek U. CYP2D6 and CYP1A1 mutations in the Turkish population. Cell Biochem Funct. 2005;23(2):133-5. DOI: 10.1002/cbf.1222.
20. Koseler A, Ilcol YO and Ulus IH. Frequency of mutated allele CYP2D6*4 in the Turkish population. Pharmacology. 2007;79:203-6. DOI: 10.1159/000100959.
21. Aynacıoğlu, AS, Sachse C, Bozkurt A. Low frequency of defective alleles of cytochrome P450 enzymes 2C19 and 2D6 in the Turkish population. Clin Pharmacol Ther. 1999;66:185-92. DOI: 10.1053/cp.1999.v66.100072001.

22. Sahin S, Aydogan L, Benli I, Ozyurt H. Distribution of HLA-B27 and CYP2D6*4 mutations in the middle Black Sea area (Tokat) of Turkey. Genetics and Molecular Research 2011;10(4):3987-91. DOI: 10.4238/2011.December.2.3.
23. Antunes MV, Linden R, Santos TV, Wallemacq P, Haufrois V, Classen JF, et al. Endoxifen levels and its association with CYP2D6 genotype and phenotype: evaluation of a southern Brazilian population under tamoxifen pharmacotheraphy. Ther Drug Monit. 2012;34:422-31. DOI: 10.1097/FTD.0b013e318260b46e.
24. Jardim DLF, Katz A. Determination of the frequency of CYP2D6 polymorphisms in Brazilian women and literature review. Rev Bras Mastol. 2014;20:55.
25. Jonrit H, Petersen S, Dankier P, Flemming N, Grandjean P, Weihe P, et al. Polymorphism of CYP2D6, CYP2C19, CYP2C9 and CYP2C8 in the Faroese population. Eur J Clin Pharmacol. 2005 Aug;61(7):491-7. DOI: 10.1007/s00228-005-0938-1.
26. Adithan C, Gerard N, Naveen AT, Koumaravelou K, Shashindran CH, Krishnamoorthy R. Genotype and allele frequency of CYP2D6 in Tamilian population. Eur J Clin Pharmacol. 2003 Oct;59(7):517-20. DOI: 10.1007/s00228-003-0657-4.
27. Ling J, Shixiu P, Jacqueline M, Edgar H, Katharina R, Matin H. Single-Step Assays to Analyze CYP2D6 Gene Polymorphisms in Asians: Allele Frequencies and a Novel*I 4B Allele in Mainland Chinese. Clinical Chemistry. 2002;48:983-88.
28. Yamada H, Dahl ML, Lannfelt L, Viitanene M, Winbland B, S joqvist F. CYP2D6 and CYP2C19 genotypes in an elderly Swedish population. Eur J Clin Pharmacol. 1998;54(6):479-81. PMID: 9776439.

J Surg Med. 2018;2(3):215-217.
DOI: 10.28982/josam.415215

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Using multiplex PCR as a diagnostic tool to detect methicillin resistant Staphylococcus aureus

Metisiline dirençli Staphylococcus aureus'u tespit etmek için bir tanı aracı olarak multipleks PCR kullanılması

Sadık Akgün [1], Hakan Sezgin Sayiner [2]

[1] Adiyaman University, Faculty of Medicine, Department of Medical Microbiology, Adiyaman, Turkey
[2] Adiyaman University, Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Adiyaman, Turkey

ORCID ID of the authors
SA: 0000-0002-1413-0450
HSS: 0000-0002-4693-3784

Abstract

Aim: The goal of this report was to deliver the methicillin resistant Staphylococcus aureus (MRSA) reports to the clinician and prevent the treatment delays, investigating the efficacy in addition to diagnostic testing and contact isolation strategies for intensive care unit (ICU) patients with MRSA.

Methods: In this report, 320 Staphylococcus aureus strains identified as coagulase positive were cultured from hospitalized ICU patients between 2015 and 2017. Wound swabs were performed and bacteria cultures were evaluated for identification and antibiotic susceptibility testing using a culture antibiogram. Among these cultures from the swabs, MRSA was identified and subsequently screened for the MecA gene using rapid Multiplex polymerase chain reaction (PCR).

Results: MRSA was detected in 67 of 320 strains, because of oxacillin resistance was detected by working with a fully automated culture antibiogram device. In addition, MRSA positivity was detected because of the high MecA gene expression in 56 of these 67 strains using rapid multiplex PCR.

Conclusion: With greater than 86% sensitivity, patients were able to get early treatment for MRSA due to the rapid screening analysis using Multiplex PCR. This method, as a diagnostic tool, may be of benefit in other diseases.

Keywords: Staphylococcus aureus, Methicillin resistant Staphylococcus aureus, Multiplex PCR, Wound culture

Öz

Amaç: Bu çalışmanın amacı, yoğun bakım ünitesi (YBÜ) hastalarında izole edilen, metisiline dirençli Staphylococcus aureus (MRSA) için tanısal test ve temas izolasyon stratejilerine ek olarak etkinliği araştırarak, MRSA raporlarını klinisyene daha hızlı bir şekilde iletmek ve tedavideki gecikmeleri önlemekti.

Yöntemler: Çalışmaya, 2015 ve 2017 yılları arasında, hastaneye yatırılmış YBÜ hastalarından alınan kültür örneklerinden izole edilen ve koagülaz pozitif olarak tanımlanan 320 Staphylococcus aureus suşu dahil edildi. Yara sürüntüleri alındı ve bakteri kültür işlemleri yapılarak, antibiyotik duyarlılık testi ve identifikasyon işlemleri için değerlendirildi. Swablardan alınan bu kültürler arasında MRSA olarak tanımlanan suşlar daha sonra hızlı Multipleks polimeraz zincir reaksiyonu (PCR) kullanılarak MecA geni için tarandı.

Bulgular: 320 suşun 67'sinde, tam otomatik kültür antibiyogram cihazı ile çalışılarak oksasilin direnci saptanarak MRSA tesbit edildi, Ayrıca hızlı Multipleks polimeraz zincir reaksiyonu (PCR) ile çalışıldığında bu 67 suşun 56'sında MecA geni tesbit edilerek, MRSA pozitifliği saptandı.

Sonuç: Multiplex PCR kullanarak hızlı tarama analizine bağlı olarak, % 86'dan fazla duyarlılık ile hastalar MRSA için erken tedavi alabildiler. Bu yöntem, bir tanı aracı olarak, diğer hastalıklarda da yararlı olabilir.

Anahtar kelimeler: Staphylococcus aureus, Metisiline dirençli Staphylococcus aureus, Multiplex PCR, Yara kültürü

Corresponding author / Sorumlu yazar:
Sadık Akgün
Address / Adres: Adıyaman Üniversitesi, Tıp Fakültesi, Tıbbi Mikrobiyoloji Bölümü, 02100, Adıyaman, Türkiye
E-mail: sakgungizem@hotmail.com

Ethics Committee Approval: Ethics committee approval was not received because of retrospective design of the study.
Etik Kurul Onayı: Etik kurul onayı çalışmanın retrospektif dizaynından dolayı alınmamıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 13.04.2018
Accepted / Kabul Tarihi: 10.05.2018
Published / Yayın Tarihi: 10.05.2018

How to cite / Atıf için: Akgün S, Sayiner HS. Using multiplex PCR as a diagnostic tool to detect methicillin resistant Staphylococcus aureus. J Surg Med. 2018;2(3):215-217.

Introduction

Staphylococcus aureus is a bacterial pathogen that causes numerous complications in humans. Methicillin-resistant Staphylococcus aureus (MRSA) has caused many problems in patients due to it multidrug resistance. MRSA strains have been detected since the early 1960s, soon after methicillin became clinically available [1,2]. MRSA continues to increase in the health facilities and it has undergone rapid epidemiological development, spreading outside the boundaries of hospitals. Due to its resistance to multiple antibiotics, new drugs options have been considered to help reduce the morbidity and mortality rates caused by MRSA [2-5].

Presently, the regulation of MRSA in hospitals is unresolved and affects hospitals worldwide. Furthermore, the use of gloves, gowns, or masks to prevent the spread of MRSA has not been proven effective [6,7]. MRSA has been estimated to contribute to ~150,000 infections in the European Union, which has resulted in 380 million euros of healthcare costs.

In order to determine the best treatment option, timely diagnosis and uncovering the antimicrobial resistance profile is very important [1,2]. Molecular methods for identification of MRSA have been based on the of the mecA gene, which is associated with methicillin resistance and encodes the penicillin-binding protein 2a (PBP-2a).

MRSA detection from non-sterile samples (i.e., nasal samples) often contain coagulase-negative staphylococci and Staphylococcus aureus, and both have the mecA gene. MRSA is differentiated from coagulase-negative staphylococci through targeting mecA from Staphylococcus aureus and femA from coagulase-negative staphylococci. There are many kits available that are suitable to determine MRSA from other methicillin sensitive bacteria [8-10].

This project was coordinated to determine a method for diagnosis of MRSA using Multiplex PCR for the mecA gene from swabs collected from ICU patients.

Materials and methods

Staphylococcus aureus was isolated from the wound swabs of 320 patients hospitalized in the ICU at our Medical Microbiology laboratory between 2015 and 2017. Initially, all of the 320 patient swab specimens were included in the study because the oxacillin resistance of coagulase positive Staphylococcus aureus strains loaded on the culture antibiogram device was unknown. The swabs were removed from the transport container and inoculated on a 5.0% sheep blood agar medium. Then, the cultures were incubated overnight at 37℃ in a bacteriological incubator. Species suspected as Staphylococcus aureus, using conventional methods (with catalase, coagulase, etc.), were examined for MRSA with a fully automated culture antibiogram (Phoenix, BD, USA) and an antibiotic sensitivity test panel (PMIC 381 BD, USA). Subsequently, multiplex real-time polymerase chain reaction (PCR) (BD-MAX, BD, USA) was evaluated as a molecular diagnostic tool to determine MRSA positivity. For the study, 2-3 Staphylococcus aureus colonies on the plates were mixed with distilled water into the tubes, vortexed at high speed for 1 minute with a table top vortexer, and mixed with PCR primers and Taq polymerase. Detection, amplification and analyses were performed using the semi-automated BD MAX platform.

In our study, statistical analyses were performed using the SPSS software (SPSS 15.0, IBM Inc., Chicago, IL, USA). Our results of continuous data analyses were given as minimum, maximum, median, and mean values, and the results of categorical (intermittent) variables as frequency and percentage.

Results

Of the 320 patients, 170 (53%) were male and 150 (47%) were female. Only 67 (20.9%) of the 320 Staphylococcus aureus strains collected were considered to be methicillin-resistant using the full-automated culture and antibiotic sensitivity test with oxacillin resistance. Thereafter, 67 strains of Staphylococcus aureus strains evaluated as MRSA by the Culture-Antibiogram device were examined by rapid PCR. Within 3 hours, mecA was detected in 56 (83.6%) of these strains and therefore reported to the clinician as MRSA. The 11 misclassified (16.4%) Staphylococcus aureus strains were reported as methicillin sensitive Staphylococcus aureus (MSSA) (Table 1).

Table 1: The number of *Staphylococcus aureus* isolated Oxacillin resistance, Non-PCR, PCR (+), and PCR (-)

Total wound culture	Men	1358 (56%)
	Women	1066 (44%)
Staphylococcus aureus isolated	320	
Oxacillin resistance	67	20.0%
PCR (+)	56	83.6%
PCR (-)	11	

Average age: 47.5, Range (oldest - youngest): 87 - 1

Discussion

In a study conducted by Lucke et al. [11] in a region with low prevalence for MRSA, 1,601 culture samples from the nose and other body regions were analyzed by culture and BDGeneOhm MRSA tests. The sensitivity, specificity, and positive and negative predictive values of the assay were found as 84.3%, 99.2%, 88.4%, and 98.9%, respectively. In a report by Widen et al. [12], BD MAX and Xpert MRSA assays were compared and good agreement (97.9%) was demonstrated. They concluded that the BD MAX MRSA assay was a reliable alternative automated system for the detection of MRSA from nares samples. In our study, the predictive values were not calculated because only the MRSA strains that were detected as culture results were tested by the PCR. However, our PCR test results were also quite high (84%) and were consistent with their study.

In a study conducted by Abbadil et al. [13] in Saudi Arabia, 55 Staphylococcus aureus strains were obtained from different hospital units. Strains were swabbed from surgical wounds (n=30) and from the other parts of the body (n=25). They performed real-time PCR on these samples and found that Staphylococcus aureus most frequently found in patients aged 21-40 years (40%). Forty five of these isolates (82%) were determined to be MRSA. With our study, the MRSA positivity in their study was found to be very close to each other.

In the study conducted by Lopez-Alcalde et al [7] they used multiplex PCR to detect MRSA directly from clinical specimens containing a mixture of staphylococci in less than an

hour. Of the 1,657 MRSA isolates tested, 1,636 (98.7%) were detected and the authors concluded that PCR is a rapid and powerful tool for MRSA detection. In our study, we found MRSA positivity close to previously reported values (84%) using the real-time multiplex PCR method.

In the study conducted by Aqel et al. [14] on nasal swabs of health care workers in Jordan, the frequency as well as phenotypic/genotypic features of MRSA was investigated. They discovered MRSA in 56 (7.8%) nasal swabs, which were all resistant to oxacillin. All samples were positive for mecA, while mecC was negative for all isolates. In our study, MRSA strains isolated from wound cultures in ICU patients were used instead of nasal swabs and subjected to real time PCR. For this reason, our numerical values were different from what they found.

In a study by Hogan et al. [15] in Madagascar, nasal MRSA carriage of a group of healthcare workers and non-medical university students was determined. They performed multiplex PCR to determine multiple methicillin resistant and sensitive strains. Of 1,548 analyzed nasal swabs, 171 (11%) were Staphylococcus aureus positive and only 20 (1.3%) were methicillin resistant. In our study, MRSA recovered from ICU patient wound swabs were found to be high (21%).

In a study conducted by Khairalla et al. [16], 1,300 samples from an Egyptian dental clinic were examined for MRSA. From the 34 mecA-positive isolates, the hand swabs from patients, nurses, and dentists were 9.8%, 6.6%, and 5%, respectively. Nasal swabs showed 11.1%, 6.7%, and 9.7%, respectively from these subjects. The environmental swabs showed 1.3% MRSA positivity. The authors reported that the results indicated augmented MRSA pathogenicity in dental wards and stressed a necessity for better surveillance/infection strategies. Because our study included MRSA strains isolated from cultured-antibiotics in patients in the ICU, the mecA gene value obtained by PCR in the studied samples was higher than in their values.

In particular, extension of antimicrobial resistance and identification may result in delays at the onset of antibiotic therapy, and thus a higher mortality and morbidity rate for patients admitted to the ICU. It may also cause a delay in contact isolation, which must be taken to prevent contamination of this microorganism with other diseases. On the other hand, it has been estimated that fast molecular tests used to remove these delays have created a usability problem. However, our study suggests that delays in treatment and isolation measures may be overcome by giving MRSA results at a lower cost and with higher sensitivity. Moreover, we believe that more work related to this issue is needed. Delays in antibiotic administration after severe sepsis recognition increases mortality. Therefore, it is important to start antibiotic treatment as soon as possible, especially in the intensive care units. For this reason, it is very important to start early treatment and diagnosis. Using the multiplex PCR method can reduce cost and time (~3 hours) as compared to culture antibiogram and antibiotic sensitivity tests, which take about 3-4 days.

References

1. Fang H, Hedin G. Rapid Screening and Identification of Methicillin-Resistant Staphylococcus aureus from Clinical Samples by Selective-Broth and Real-Time PCR Assay. J Clin Microbiol. 2003;7;2894–9.
2. Liu Y, Zhang J, and Ji Y. PCR-based Approaches for the Detection of Clinical Methicillin-resistant Staphylococcus aureus. Microbiol J. 2016;14(10):45-56.
3. Deresinski S. Methicillin-resistant Staphylococcus aureus: an evolutionary, epidemiologic, and therapeutic odyssey. Clin Infect Dis. 2005;15;40(4):562-73
4. Carroll KC. Rapid diagnostics for methicillin-resistant Staphylococcus aureus: current status. Mol Diagn Ther. 2008;12(1):15-24.
5. Green BN, Johnson CD, Egan JT, Rosenthal M. Griffith EA, Evans MW. Methicillin-resistant Staphylococcus aureus: an overview for manual therapists. J Chiropr Med. 2012 Mar;11(1):64–76.
6. Köck R, Becker K, Cookson B, van Gemert-Pijnen JE, Harbarth S, Kluytmans J, et al. Methicillin-resistant Staphylococcus aureus (MRSA): burden of disease and control challenges in Europe. Euro Surveill. 2010;41;14:15.
7. Lopez-Alcalde J, Mateos-Mazon M, Guevara M, Conterno LO, Sola I, Cabir Nunes S, et al. Gloves, gowns and masks for reducing the transmission of meticillin-resistant Staphylococcus aureus (MRSA) in the hospital setting. Cochrane Database Syst Rev. 2015;6(7):CD007087.
8. Huletsky A, Giroux R, Rossbach V, Gagnon M, Vaillancourt M, Bernier M, et al. New real-time PCR assay for rapid detection of methicillin-resistant Staphylococcus aureus directly from specimens containing a mixture of staphylococci. J Clin Microbiol. 2004;42(5):1875-84.
9. Bennimath VD, Gavimath CC, Kalburgi PB, Kelmani C. Amplification and Sequencing of MecA Gene From Methicillin Resistance Staphylococcus aureus. Int. J. Adv. Biotechnol. Res. 2011;2(3):310-14.
10. Bakthavatchalam YD, Nabarro LE, Veeraraghavan B. Evolving Rapid Methicillin-resistant Staphylococcus aureus Detection: Cover All the Bases. J Glob Infect Dis. 2017;9(1):18–22.
11. Lucke K, Hombach M, Hug M, Pfyffe GE. Rapid detection of methicillin-resistant Staphylococcus aureus (MRSA) in diverse clinical specimens by the BD GeneOhm MRSA assay and comparison with culture. J Clin Microbiol. 2010;48(3):981-4.
12. Widen R, Healer V, Silbert S. Laboratory Evaluation of the BD MAX MRSA Assay. J Clin Microbiol. 2014;52(7):2686–8.
13. Abbadi S, Yousse H, Nemenqani D, Abdel-Moneim AS. Rapid Identification of Methicillin Resistant Staphylococcus aureus Using Real Time PCR. Advances in Infectious Diseases. 2013;3;44-9.
14. Aqel AA, Alzoubi HM, Vickers A, Pichon B, Kearns AM. Molecular epidemiology of nasal isolates of methicillin-resistant Staphylococcus aureus from Jordan. J Infect Public Health. 2015;8(1):90-7.
15. Hogan B, Rakotozandrindrainy R, Al-Emran H, Dekker D, Hahn A, Jaeger A, Poppert S, et al. Prevalence of nasal colonisation by methicillin-sensitive and methicillin-resistant Staphylococcus aureus among healthcare workers and students in Madagascar. BMC Infect Dis. 2016 Aug 15;16(1):420.
16. Khairalla AS, Wasfi R, Ashour HM. Carriage frequency, phenotypic, and genotypic characteristics of methicillin-resistant Staphylococcus aureus isolated from dental health-care personnel, patients, and environment. Sci Rep. 2017 Aug 7;7(1):7390.

J Surg Med. 2018;2(3):218-222.
DOI: 10.28982/josam.417473

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Positive association of neck circumference and cardiometabolic risk factors in Ekiti, Nigeria

Nijerya'da Ekiti'de boyun çevresi ve kardiyometabolik risk faktörlerinin pozitif ilişkisi

Taiwo Hussean Raimi [1], Samuel Ayokunle Dada [1], Abimbola Solanke [2]

[1] Department of Medicine, Ekiti State University /Ekiti State University Teaching Hospital, Ado-Ekiti, Nigeria
[2] Department of Radiology, Ekiti State University Teaching Hospital, Ado-Ekiti, Nigeria

ORCID ID of the authors
THR: 0000-0002-0092-5324
SAD: 0000-0003-4235-2250
AS: 0000-0003-1122-0546

Corresponding author / Sorumlu yazar:
Taiwo Hussean Raimi
Address / Adres: Department of Medicine, Ekiti State University, P.M.B. 5355, Ado-Ekiti, Ekiti State, Nigeria
E-mail: taiwo.raimi@eksu.edu.ng

Ethics Committee Approval: The ethic and research committee of EKSUTH approved the study (EKSUTH/A67/2018/001).
Etik Kurul Onayı: EKSUTH'ın etik ve araştırma komitesi çalışmayı onayladı (EKSUTH / A67 / 2018/001).

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 20.04.2018
Accepted / Kabul Tarihi: 11.05.2018
Published / Yayın Tarihi: 11.05.2018

Abstract

Aim: The association between neck circumference (NC) and cardiometabolic risk factors in Southwest Nigeria is unknown. The study aimed at determining the relationship between NC and cardiometabolic risk factors.

Methods: Result of a cross-sectional health survey involving residents of Ado-Ekiti/Ika community in Ekiti State was analyzed. Clinical measurements of body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR), neck circumference, systolic/diastolic blood pressures (SBP & DBP) were taken, and random blood glucose (RBG) determined. Bivariate correlations and linear regression models were computed for each sex.

Results: There were 211 participants out of which 78 (37.0%) were men. Among men, NC was significantly correlated with weight (r=0.412, p<0.001) and BMI (r=0.362, p<0.01). Among women, NC correlated with weight (r=0.319, p<0.001), BMI (r=0.228, p<0.01), WC (r=0.238, p<0.01), SBP (r=0.444, p<0.001), DBP (r=0.423, p<0.05), and RBG (r=0.203, p<0.05). NC independently predicted SBP, ORs (95%CI), 2.707 (1.468-3.946) and DBP, ORs (95%CI), 1.780 (0.950-2.611) in women, but not in men. While only the NC of men with general obesity was greater than those who do not have, 39.27(5.68)cm vs 36.96(3.46)cm, p=0.04, the NC of women who were obese or had hypertension were significantly greater than those who were not: general obesity, 33.17(2.58)cm vs 31.57(3.08cm), p=0.002; central obesity, 32.88(2.99)cm vs 31.09(2.62)cm, p<0.001; hypertension, 34.39(2.77)cm vs 31.88(2.88)cm, p=0.001). Compared with those in the upper tertile, men with NC in the middle tertile had lower mean weight [60.82 (8.67) kg vs 68.90 (10.08) kg, p=0.005], BMI [21.31 (2.54) kgm2 vs 23.72 (3.77) kgm2, p=0.022], WC [78.32 (5.57) cm vs 85.14 (8.72), p=0.003], and WHtR [0.464 (0.06) vs 0.50 (0.06), p=0.004].Compared with those in the upper tertile, women with NC in the lower tertile had lower mean weight [56.81(9.80) kg vs 66.08(13.50)kg, p=0.031], SBP [107.53 (15.59) mmHg vs 132.38 (15.85) mmHg, p<0.001], and DBP [69.27 (10.91) mmHg vs 84.69 (10.52) mmHg, p<0.001].

Conclusions: Neck circumference has positive association with, and predicts cardiometabolic risk factors, and may serve as an index of obesity in Ekiti, Nigeria.

Keywords: Cardiometabolic risk factors, Correlations, Neck circumference, Obesity, Hypertension

Öz

Amaç: Güneybatı Nijerya'da boyun çevresi (NC) ve kardiyometabolik risk faktörleri arasındaki ilişki bilinmemektedir. Çalışma, NC ve kardiyometabolik risk faktörleri arasındaki ilişkiyi belirlemeyi amaçlamıştır.

Yöntemler: Ekiti Devletinde Ado-Ekiti / Ika topluluğu sakinlerini içeren kesitsel bir sağlık araştırması sonuçları analiz edildi. Vücut kitle indeksi (BMI), bel çevresi (WC), bel-boy oranı (WHtR), boyun çevresi, sistolik / diyastolik kan basınçları (SBP ve DBP) klinik ölçümleri alındı ve rastgele kan şekeri (RBG) belirlendi. Her cinsiyet için iki değişkenli korelasyonlar ve doğrusal regresyon modelleri hesaplandı.

Bulgular: 78'i (%37,0) erkek olan 211 katılımcı vardı. Erkekler arasında NC, ağırlıkla (r=0,412, p<0,001) ve BMI (r=0.362, p<0,01) ile anlamlı olarak koreleydi. Erkeklerde olmamakla birlikte kadınlar arasında NC (r=0,319, p<0,001), BMI (r=0,228, p<0,01), WC (r=0,238, p<0,01), SBP (r=0,444, p<0,001) ile korele bulundu. DBP (r=0,423, p<0,05) ve RBG (r=0,203, p<0,05). NC bağımsız olarak, kadınlarda SBP, OR (%95 CI), 2,707 (1,468-3,946) ve DBP, OR (%95 CI), 1,780 (0,950-2,611). Genel obezitesi olan erkeklerin sadece NC'si olmayanlardan 39,27 (5,68) cm'ye karşılık 36,96 (3,46) cm, p=0.04 iken, obez olan veya hipertansiyonu olan kadınların NC'si, değil: genel obezite, 33,17 (2,58) cm vs 31,57 (3,08 cm), p=0.002; santral obezite, 32,88 (2,99) cm'ye karşı 31,09 (2,62) cm, p<0.001; hipertansiyon, 34,39 (2,77) cm'ye karşı 31,88 (2,88) cm, p = 0.001) idi. Üst tersiyer ile karşılaştırıldığında, orta hüviyette NC olan erkeklerin oranı daha düşüktü [60,82 (8,67) kg / 68,90 (10,08) kg, p=0,005], BMI [21,31 (2,54) kg/m2 ve 23,72 (3,77) kg/m2 idi. , p=0,022], WC [78,32 (5,57) cm'ye karşı 85,14 (8,72), p=0,003] ve WHtR [0,464 (0,06) / 0,50 (0,06), p=0,004]. Üst tersiyerde bulunanlarla karşılaştırıldı, alt kadranda KKY'li kadınlar daha düşük ortalama ağırlığa sahipti [56,81 (9,80) kg / 66,08 (13,50) kg, p=0,031], SBP [107,53 (15,59) mmHg ve 132,38 (15,85) mmHg, p=0,000] ve DBP [69,27 (10,91) mmHg, 84,69 (10,52) mmHg, p=0,000].

Sonuçlar: Boyun çevresi kardiyometabolik risk faktörleri ile pozitif ilişkilidir ve tahmin eder ve Nijerya'daki Ekiti'de bir obezite endeksi olarak hizmet edebilir.

Anahtar kelimeler: Kardiyometabolik risk faktörleri, Korelasyonlar, Boyun çevresi, Obezite, Hipertansiyon

How to cite / Atıf için: Raimi TH, Dada SA, Solanke A. Positive association of neck circumference and cardiometabolic risk factors in Ekiti, Nigeria. J Surg Med. 2018;2(3):218-222.

Introduction

Worldwide, obesity is a major cause of morbidity and mortality [1]. It is associated with diseases such as diabetes, hypertension, ischemic heart disease, stroke, sleep apnea, osteoarthritis, gall bladder stones, and cancers [2]. The World Health Organization (WHO) estimated the global prevalence of obesity in adults to be 36% in 2016 [2]. A study involving 5,392 participants in five geopolitical zones in Nigeria found the prevalence of obesity to be 17.2% [3]. This is expected to rise due to adoption of western lifestyle amongst other reasons.

A number of anthropometric indices such as body mass index (BMI), waist circumference (WC), waist to hip ratio (WHpR), and waist to height ratio (WHtR) are in use as surrogates of excess body fat, which is what obesity actually connotes [2-4]. These obesity indices correlate with both total and regional body fat [5]. However, some of these indices have their drawbacks. For example, body mass index may over-estimate or under-estimate body fat depending on the build of individual or certain races [6,7]. Additionally, measurement of WC and hip circumference (HC) may be greeted with reservations in certain cultures, especially among females, who may feel awkward when such body parts are being examined [8]. Use of different landmarks while measuring WC is another potential drawback [9]. In addition to these indices, imaging techniques such as ultrasonography, computed tomography, magnetic resonance imaging, and dual energy x-ray absorptiometry (dexa scan) are used to diagnose obesity. These give better assessment of body fat than anthropometric indices, but due to cost, non-availability, and the required technicalities, they are mostly employed in research settings.

Recently, there is a growing interest in the utility of neck circumference (NC) in identifying people with obesity. This new index of upper body adiposity is easy to determine, does not require much body exposure, and was found to correlate with other obesity indices and body fat [10-14]. In the Framingham Heart Study, NC was found to be positively associated with BMI, visceral adipose tissue (VAT) and other cardiovascular disease risk factors [10]. A study conducted among the Turks [11,13] and Saudi Arabs [14] revealed that NC had positive correlation with indices of general and central obesity. Similar studies among the Chinese [15-17], Indians [18,19], Indonesians [20], and other Asian populations [21], also confirmed the positive association between NC with established anthropometric indices and cardiovascular risk factors. Specifically, Fan et al., [22] examined the relationship between NC and arterial hypertension, and found that NC predicted blood pressure, independent of other anthropometric indices.

There are scanty reports on the relationship between NC and established obesity indices and cardiovascular (CVD) risk factors in Nigeria. Specifically, no report(s) has emanated from southwest Nigeria. The aim of this study is to determine the association between NC and the established obesity indices, as well as CVD risk factors in Ekiti State, Nigeria. We hypothesize that NC will correlate with obesity indices and CVD risk factors.

Materials and methods

A health survey with cross-sectional design was conducted among some residents of Ado-Ekiti and Ika community between August and October 2017. With the aid of a questionnaire, relevant demographic and medical history was obtained from the participants. This included age, gender, previous diagnosis of hypertension and diabetes, smoking, and use of alcohol. Clinical measurements of height, weight, waist circumference, neck circumference and blood pressure were taken. Random plasma glucose (RBG) was also taken. Written informed consent was obtained from the participants. The ethic and research committee of EKSUTH approved the study (EKSUTH/A67/2018/001).

Anthropometric and Clinical measurements

Weight was measured with a bathroom weighing scale to the nearest 0.1kg, while the participant wore light clothing. Height was determined with a stadiometer to the nearest 0.1m while standing without shoes, head gear or cap. Body mass index was taken as weight (kg)/height^2 (m). General obesity was defined according to the WHO classification: <18.5 kg/m^2, underweight; 18.5 to 24.9 kg/m^2, normal; 25.0 to 29.9 kg/m^2, overweight; ≥30kg/m^2, obese [2]. Waist circumference was measured after expiration to the nearest 0.5cm, with a non-stretchable tape rule along the umbilicus while standing. Waist to height ratio was taken as waist circumference (cm)/height (cm). Central obesity was defined as follows: (1) WC ≥94cm in men and WC ≥80cm in women [3]; (2) WHtR >0.50 in both men and women [4]. Neck circumference was measured in centimeters below the laryngeal prominence and perpendicular to the long axis of the neck. While taking this reading, the participant was asked to look straight ahead, with shoulders down, but not hunched.

The blood pressure was measured from the left upper arm with the participants in sitting position. Accussons' mercury sphygmomanometer attached to appropriate cuff sizes was used. The first and fifth Koroktoff sounds were taken as the systolic and diastolic blood pressures respectively. Hypertension was defined as blood pressure ≥140/90mmHg [23]. RBG was determined with a glucometer (Accucheck, Roche diagnostics). Those with goiter, pregnant women and nursing mothers were excluded.

Statistical Analysis

Categorical variables were expressed as percentages and compared with Chi-Square, while continuous variables were expressed as mean (standard deviation) and compared with Student's t-test. Pearson's correlation was used to determine the relationship between NC and the traditional obesity indices and blood pressure. Multiple linear regression analysis was used to determine the predictive ability of NC for the cardiometabolic factors. The NC was further categorized, and analysis of variance (ANOVA) was employed to compare the means of the blood pressure and obesity indices in different tertiles of NC. Statistical analyses were done with SPSS (IBM SPSS) version 20.0 (Chicago, Illinois, USA). Statistical significance was taken as $p<0.05$.

Results

There were 211 participants out of which 78 (37.0%) were men. The mean BMI and WHtR were greater in women:

Men vs Women [BMI, 22.92(3.63) kg/m^2 vs 24.12(4.94) kg/m^2, p=0.045; WHtR, 0.49(0.06) vs 0.52(0.08), p=0.006]. Compared to women, the mean neck circumference was greater in men [37.47(4.12) cm vs 32.22(2.98) cm, p<0.001]. The mean SBP and DBP were higher in men: Men vs Women [SBP, 124.55(14.17) mmHg vs 117.32 (14.17) mmHg, p=0.006]; [DBP, 79.61(9.89) mmHg vs 74.98(14.91) mmHg, p=0.008] (Table 1). The result shows that among men, NC positively correlated with weight (r=0.412, p<0.001) and BMI (r=0.362, p<0.01). Similarly among women, NC revealed a positive correlation with weight (r=0.319, p<0.001), BMI (r=0.228, p<0.01), WC (r=0.238, p<0.01), SBP (r=0.444, p<0.001), DBP (r=0.423, p<0.05), and RBG (r=0.203, p<0.05) (Table 2).

Table 1: Clinical characteristics of the participants according to gender

Characteristics	Male n=78 Mean(sd)	Female n=133 Mean(sd)	p
Age	37.93(14.61)	38.21(11.69)	0.883
Weight	66.19(10.48)	62.16(12.91)	0.020
Height	1.70(0.11)	1.61(0.08)	<0.001
BMI	22.92 (3.63)	24.12(4.94)	0.045
WC	83.98(9.21)	83.52(11.61)	0.751
WHtR	0.49 (0.06)	0.52(0.08)	0.006
NC	37.47(4.12)	32.22(2.98)	<0.001
SBP(mmHg)	124.55(14.17)	117.32(14.17)	0.006
DBP(mmHg)	79.61(9.89)	74.98(14.91)	0.008
RBG	5.47(1.04)	5.17(1.11)	0.059

BMI: body mass index, WC: waist circumference, WHtR: waist to height ratio, DBP: diastolic blood pressure, SBP: systolic blood pressure, RBG: random blood glucose

Table 2: Correlation between neck circumference and cardiovascular risk factors by gender

Variables	Men R	p	Women R	p
Age	-0.457	<0.001	0.255	0.004
Weight	0.412	<0.001	0.319	<0.001
BMI	0.362	0.001	0.228	0.008
WC	0.004	0.971	0.238	0.006
WHtR	-0.034	0.766	0.163	0.061
SBP	0.162	0.158	0.444	<0.001
DBP	0.072	0.533	0.423	0.020
RBG	-0.204	0.077	0.203	0.020

BMI: body mass index, HC: hip circumference, WC: waist circumference, WHtR: waist to height ratio, DBP: diastolic blood pressure, SBP: systolic blood pressure, RBG: random blood glucose

In a model that included age, BMI and WC, NC independently predicted systolic and diastolic blood pressures in women, but not in men. The ORs (95%CI) for NC in women for SBP and DBP were 2.707 (1.468-3.946) and 1.780 (0.950-2.611) respectively. The R^2 for the model is 0.288 (28.8%) for SBP and 0.241 (24.1%) for DBP. WHtR was not included in the regression due to collinearity with BMI (Table 3).

The NC of the participants who were overweight or obese was significantly greater than those who had normal BMI (men, 39.27(5.68) cm vs 36.96(3.46) cm, p=0.04; women, 33.17(2.58) cm vs 31.57(3.08) cm, p=0.002).

Additionally, the NC of women who had central obesity and hypertension was greater than those without these CVD risk factors [central obesity, 32.88(2.99) cm vs 31.09(2.62) cm, p<0.001; hypertension, 34.39(2.77) cm vs 31.88(2.88) cm, p=0.001] (Table 4).

Table 4: Mean neck circumference of those with or without cardiovascular risk factors

CVD risk_factors		n	Men NC Means(sd)	P	N	Women NC Means (sd)	p
BMI	Normal	61	36.96(3.46)	0.040	79	31.57(3.08)	0.002
	Overweight / obese	17	39.27(5.68)		54	33.17(2.58)	
WHtR	Normal	49	37.29(2.64)	0.685	53	31.69(2.99)	0.096
	Obese	29	37.77(5.88)		80	32.57(2.94)	
WC	Normal	68	37.74(3.06)	0.449	49	31.09(2.62)	<0.001
	Obese	10	35.61(8.44)		84	32.88(2.99)	
BP	Normal	68	37.34(3.87)	0.553	115	31.88(2.88)	0.001
	Raised	9	38.61(6.01)		18	34.39(2.77)	

CVD: cardiovascular disease, NC: neck circumference, BMI: body mass index, WHtR: waist to height ratio, WC: waist circumference, BP: blood pressure

Compared to those with NC is in the lower tertile, women with NC in the middle and/or upper tertiles had greater mean weight, BMI, WC, WHtR, SBP, and DBP. For lower vs upper tertile: Weight [56.81(9.80) kg vs 66.08(13.50) kg, p=0.031]; SBP [107.53(15.59) mmHg vs 132.38(15.85) mmHg, p<0.001; DBP [69.27(10.91) mmHg vs 84.69(10.52) mmHg, p<0.001]. For lower vs middle tertile: Weight [56.81(9.80) kg vs 67.36(13.64) kg, p<0.001]; BMI [22.46(3.99)kgm2 vs 25.92(5.44) kgm2, p<0.001]; WC [79.69(9.42)cm vs 87.18(12.91), p=0.001]; WHtR [0.50(0.06) vs 0.54(0.09), p=0.012]; SBP [107.53(15.59) mmHg vs 125.0(27.55) mmHg, p<0.001; DBP [69.27(10.91) mmHg vs 79.27(17.14) mmHg, p=0.001] (Table 5).

Table 5: Mean of anthropometric and clinical characteristics of in women according to neck circumference tertiles

Characteristics	NC mean (sd) Lower tertile N=64	Upper tertile N=13	P	Lower tertile N=64	Middle tertile N=56	p
Weight(kg)	56.81(9.80)	66.08(13.50)	0.031	56.81(9.80)	67.36(13.64)	<0.001
BMI(kgm^2)	22.46(3.99)	24.53(4.37)	0.321	22.46(3.99)	25.92(5.44)	<0.001
WC (cm)	79.69(9.42)	86.65(10.04)	0.101	79.69(9.42)	87.18(12.91)	0.001
WHtR	0.50(0.06)	0.53(0.06)	0.347	0.50(0.06)	0.54(0.09)	0.012
SBP(mmHg)	107.53(15.59)	132.38(15.85)	<0.001	107.53(15.59)	125.0(27.55)	<0.001
DBP(mmHg)	69.27(10.91)	84.69(10.52)	<0.001	69.27(10.91)	79.27(17.14)	0.001
RBG(mmol/L)	5.02(0.65)	5.89(0.50)	0.296	5.02(0.65)	5.19(1.28)	0.778

CVD: cardiovascular disease, NC: neck circumference, BMI: body mass index, WHtR: waist to height ratio, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, SD: standard deviation

Men with NC in the upper tertile had greater mean weight, BMI, WC, and WHtR compared with those in the middle tertile. For middle vs upper tertile: Weight [60.82(8.67) kg vs 68.90(10.08) kg, p=0.005]; BMI [21.31(2.54) kgm^2 vs 23.72(3.77) kgm^2, p=0.022]; WC [78.32(5.57) cm vs 85.14(8.72) cm, p=0.003]; WHtR [0.464(0.06) vs 0.50(0.06), p=0.004].

Table 3: Predictors of systolic and diastolic blood pressures according to gender

	Predictor Variable	Women B	95%CI	p	Model R^2	Men B	95%CI	p	Model R^2
SBP									
Model 1	NC	3.491	2.274-4.707	<0.001	19.7%	0.555	-0.221-1.332	0.158	2.6%
Model 2	NC	2.707	1.468-3.946	<0.001	28.8%	0.130	-0.814-1.075	0.784	10.0%
	BMI	0.663	-0.533-1.1859	0.275		0.254	-0.899-1.407	0.662	
	WC	-0.131	-0.697-0.435	0.648		0.363	-0.061-0.787	0.092	
	Age	0.588	0.222-0.954	0.002		0.130	-0.440-1.077	0.166	
DBP									
Model 1	NC	2.115	1.332-2.898	<0.001	17.9%	0.172	-.376-.720	0.533	0.5%
Model 2	NC	1.780	0.950-2.611	<0.001	24.1%	0.093	-0.737-0.551	0.774	12.1%
	BMI	0.231	-0.571-1.032	0.570		-0.034	-0.820-0.752	0.931	
	WC	-0.113	-0.493-0.266	0.555		0.364	0.075-0.6532	0.014	
	Age	0.359	0.114-0.604	0.004		-0.149	-0.325-0.028	0.097	

BMI: body mass index, NC: neck circumference, WC: waist circumference, DBP: diastolic blood pressure, SBP: systolic blood pressure

No statistically significant difference was observed in the SBP, DBP and RBG of the two groups. Only 4 men had NC in the lower tertile. Therefore, no comparison was made (Table 6).

Table 6: Mean of anthropometric and clinical characteristics of men according to neck circumference tertiles

Characteristics	Middle tertile n=22	Upper tertile n=52	p
Weight(kg)	60.82(8.67)	68.90(10.08)	0.005
BMI(kgm^2)	21.31(2.54)	23.72(3.77)	0.022
WC (cm)	78.32(5.57)	85.14(8.72)	0.003
WHtR	0.464(0.06)	0.50(0.06)	0.004
SBP(mmHg)	118.76(11.18)	126.52(14.87)	0.085
DBP(mmHg)	75.67(1.26)	80.88(9.13)	0.101
RBG(mmol/L)	5.53(0.86)	5.33(1.05)	0.728

CVD: cardiovascular disease, NC: neck circumference, BMI: body mass index, WHtR: waist to height ratio, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, RBG: random blood glucose

Discussion

NC is an upcoming upper body obesity index. Its determination is easy, not influenced by meal, footwear or clothing, is inexpensive and requires minimal or insignificant body exposure. This study examined the correlation between NC and other obesity indices. The correlation with blood pressure and random blood glucose were also determined. Additionally, the predictive ability of NC for blood pressure was determined. Furthermore, we compared the NC of those who had obesity and hypertension versus those who did not, as well as the mean of CVD risk factors at different tertiles of NC.

The mean NC in men and women who participated in this study was 37.47(4.12) cm and 32.22(2.98) cm, respectively. The values are similar to what Zhou et al., [15], found but lower than the findings of Alfadhi et al [14], and Lindarto et al., [20]. It was however higher than what Adamu et al., [24] found. Compared with our participants, those of Alfadhi et al [14], and Lindarto et al., [20] had higher mean BMI and WC. The participants in the study by Lindarto et al., [20] were also older than ours. Contrariwise, those who took part in the study by Adamu et al., [24] were younger, and had a lower mean BMI and WC. The differences are not unexpected given the relationship between NC with age, BMI and WC. Consistent with previous studies men had a higher mean NC [14,18,21].

We found a significant correlation between neck circumference with weight, and BMI in both men and women. Additionally, NC significantly correlated with WC, SBP, DBP and RBG in women but not in men. The association was however weak to modest. We found no correlation between NC and WHtR in this study. Other workers also found significant correlation between NC and indices of general and central obesity, blood pressure and blood glucose [11,17,21,25,26]. Additionally, some workers also found correlation between NC and other metabolic parameters such as serum total cholesterol, high density lipoprotein (HDL-C), triglycerides, C-reactive protein and insulin resistance [26]. NC is a surrogate for upper body subcutaneous adipose tissue and has been found to correlate with VAT [10,16]. Since BMI and WC correlates with VAT, it is unexpected that NC also correlated with these obesity indices.

The correlation between NC and blood pressure may be related to the hemodynamic changes that accompany neck fat deposition. Ectopic fat in the neck is associated with obstructive sleep apnea (OSA), which in turn may lead to increased sympathetic tone and endothelial dysfunction [27]. These will eventually lead to increased peripheral resistance and hypertension. This fat depot may also cause insulin resistance, which is associated with activation of sympathoadrenal axis, poor renal sodium handling, increased vascular resistance and stimulation of renin-angiotensin-aldosterone system, resulting in raised blood pressure [28]. Further, ectopic fat secrets adipocytokines, which are implicated in insulin resistance, and vascular inflammation [27]. These metabolic changes may result in dysglycaemia, and may explain the correlation between NC and RBG in this study. Other workers also reported positive correlation between NC and plasma glucose [14,17].

In this study, linear regression analysis demonstrated that NC predicted SBP and DBP, even after controlling for factors such as age, BMI and WC. However, gender-specific analysis revealed that NC predicted blood pressure only in women. In the Framingham Heart study, Preis et al. [10] found that NC was positively associated with SBP and DBP only in men, after adjustment for visceral adipose tissue (VAT) and BMI. Some workers also found varied relationship between NC and cardiometabolic risk factors in the men and women [18]. However, Zhou et al. [15] and Fan et al. [22] found that NC predicted hypertension in both men and women. The effect remained after adjustment for BMI, WC, WHpR and age. Using receiver operating characteristics (ROC) curve analysis, some workers also found that NC predicted arterial blood pressure with a large area under curve [29]. In addition to the relationship between NC and hypertension mentioned above, subcutaneous adipose tissue in the neck contributes to efflux of free fatty acids (FFA) which promotes insulin resistance. Some of the gender differences observed in the relationship between NC and BP may be due to varied metabolism of fatty acids in men and women [10]. Taken together, these findings suggest that NC is related to hypertension independent of other obesity indices.

In this study, the NC of men and women who were overweight or had general obesity were higher than those who were not. Among women, but not in men, the NC of those who had central obesity and hypertension were greater than those who were not. Some workers evaluated the predictive ability of NC for obesity and insulin resistance, and found that the mean NC of participants with overweight/general obesity was higher than those with normal weight [17]. Kumar et al. [18] examined the relationship between NC and metabolic syndrome among Indians, and found that compared with those without the syndrome, more people with metabolic syndrome had abnormal NC. Other workers also reported a higher mean NC in people with metabolic syndrome [25].

The current study further revealed that compared with those in the lower tertile, the mean of CVD risk factors were higher in those with NC in the middle/upper tertiles. In men no difference was found in the mean blood pressure and random blood glucose, while in women no difference was found in the mean random blood glucose. Saka et al. [11] and Selvan et al. [25] reported that participants with high NC were more likely to have cardiometabolic syndrome. Additionally, Selvan et al. [25] showed that more people in the higher tertile of NC had obesity

(general and central) and dyslipidemia, but not hypertension or diabetes mellitus. In a study, Joshipura and associates [26] divided the participants into two groups (normal or high) based on NC, and compared the mean of the CVD risk factors or percentages (for categorical variables) of those with abnormal CVD risk factors. These risk factors include blood pressure, plasma glucose, BMI, WC, HOMA-IR, body fat percentage, and lipids. They found the CVD risk factors to be more prevalent in those with high NC. Additionally the mean of CVD factors were higher in that group.

Summarily this study established a positive association between NC and CVD risk factors. Determination of NC can be used to identify people with adverse cardiometabolic profile, especially among women. As mentioned earlier, some of the gender differences observed in the relationship between NC and CVD risk factors may be due to varied metabolism of fatty acids in men and women [10].

This study is limited by cross-sectional design and small sample size. The findings may therefore not be generalized until a large scale study is conducted. Further, relationship between neck circumference and cardiometabolic risk factors such as triglycerides, total, low-density and high density cholesterol were not explored.

In conclusion, neck circumference has positive association with, and predicts cardiometabolic risk factors in Ekiti, Nigeria. It may serve as an index of obesity in the population studied.

References

1. World Health Organization, http://www.who.int/mediacentre/factsheets/fs311/en/
2. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. WHO Technical Report Series 894. Geneva: World Health Organization, 2000.
3. Okafor C, Gezawa I, Sabir A, Raimi T, Enang O. Obesity, overweight, and underweight among urban Nigerians. Nig J Clin Pract. 2014;17(6):743-9. doi:10.4103/1119-3077.144389
4. Alberti KG, Zimmet P, Shaw J. The metabolic syndrome-a new worldwide definition. Lancet. 2005;366(9491):1059-62.
5. Ashwell M, Gibson S. Waist-to-height ratio as an indicator of 'early health risk': simpler and more predictive than using a 'matrix' based on BMI and waist circumference. BMJ Open. 2016 Mar 14;6(3):e010159. doi:10.1136/bmjopen-2015-010159
6. Kim MK, Han K, Kwon HS, Song KH, Yim HW, Lee WC, et al. Normal weight obesity in Korean adults. Clin Endocrinol (Oxf). 2014;80(2):214-20. doi:10.1186/2052-9538-1-9
7. Pasco JA. Body mass index and measures of body fat for defining obesity and underweight: a cross-sectional, population-based study. BMC Obes. 2014 Jun 23;1:9. doi: 10.1186/2052-9538-1-9.
8. Dunkley AJ, Stone MA, Patel N, Davies MJ, Khunti K. Waist circumference measurement: knowledge, attitudes and barriers in patients and practitioners in a multi-ethnic population. Family Practice. 2009;26(5):365-71.
9. Brown RE, Randhawa AK, Canning KL, Fung M, Jiandani D, Wharton S, et al. Waist circumference at five common measurement sites in normal weight and overweight adults: which site is most optimal? Clin Obes. 2018;8(1):21-9. doi:10.1111/cob.12231
10. Preis SR, Massaro JM, Hoffmann U, D'Agostino RB Sr, Levy D, Robins SJ, et al. Neck circumference as a novel measure of cardiometabolic risk: the Framingham Heart study. J Clin Endocrinol Metab. 2010;95(8):3701-10. doi:10.1210/jc.2009-1779
11. Saka M, Türker P, Ercan A, Kızıltan G, Baş M. Is neck circumference measurement an indicator for abdominal obesity? A pilot study on Turkish Adults. Afr Health Sci. 2014;14(3):570-5. doi 10.4314/ahs.v14i3.11
12. Volaco A, Martins CM, Soares JQ, Cavalcanti AM, Moyses ST, Filho RP, et al. Neck Circumference and its Correlation to Other Anthropometric Parameters and Finnish Diabetes Risk Score (FINDRISC). Curr Diabetes Rev. 2017 Oct 2. pii: CDR-EPUB-86087 doi: 10.2174/1573399813666171002113442
13. Ozkaya I, Tunckale A. Neck Circumference Positively Related with Central Obesity and Overweight in Turkish University Students: A Preliminary Study. Cent Eur J Public Health. 2016;24(2):91-4. doi:10.21101/cejph.a4555
14. Alfadhli EM, Sandokji AA, Zahid BN, Makkawi MA, Alshenaifi RF, Thani TS, et al. Neck circumference as a marker of obesity and a predictor of cardiometabolic risk among Saudi subjects. Saudi Med J. 2017;38(12):1219-23. doi: 10.15537/smj.2017.12.20926
15. Zhou JY, Ge H, Zhu MF, Wang LJ, Chen L, Tan YZ, et al. Neck circumference as an independent predictive contributor to cardio-metabolic syndrome. Cardiovasc Diabetol. 2013;12:76. doi:10.1186/1475-2840-12-76
16. Li HX, Zhang F, Zhao D, Xin Z, Guo SQ, Wang SM, et al. Neck circumference as a measure of neck fat and abdominal visceral fat in Chinese adults. BMC Public Health. 2014;14:311. doi: 10.1186/1471-2458-14-311
17. Wang X, Zhang N, Yu C, Ji Z. Evaluation of neck circumference as a predictor of central obesity and insulin resistance in Chinese adults. Int J Clin Exp Med. 2015 Oct 15;8(10):19107-13. eCollection 2015.
18. Kumar NV, Ismail MH, Mahesha P, Girish M, Tripathy M. Neck circumference and cardio- metabolic syndrome. J Clin Diagn Res. 2014;8(7):23-5. doi: 10.7860/jcdr/2014/8455.4641
19. Verma M, Rajput M, Sahoo SS, Kaur N. Neck Circumference: Independent Predictor for Overweight and Obesity in Adult Population. Indian J Community Med. 2017;42(4):209-13. doi: 10.4103/ijcm.IJCM_196_16
20. Lindarto D, Shierly, Syafril S. Neck Circumference in Overweight/Obese Subjects who Visited the Binjai Supermall in Indonesia. Open Access Maced J Med Sci. 2016;4(3):319-23. doi:10.3889/oamjms.2016.072
21. Qureshi NK, Hossain T, Hassan MI, Akter N, Rahman MM, Sultana MM, et al. Neck Circumference as a Marker of Overweight and Obesity and Cut-off Values for Bangladeshi Adults. Indian J Endocrinol Metab. 2017;21(6):803-8. doi: 10.4103/ijem.IJEM_196_17
22. Fan S, Yang B, Zhi X, He J, Ma P, Yu L, et al. Neck circumference associated with arterial blood pressures and hypertension: A cross-sectional community-based study in northern Han Chinese. Sci Rep. 2017;7(1):2620. doi:10.1038/s41598-017-02879-7
23. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;42:1206–52.
24. Adamu L, Asuku A, Taura M, Tela I, Datti SS, Imam A. Neck circumference: An upcoming tool of adiposity indices. Niger J Basic Clin Sci. 2013;10(2):82-5. doi:10.4103/0331-8540.122766
25. Selvan C, Dutta D, Thukral A, Nargis T, Kumar M, Mukhopadhyay S, et al. Neck height ratio is an important predictor of metabolic syndrome among Asian Indians. Indian J Endocrinol Metab. 2016;20(6):831-7. doi:10.4103/2230-8210.192927
26. Joshipura K, Munoz-Torres F, Vergara J, Palacios C, Perez CM. Neck Circumference May Be a Better Alternative to Standard Anthropometric Measures. J Diabetes Res. 2016;2016:6058916. doi:10.1155/2016/6058916
27. Ceccato F, Bernkopf E, Scaroni C. Sleep apnea syndrome in endocrine clinics. J Endocrinol Invest. 2015;38(8):827-34. doi: 10.1007/s40618-015-0338-z
28. Simonenko VB, Goriutskii VN, Dulin PA. The role of insulin resistance in pathogenesis of arterial hypertension. Klin Med (Mosk). 2014;92(9):27-33.
29. Assyov Y, Gateva A, Tsakova A, Kamenov Z. A comparison of the clinical usefulness of neck circumference and waist circumference in individuals with severe obesity. Endocr Res. 2017;42(1):6-14. doi:10.3109/07435800.2016.1155598

J Surg Med. 2018;2(3):223-227.
DOI: 10.28982/josam.417158

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Comparative study of Mycobacterium tuberculosis and Mycobacterium bovis protein profiles

Mycobacterium tuberculosis ve Mycobacterium bovis protein profillerinin karşılaştırmalı çalışması

Mohammad Kazem Sharifi Yazdi [1], Amir Houshang Beheshnejad [2], Azim Hedayatpour [3], Sara Sharifi-yazdi [4], Fariborz Mehrani [5]

[1] Zoonosis Research Center, Department of Medical Laboratory Sciences, Tehran University of Medical Sciences, Tehran, Iran
[2] Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran
[3] Department of Anatomy , School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[4] Medical student, School of Medicine, Tehran University of Medical Sciences,Tehran, Iran.
[5] Anesthesia Department, School of Allied Medicine, Tehran University of Medical Sciences, Tehran, Iran

ORCID ID of the authors
MKSY: 0000-0001-9060-5908
AHB: 0000-0002-3485-4587
AH: 0000-0002-1036-0697
SS: 0000-0001-9350-2947
FM: 0000-0001-8917-5285

Corresponding author / Sorumlu yazar:
Mohammad Kazem Sharifi Yazdi
Address / Adres: Zoonosis Research Center, Department of Medical Laboratory Sciences, Tehran University of Medical Sciences, Tehran, Iran
Tel: +982188983919
E-mail: mksharifi@tums.ac.ir

Ethics Committee Approval and Financial Disclosure: This research was supported by Tehran University of Medical Sciences and Health Services Grant 22146.
Etik Kurul Onayı ve Finansal Destek: Bu araştırma Tıp Bilimleri Tahran Üniversitesi ve Sağlık Hizmetleri Grant No: 22146 tarafından desteklenmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Received / Geliş Tarihi: 21.04.2018
Accepted / Kabul Tarihi: 10.05.2018
Published / Yayın Tarihi: 12.05.2018

Abstract

Aim: Despite the drug resistance Mycobacterium bovis and Mycobacterium tuberculosis (MTB) are still regarded as two of the global health problems in the world. In the present study, a comparison was made between protein profiles of Mycobacterium bovis and MTB in order to achieve effective biomarkers for diagnosis of tuberculosis.

Methods: The clinical samples, sputum and gastric lavage (and the other samples) were processed by N-acetyl-L-cysteine-sodium hydroxide methods and consequently were cultured on Lowenstein–Jensen medium. Mycobacterium tuberculosis and bovis strains were distinguished according to the biochemical tests and susceptibility testing system. Colonies were grown in 7H9 medium and membrane and secretory proteins were extracted, purified by ammonium sulfate and refrigerated alcohol methods.

Results: The protein contents were measured by Bradford method. Comparison of protein bands in each strain were performed by one dimensional electrophoresis.

The major discrepancy between the two strains in the banding separation membrane proteins could be observed in 45 and 60 KDa and also less than 45 and 14 KDa.

Conclusion: The results showed that discrepancy in the proteins bands could be used as protein effective biomarker for tuberculosis diagnosis. We should use antibody against tuberculosis for further investigation for rapid tuberculosis diagnosis.

Keywords: Mycobacterium bovis, Mycobacterium tuberculosis, Membrane and Secretory protein

Öz

Amaç: İlaç direncine rağmen Mycobacterium bovis ve Mycobacterium tuberculosis (MTB) hala dünyadaki küresel sağlık sorunlarından iki tanesi olarak kabul edilmektedir. Bu çalışmada, tuberküloz tanısı için etkili biyobelirteçler elde etmek amacıyla Mycobacterium bovis ve MTB protein profilleri arasında bir karşılaştırma yapılmıştır.

Yöntemler: Klinik örnekler, balgam ve gastrik lavaj (ve diğer örnekler), N-asetil-L-sistein-sodyum hidroksit yöntemleri ile işlendi ve sonuç olarak Lowenstein-Jensen ortamı üzerinde kültürlendi. Mycobacterium tuberculosis ve bovis suşları biyokimyasal testlere ve duyarlılık test sistemine göre ayrıldı. Koloniler 7H9 ortamında büyütülmüş ve membran ve sekretuar proteinler ekstrakte edilmiş, amonyum sülfat ve soğutulmuş alkol metotları ile saflaştırılmıştır.

Bulgular: Protein içerikleri Bradford metodu ile ölçüldü. Her bir suşta protein bantlarının karşılaştırması tek boyutlu bir elektroforez ile gerçekleştirilmiştir. Bant ayırma membranı proteinlerindeki iki suş arasındaki temel farklılık, 45 ve 60 KDa'da ve ayrıca 45 ve 14 KDa'dan daha az olarak gözlemlenebildi.

Sonuç: Sonuçlar, protein bantlarındaki farklılıkların tuberküloz tanısı için protein etkin biyobelirteç olarak kullanılabileceğini gösterdi. Hızlı tuberküloz teşhisi için ileri tetkiklerde tuberküloz'a karşı antikor kullanmalıyız.

Anahtar kelimeler: Mycobacterium bovis, Mycobacterium tuberculosis, Membran ve sekretuvar protein

How to cite / Atıf için: Sharifi Yazdi MK, Beheshnejad AH, Hedayatpour A, Sharifi-yazdi S, Mehrani F. Comparative study of Mycobacterium tuberculosis and Mycobacterium bovis protein profiles. J Surg Med. 2018;2(3):223-227.

Introduction

Tuberculosis is a global problem. In 2014, estimates indicate that 9.6 million new tuberculosis cases, that with early diagnosis and proper treatment, nearly all of them were preventable [1]. The world "Stop tuberculosis strategy" program for the period 2006-2015 was planned to achieve this goal [2]. Mycobacterium bovis is one of the oldest and most important zoonosis diseases as well as one of the numerous global health challenges. The mortality rate of M. bovis is more than Mycobacterium tuberculosis [3].

The complex of Mycobacterium tuberculosis (MTB), including M. tuberculosis, M. africanum, M. bovis, Bovis BCG, M. caprae, M. microti, M. pinnipedii, M. dassie bacillus and M. canettii, although shows different phenotype characteristics in their biochemical tests, but they have high similarity in genetic terms [4]. To differentiate complex members is essential to promote successful treatment, especially in areas where the disease is epidemic or exposure to human and animal is high [5]. The classic diagnosis method between M. tuberculosis and M. bovis based on drug sensitivity, pyrazinamida activity, nitrate reduction, niacin accumulation and growth in the thiophene 2-carboxylic acid hydrazide [6]. The only way to protect people against tuberculosis are early diagnosis, protection and treatment and the current differential methods used despite their value do not meet the need for rapid diagnostic methods. Furthermore M. tuberculosis strains resistant to antibiotics, lack of a comprehensive performance BCG vaccine in adult makes necessity for the development of rapid diagnostics and prevention will become a is a global necessity [7]. One of the suitable ways in the field is the study of protein profiles of M. bovis and MTB in order to achieve effective biomarkers for diagnosis of tuberculosis. As mentioned above MTB complex shows different phenotypic profile and drug sensitive strains of MTB are spread almost all parts of the country that makes important from epidemiological point to study. Membrane and secretory protein have effective role in stimulating cellular immunity and are important in diagnosis of tuberculosis. MTB cultures filters contain various antigens in which many of them are identifiable by monoclonal antibody and are evaluated. Many of these antibodies are secreted proteins released by the cell wall or dead bacteria. These are able to generate an immune response in the early stages of infection in patients [8]. Although complete information of genomic and proteomic of M. tuberculosis had been obtained but unfortunately not appropriate candidates for vaccine nor have protein profile model to distinction between species been introduced.

Ying Xiong et al. [9] had studied membrane proteins of H37Rv strains of M. tuberculosis by one-dimensional gel electrophoresis and mass spectrometry They could integral 349 membrane protein, in which 42 of them was reported and discussed for the first time. The aim of this study was to evaluate differences in protein profiles of strains of Mycobacterium tuberculosis and M. bovis in order to obtained suitable biomarker to diagnosis between the two strains.

Materials and methods

In total 100 samples including 80% sputum sample,7% gastric lavage ,5% axillary node aspirate, 3.5% biopsies, 2% hip, and 1.5% bronchial washings were collected. Two standard strains of RB1P11 and 7.121 were used as control. The samples were cultivated by N-acetyl-L-cysteine in Lowenstein - Jensen Medium and thiophene2 carboxylic acid hydrazide medium were used for differentiation of M. bovis and M. tuberculosis. After 8 weeks, Niacin, Catalase and Nitrate reduction and antibiotic susceptibility tests were carried out to identify the strains. Out of 100 tested samples, five were positive. The biochemical and drug sensitivity test showed that these strains were sensitive Mycobacterium tuberculosis. These strains were cultured in Middlebrook 7H9 medium for 4 weeks. The supernatants of stationary-phase liquid cultures were collected and used to extract proteins [10]. In order to extract membrane and secretory proteins, strains were cultured into Middle Brook 7H9 broth at 37 ° C and maintained for 4 weeks in order to get in logarithmic growth phase. After that it was centrifuged at 3000 rpm at 3°C for 45 minutes, then the supernatant was removed. The supernatant was washed with phosphate-buffered saline (PBS). The extraction buffer was (10 mM Tris containing protease inhibitors (PMSF) 1mM, DNase 1 mg and Triton x114 - 5%. The resulting solution was centrifuged at 5000 rpm at -3 °C for an hour. Composition with saturated solution of ammonium-sulfate 70% was used to distinct available proteins in the resulted supernatant and kept in Refrigerator for 18 hours. Samples were centrifuged at -4°C at 15000 rpm and obtained deposits were solved in 1×PBS.

Amount of protein in deposited solutions was obtained by Bradford protein analysis. Dialysis in 1x PBS was used to remove existing salts in the protein solutions. Protein solution inside the dialysis bag was placed in a solution of PBS 1x for 24 hours and the buffer was replaced on a regular basis, at least 3 times [11-13]. Ultimately, deposited proteins were investigated by SDS-PAGE, Blue Silver Staining and Coomasie Blue R-250. SDS-PAGE for membrane and secretory proteins was performed with 10% and 12.5 % Gel.

Results

From 100 random samples cultivated in Lowenstein – Jensen solid Medium, 5 samples of susceptible M. tuberculosis were selected by biochemical and antibiotic susceptibility testing methods along with 5 M. bovis strains cultivated in Middlebrook 7H9 medium. The concentration of proteins was defined by Bradford method after they were extracted and standard curve was drawn with bovine serum albumin 1 mg/ml as standard protein. The concentration of membrane and secretory proteins were reported 40-70 and 1-5, respectively. SDS-PAGE of membrane proteins by Gel 10% was carried out with Blue Silver Staining. It was resulted that all strains of M. bovis in 5 different patients have same protein patterns and all susceptible strains of M. tuberculosis in 5 different patients also have same protein pattern. 15-85KDa and 15-120KDa bands were observed in strains of M. bovis and M. tuberculosis, respectively. Differences of candidate strains of the susceptible M. tuberculosis and M. bovis are revealed in picture [2] with arrow and it can be seen

that major differences of these two strains is related to the weighted ranges of 45 and 60 KDa bands.

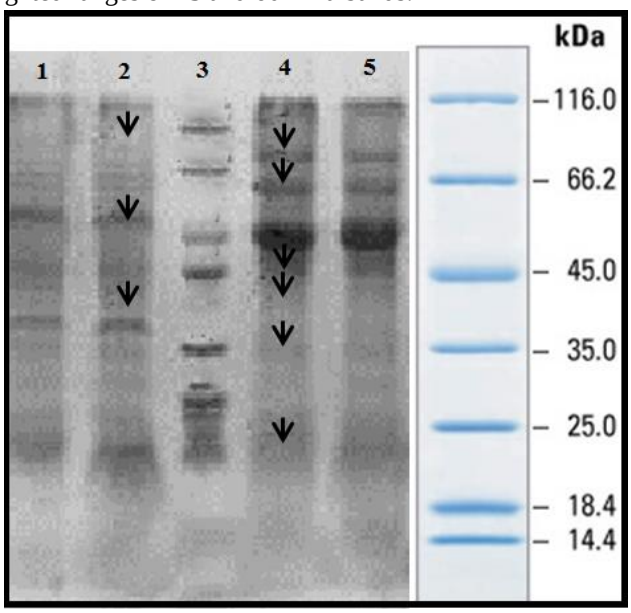


Figure 1: Gel 10%. Columns 1-2, membrane proteins of M. bovis strains-columns 3-5, membrane proteins of susceptible M. tuberculosis strains. Protein extraction using Ammonium sulfate and Blue Silver Staining methods

SDS-PAGE of secretory proteins were done using 12.5% Gel with Blue Silver Staining and it was perceived that all strains of M. bovis in 5 patients are with same protein pattern and all strains of susceptible M. tuberculosis in 5 different patients also are with same pattern.

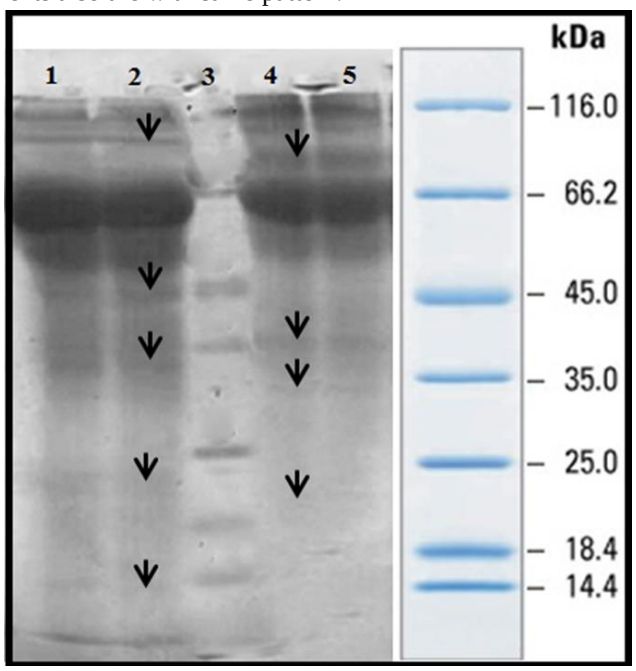


Figure 2: 12.5% Gel, columns 1, 2 secretory proteins of standard M. bovis and columns 3-5 M. tuberculosis secretory proteins. Protein extraction using Ammonium sulfate and Blue Silver Staining methods

As it is shown from the 25 KDa to less than 66.2KDa Mycobacterium bovis, Mycobacterium tuberculosis strains clearly had different bands. For example, from the 45 to 50 kDa protein bands of M. bovis are differing from M. tuberculosis. Between band 10 to 66.2 KDa only 1 or 2 bands are seen with mycobacterium tuberculosis, while 7 different protein bands are seen with Mycobacterium bovis. Results of gel electrophoresis, SDS-PAGE on 10% (Figure 1), with Blue Silver staining for membrane proteins of M. bovis and M. tuberculosis were not same and shows identical and distinct differences in the band 14 to 25 kDa. Mycobacterium tuberculosis has some bands which are not seen in Mycobacterium bovis (protein band of 15KDa). Furthermore in region 25 to 35 KDa Mycobacterium tuberculosis had 32 to 34 KDA which cannot be seen in Mycobacterium bovis.30 kDa protein was seen in M. bovis and was not seen Mycobacterium tuberculosis. Mycobacterium tuberculosis has a 45 kDa protein that is expressed in a very clear and distinct and was not seen in M. bovis. The 50-48 kDa protein band seen M. bovis and band of around 60, 70 and above 116 kDa in Mycobacterium tuberculosis gel electrophoresis of proteins secreted by 12% and Blue Silver staining (G250) differences in protein expression between the two strains of Mycobacterium bovis strains seen. These differences in the protein bands in the area 13, 23, 32, 44, 115 kDa are seen in mycobacterium tuberculosis and not in M. bovis. On the other hand proteins with molecular weight 18,30,36,85 kDa are seen in Mycobacterium tuberculosis and not in M. bovis (Figure 2). Differences of candidate strains are displayed by arrow in figure 3. Weighted range of 14- 45 bands is the most significant differences of these two strains.

In 15-115 KDa and 18-114 KDa bands were observed in strains of M. bovis and M. tuberculosis.

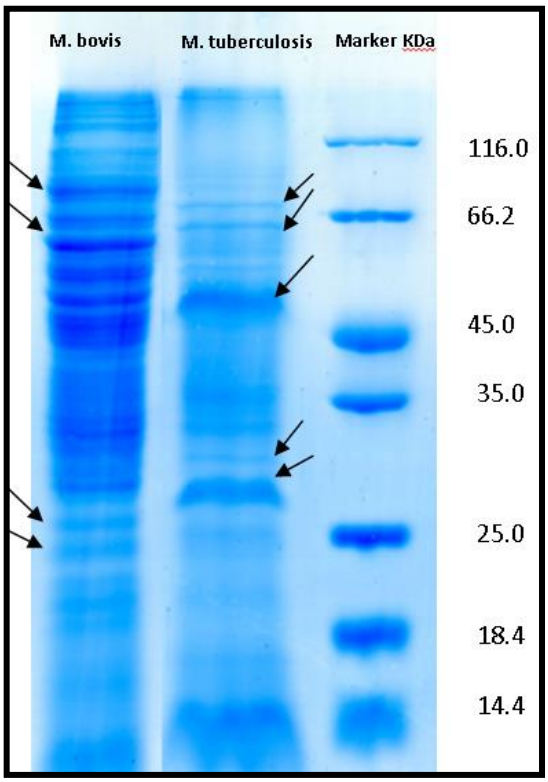


Figure 3: Comparison of protein profiles of Mycobacterium tuberculosis and Mycobacterium bovis by SDS-PAGE, polyacryamide gel 10%,, Blue Silver Staining and Coomasie Blue R-250

Discussion

Considering that M. tuberculosis diagnostic methods including susceptible and resistant to drug susceptible mycobacterium and even M. bovis are based on microbiologic methods such as direct smear, cultivation and PCR methods. But cultivation always is considered as gold standard method. The necessity of rapid treatment and easy diagnosis are inevitable considering the Low susceptibility of some of these methods such as direct view slide or long response time to suspected patients to tuberculosis including cultivation in specific

mycobacterium medium. In this study we tried to compare patterns of membrane and secretory proteins between candidate strains of M. tuberculosis and M. bovis using SDS- PAGE method.

The liquid Middlebrook 7H9 medium was used in the current study and makes bacteria able to synchronize in addition to making possible the study of secretory proteins. Having mineral salts, enrichment materials (such as Albumin), Catalase, dextrose, Sodium Chloride, Glycerol and Polysorbate80 are among its other advantages [14].

In 1998, Cole et al [15] determined the complete genome sequence of M. tuberculosis H37Rv and defined the sequences of 3924 Gene. With the help of these genetic information, proteome analysis was done through combination of two-dimensional electrophorese and mass spectrometry. Almost 800 coding secretory proteins have been recognized by M. tuberculosis genome.

In 2003, Jens Mattow et al [16] analyzed supernatant proteins of mycobacterium tuberculosis cultivation using combination of two-dimensional gel electrophoresis and mass spectrometry and determined the N- terminal sequence. About 1250 protein pieces of M. tuberculosis H37Rv were identified. This study showed 137 different proteins from which 42 proteins were explained as secretory proteins. Comparison of M. tuberculosis H37Rv and weakened M. bovis BCG Ccopenhageh showed 39 specific protein pieces for M. tuberculosis which had 27 different proteins and can be as a candidate of antigens in order to produce new vaccine.

Xing Xiong et al [9] investigated the membrane proteins of M. tuberculosis H37Rv using one-dimensional electrophoresis and mass spectrometry and reported 349 integral fully membrane proteins and 42 membrane proteins was discussed for the first time.

Malen et al [17] compared membrane proteins of M. tuberculosis H37Rv and H37Ra strains and examined the properties of more than 1700 proteins of both strains. Almost all identified proteins were too much similar, although strains were different in 5 or more proteins in 29 membrane or membrane associated proteins. 19 proteins and lipoproteins were the most frequent in H37Rv, while 10 proteins had the most frequency in H37Ra. 66 lipoproteins were the same in both strains, although 7 and 3 lipoproteins were just observed in H37Rv and H37Ra, respectively. Standard strains of ATCC and solid medium (7H10) were used in this study. Singhal et al [18] examined the intra cellular proteins of M. tuberculosis clinical isolates. Susceptible to drug M. tuberculosis (susceptible to at least 5 first-line drugs of ST-11 EA13-IND family) and resistant to drug M. tuberculosis (resistant to isoniazid rifampin and streptomycin from st288-CAS2 family) were selected from pulmonary disease center of JALMA (India). The liquid Sautons medium was used and bacteria were isolated in the late exponential phase (third week). Some protein were upregulate in comparison of 2DE and MS. 4 proteins were common in both groups AND 3 proteins belonged to metabolism and bacterial respiratory chain specifically. Results indicated that most proteins of upregulate / expressed were related to cellular metabolism and bacterial respiratory. Macrophage cell culture (THP-1) and cell infection with mycobacterium are also used. Overall, identified proteins contribute to bacteria compatibility with the environment and understanding the protein action is consistent with macrophage condition. Induction of their expression in in vitro may result in the interpretation of M. tuberculosis strategy in creation of infection and increase of TB cell survival. Accurate identification of the proteins allows us to involve them in structural operation of TB and growth of mycobacterium in the environment [18]. Shi et al [19] investigated the use of zinc in mice food for the cellular and humoral immune response with antigens ESAT-6 and CEP10 of Mycobacterium bovis BCG strains causes a drop in plasma cytokine levels. This has not caused changes in effect of immunization by these antigens at the time of vaccination. When comparing the bands of susceptible M. tuberculosis in the current study with membrane proteins of M. tuberculosis H37Rv in the Xiong [9] study it can be state that clinical sample and standard strain of H37Rv are the same in terms of protein expression. Among main differences of the current study and the Xiong study, protein bands of 45 and 60 KDa can be noted.

It seems that the expression differences of protein bands of the two strains probably can be used as marker protein and even effective biomarker in differentiation of susceptible M. tuberculosis and M. bovis from each other in the case of more comprehensive purification and using a suitable method because differentiation of strains is important in cases that their distinguishing is not completely clear. Treatment of patients with M. bovis and M. tuberculosis is usually similar. Thus, difference of protein profile between these strains result in the early diagnosis and separation and consequently reducing health care costs. Selection of specific proteins able to show the differences of the strains can cause determination of these proteins to be as appropriate diagnostic biomarker. So that observation of differences in protein bands in the current study can be the beginning of different profile selection to determine the suitable candidate protein.

In this study, complementary studies including two-dimensional electrophoresis and mass spectrometry for protein difference in the observed weighted ranges will lead to more efficient purification of these Proteins in the future. Moreover, the protein difference can be useful to identify effective isotopes in immune responses of the host.

Acknowledgment

This research was supported by Tehran University of Medical Sciences and Health Services Grant 22146.

References

1. Global tuberculosis Report. 2015. World health organization, 2015
2. World Health Organization. Global tuberculosis control; surveillance planning, financing. WHO Report. Geneva, Switzerland: WHO; 2014.
3. Majoor CJ, Magis-Escurra C, Van Ingen J, Boeree MJ, Van Soolingen D. Epidemiology of Mycobacterium bovis disease in humans, The Netherlands, 1993–2007. Emerg Infect Dis. 2011;17:457-63.
4. Somoskovi A, Dormandy J, Parsons LM, Kaswa M, SengGoh K, Rastogi N, et al. Sequencing of the pncA gene in members of the Mycobacterium tuberculosis complex has important diagnostic applications: identification of a speciesspecific pncA mutation in “Mycobacterium canettii” and the reliable and rapid predictor of pyrazinamide resistance. JCM. 2007;45:595-99.
5. Barouni AS, Augusto CJ, Lopes MT, Zanini MS, Salas CE. A pnca polymorphism to differentiate between Mycobacterium bovis and Mycobacterium tuberculosis. Mol Cell Probes. 2004;18:167–70.
6. Monteros LE, Galan JC, Gutierrez M, Samper S, Garcia Marin JF, Martin C, et al. Allele- specific PCR method based on pncA and oxyR sequences

for distinguishing Mycobacterium bovis from Mycobacterium tuberculosis: intraspecific M. bovispnca sequence polymorphism. J Clin Microbiol. 1998;36:239–42.
7. Barker LF, Brennan MJ, Rosenstein PK, Sadoff JC. Tuberculosis vaccine research: the impact of immunology. Curr Opin Immunol 2009;21:331-38.
8. Sonnenberg MG, Belisle JT. Definition of Mycobacterium tuberculosis culture filtrate proteins by two-dimensional polyacrylamide gel electrophoresis, N terminal amino acid sequencing, and electrospray mass spectrometry. Infect Immun 1997; 65:4515-24.
9. Xiong Y, Chalmers MJ, Gao FP, Cross TA, Marshall AG. Identification of Mycobacterium tuberculosis H37Rv integral membrane proteins by one-dimensional gel electrophoresis and liquid chromatography electrospray ionization tandem mass spectrometry. J Proteome Res. 2005;4:855-61.
10. Mollenkopf HJ, Grod L, Mattow J, Stein M, Knapp B, Ulmer J, et al. Application of mycobacterial proteomics to vaccine design: improved protection by Mycobacterium bovis BCG prime-Rv3407 DNA boost vaccination against tuberculosis. Infect Immun. 2004;72:6471–79.
11. Kubica G, Kent P. Public health microbiology. A guide for the lever laboratory. Atlanta, Georgia: Public Health Service, Genters for Disease Control; 1985.
12. Farnia P, Mohammadi F, Mirsaedi M, Zia Zarifi A, Tabatabee J, Bahadori M, et al. Bacteriological follow-up of pulmonary tuberculosis treatment: a study with a simple colorimetric assay. Microbes Infect. 2004;6:972-76.
13. Dennison C, ed. A guide to protein isolation. New York: Kluwer Academic Publisher; 2002.
14. Bradford MM. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. Anal Biochem. 1976;72:248–54.
15. Cole ST, Brosch R, Parkhill J, Garnier T, Churcher C, Harris D, et al. Deciphering the biology of Mycobacterium tuberculosis from the complete genome sequence. Nature. 1998 Jun 11;393(6685):537-44.
16. Mattow J, Schable UE, Schmidt F, Hagens K, Siejak F, Brestrich G, et al. Comparative proteome analysis of culture supernatant proteins from virulent Mycobacterium tuberculosis H37Rv and attenuated M. bovis BCG Copenhagen. Electrophoresis. 2003;24:3405–20.
17. Malen H, De Suza GA, PathakSh, Softeland T, Wiker HG. Comparison of membrane proteins of Mycobacterium tuberculosis H37Rv and H37Ra strains. BMC Microbiol. 2011;11:18.
18. Singhal N, Sharma P, Kumar M, Joshi B, Bisht D. Analysis of intracellular expressed proteins of Mycobacterium tuberculosis clinical isolates. Proteome Sci. 2012 Mar 1;10(1):14. DOI: 10.1186/1477-5956-10-14.
19. Shi L, Zhang L, Li C, Hu X, Wang X, Huang Q, Zhou G. Dietary zinc deficiency impairs humoral and cellular immune responses to BCG and ESAT-6/CFP-10 vaccination in offspring and adult rats. Tuberculosis (Edinb). 2016 Mar;97:86-96.

J Surg Med. 2018;2(3):228-232.
DOI: 10.28982/josam.416286

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Troponin I levels before bypass surgery after acute myocardial infarction; When to operate?

Akut miyokardiyal infarktüs sonrası bypass cerrahisinden önce troponin I seviyeleri: Ne zaman opere etmeli?

Mihriban Yalçın [1], Eda Gödekmerdan Katırcıoğlu [1], Serkan Yazman [1], Kaptanıderya Tayfur [1], Melih Ürkmez [1]

[1] Ordu State Hospital, Department of Cardiovascular Surgery, Ordu, Turkey

ORCID ID of the authors
MY: 0000-0003-4767-0880
EGK: 0000-0003-0724-4051
SY: 0000-0002-6035-1123
KT: 0000-0002-4539-1055
MÜ: 0000-0002-5745-5941

Corresponding author / Sorumlu yazar:
Mihriban Yalçın
Address / Adres: Sahincili Mah, Ordu Devlet Hastanesi, 52200, Ordu, Türkiye
E-mail: mihribandemir33@hotmail.com

Ethics Committee Approval: Ethics committee approval was not received because of retrospective design of the study.
Etik Kurul Onayı: Etik kurul onayı çalışmanın retrospektif dizaynından dolayı alınmamıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 17.04.2018
Accepted / Kabul Tarihi: 31.05.2018
Published / Yayın Tarihi: 31.05.2018

Abstract

Aim: Measurement of cardiac troponin I (cTnI) preop coronary artery bypass surgery (CABG) may be a determinant of surgical risk in patients with myocardial infarction (MI). Our aim is to explain the prognostic value of the preoperative serum levels of cardiac troponin I in patients with a recent acute MI under relatively stable clinical conditions.

Methods: This study was a retrospective single-center study in a small state hospital in Turkey. Included were 65 patients that had undergone a first-time isolated CABG between January 2012 and December 2014 due to acute MI. Samples for preoperative cTnI measurements were collected daily prior to the operation. Patients were enrolled in this study if they had nonST or ST elevation MI and had also undergone an early isolated CABG. We evaluated the association between serum levels of cTnI 24 hours before CABG and postoperative in-hospital patient outcomes.

Results: In cases with mortality troponin was high but it was not statistically significant. There was a significant poor positive correlation between admission troponin and intensive care unit (ICU) stay and the duration of discharge. No statically significant correlation was found between troponin levels and other postoperative in- hospital patient outcomes.

Conclusion: Although there was no significant correlation between troponin values and postoperative data troponin was higher than those without mortality. Therefore we suggest that if the vital signs are stable for patients with AMI preparing to undergo CABG, surgery should be delayed until troponin falls to nearly normal values.

Keywords: Acute myocardial infarction, Coronary artery bypass surgery, Troponin I

Öz

Amaç: Kardiyak troponin I'in (cTnI) preop ölçümü miyokard infarktüsü (MI) olan hastalarda cerrahi riskin belirleyicisi olabilir. Amacımız, son zamanlarda akut miyokard infarktüsü geçirmiş olan hastalarda nispeten stabil klinik koşullar altında kardiyak troponin I'in preoperatif serum düzeylerinin prognostik değerini açıklamaktır.

Yöntemler: Bu çalışma küçük bir devlet hastanesinde yapılmış retrospektif bir çalışmadır. Akut MI nedeniyle Ocak 2012 ile Aralık 2014 arasında ilk kez izole KABG geçiren 65 hasta alındı. Ameliyat öncesi cTnI ölçümleri için numuneler operasyondan önce günlük olarak toplandı. Hastalar, ST veya nonST MI geçirmiş ve erken izole KABG geçirmişlerse bu çalışmaya dahil edildi. KABG'den 24 saat önce cTnI serum seviyeleri ile postoperatif hasta sonuçları arasındaki ilişkiyi değerlendirdik.

Bulgular: Mortalite olan olgularda troponin yüksek olmasına rağmen istatistiksel olarak anlamlı değildi. Giriş troponin ve yoğun bakım ünitesinin (YBÜ) kalış süresi ve taburculuk süresi arasında anlamlı derecede zayıf bir korelasyon vardı. Troponin düzeyleri ile diğer postoperatif hastane içi hasta sonuçları arasında istatistiksel olarak anlamlı bir ilişki bulunmadı.

Sonuç: Troponin değerleri ile postoperatif veriler arasında anlamlı bir korelasyon olmamasına rağmen, troponin mortalite olanlarda olmayanlara göre daha yüksekti. Bu nedenle, KABG'ye girmeye hazırlanan AMI hastaları için yaşamsal belirtiler stabil ise, troponinin neredeyse normal değerlere düşmesine kadar ameliyatın ertelenmesi gerektiğini öneriyoruz.

Anahtar kelimeler: Akut miyokard infarktüsü, Koroner arter baypas cerrahisi, Troponin I

How to cite / Atıf için: Yalçın M, Katırcıoğlu EG, Yazman S, Tayfur K, Ürkmez M. Troponin I levels before bypass surgery after acute myocardial infarction; When to operate? J Surg Med. 2018;2(3):228-232.

Introduction

Cardiac troponins (I and T) are highly sensitive and serologic biomarkers specific to myocardial tissue that are used for the definition of acute myocardial infarction (AMI). They improve the detection criteria for AMI [1]. Myocardial infarction is now defined as a troponin concentration above the 99th percentile of a healthy reference population in the setting of myocardial ischemia [2]. Because troponins are truly cardio-specific, they are the gold standard for biochemical testing for myocardial cell injury. Cardiac troponin I (cTnI, molecular mass 22 500 Da) is a regulatory protein unique to heart muscle. cTnJ is the only TnI isotype located in the myocardium and an inhibitor of the troponin-tropomyosin regulatory complex that confers calcium sensitivity to actomyosin [3]. Cardiac troponin T may cross-react with troponin found in other muscles, producing false positive or increased results when there is no myocardial damage [4]. Because cTnI is not found in skeletal muscle, cTnI is highly sensitive and specific for myocardial necrosis [5]. cTnI estimates infarct size after reperfusion. It is a specific marker of cardiac damage during coronary artery bypass surgery [6]. In addition, cTnI has no cross-reactivity with skeletal muscle isoforms and does not increase in healthy people, even under excessive muscular activity or as the result of non-cardiac operations.

After CABG, risk factors for death or cardiac events have been described. To predict postoperative outcomes, several models have developed [7]. Cardiac troponins have been routinely measured as part of preoperative preparation at hospitals for several years.

The primary aim of the present study was to verify the influence of preoperative cTnI values on the incidence of major postoperative complications and mortality of patients who had experienced an AMI within the previous two weeks before undergoing CABG in stable clinical conditions.

Materials and methods

The study population consisted of 71 consecutive patients who had been admitted via the emergency department of Ordu State Hospital with an AMI. From January 2012 to December 2014, the 65 patients, 14 females and 51 males, underwent elective, isolated, first-time CABG operations with cardiopulmonary bypass. The angiogram for patients with AMI revealed more severe coronary artery disease requiring CABG. But these patients did not require an immediate operation. Samples for preoperative cTnI measurements were collected daily prior to the operation. We evaluated the association between serum levels of cTnI at admission and 24 hours before CABG and postoperative in-hospital patient outcomes. Low cardiac output syndrome, IABP necessity and mechanical ventilation lasting longer than 72 hours, acute renal failure, and in-hospital death are considered major postoperative complications

If any of the following preoperative criteria were present, patients were excluded from the study: (1) reoperations, (2) any concomitant heart surgery besides CABG, or (3) any concomitant AMI mechanical complications. Among the 71 patients, 6 excluded because of these criteria. A cTnI value above 0.3 ng/mL was considered abnormal (Reference range 0.00-0.30 ng/mL). In all patients, standard anesthetic and monitoring techniques were used. Internal thoracic artery and saphenous vein grafts were used as graft conduits. A standard cardiopulmonary bypass was achieved by ascending aortic and two-stage venous cannulation. Myocardial protection was achieved by using antegrade crystalloid cardioplegic arrest and additional topical cooling.

Postoperatively, patients were admitted to the intensive care unit (ICU). Postoperative management of patients was standardized. If patients were hemodynamically stable, they were discharged from the ICU to the general cardiothoracic ward, usually on the second postoperative day. Patients were generally discharged from the hospital on postoperative day 7–10. The patients were followed during hospitalization for incidence of death and postoperative complications. The median time from arrival to CABG for AMI patients was approximately 170 hours (about seven days).

Statistical analysis

The data obtained in this study were analyzed using SPSS (Statistical Package for the Social Sciences) program 22.0 for Windows. In the evaluation of the data for descriptive statistical methods, number, percentage, mean, and standard deviation were used. A t-test was used to compare continuous quantitative data between two independent groups. A one-way analysis of variance (ANOVA) test was used to compare continuous quantitative data between more than two independent groups. After the ANOVA test, the Scheffe test was used to determine differences as a complementary post-hoc analysis. A correlation between continuous variables in this study was performed. The findings are evaluated to be in the 95% confidence interval and at the 5% significance level.

Results

Of the 51 (78.5%) male and 14 (21.5%) female patients, 44 (67.7%) were nonST MI, 11 (16.9%) had anterior MI, and 10 (15.4 %) had inferior MI. Preoperative characteristics of the patients are seen on table 1.

CABGX2 was performed for 13 (20.0%) patients; CABGX3 for 30 (46.2%) patients; CABGX4 for 18 (27.7%) patients; and CABGX5 for 4 (6.2%) patients. Mortality was 9.4% (6 patients). Four patients (6.2%) had wound infections 6 (9.4 %) had ARF; 2 (3.1%) had lasting mechanical ventilation; 4 (6.2%), bleeding revision; and 1 (1.6%) LCOS. IABP was used in 8 (12.3%) patients.

Figure 1 shows with Roc analysis to maintain a cut-off value. Shown are 58 positive values, six negative values and one missing value. The area under the ROC curve was not statistically significant ($p > 0.05$). Because the ROC curve was not meaningful, a cut-off value could not be obtained. Figure 2 shows ROC analysis for troponin at admission.

Table 2 shows the mean values of troponin at admission and 24 hours before operation. According to the ANOVA test, the mean of troponin at admission, values were statistically significant ($F=154.906$; $p=0<0.05$) as expected. A complementary post-hoc analysis was conducted to determine the sources of the differences. The first troponin values of patients with anterior MI (17.869 ± 5.747) were higher than of

those with NonST MI (2.493 ± 1.156) and the first troponin values of inferior MI (9.470 ± 2.458) were higher than the first troponin values (2.993 ± 1.156) of NonST MI. After all, the mean of troponin values 24 hours before operation was not statistically significant (p>0.05) compared to the average of the groups.

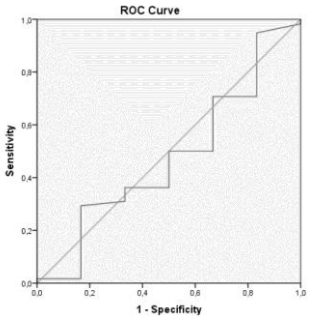


Figure 1: Roc analysis for troponin

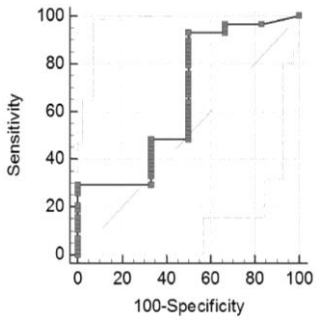


Figure 2: Roc analysis for troponin at admission

Table 1: Descriptive parameters

Parameters	Groups	n	%
Gender	Male	51	78.5
	Female	14	21.5
	Total	65	100.0
Myocardial Infarction	Nonst MI	44	67.7
	Anterior MI	11	16.9
	İnferior MI	10	15.4
	Total	65	100.0
Cardiovascular risk Factors	DM	40	61.5
	HT	55	84.6
	HL	52	80.0
	Family History	52	80.0
	Obesity	40	61.5
Comorbidity	Stroke	5	7.7
	COPD	22	33.8
	PAD	10	15.4
Operations	CABGx2	13	20.0
	CABGx3	30	46.2
	CABGx4	18	27.7
	CABGx5	4	6.2
	Total	65	100.0
Mortality	No	58	90.6
	Yes	6	9.4
	Total	64	100.0
Complications	None	47	73.4
	Wound Infection	4	6.2
	ARI	6	9.4
	ARDS	2	3.1
	Revision for bleeding	4	6.2
	LCOS	1	1.6
	Total	64	100.0
IABP	No used	57	87.7
	Used	8	12.3
	Total	65	100.0

ARDS: acte respiratory distress syndrome, ARI: acute renal insufficiency, CABG:coronary artery bypass greft, COPD: chronic obstructive pulmonary disease, DM: diyabetes mellitus, HL: hyperlipidemia, HT: hypertension, IABP: intra aortic balloon pump, LCOS: low cardiac output syndrome, PAD: peripheral arterial disease

Table 2: The mean value of troponin according to myocardial infarction

	Group	n	Mean	Sd	F	p	Diff.
Troponin at admission	NonST MI	44	2.993	1.156	154.906	0.000	2 > 1 3 > 1
	Anterior MI	11	17.869	5.747			
	Inferior MI	10	9.470	2.458			
	Group	N	Mean	Sd	F	p	
Troponin 24 hours before operation	NonST MI	44	2.570	10.492	0.304	0.739	
	Anterior MI	11	4.473	4.198			
	Inferior MI	10	1.541	2.286			

MI: myocardial infarction, Diff: Difference

There was no statistically significant difference between the number of bypasses and troponin at admission according to the ANOVA test. (F=1.506; p=0.222; >0.05). IABP was used in 8 patients. There was no statistically significant (p=0.188 for troponin at admission and p=0.894 for troponin 24 hours before) difference for values of troponin in the use of IABP.

Table 3 shows that the result of the t-test to determine whether there was a difference between the mortality and the mean values of troponin variable was not statistically significant (p>0.05). In cases with mortality troponin was high but it was not statistically significant. Table 4 shows, as expected, there was a significant poor positive correlation (r=0.317; p=0.011; <0.05) between ICU stay and discharge time period. There was a significant poor positive correlation between admission troponin and ICU stay (r=0.249; p=0.045; <0.05) and the duration of discharge (r = 0.312; p=0.012; <0.05). The relationship between other variables is not statistically significant (p> 0.05).

Table 3: The mean value of troponin according to the mortality

	Mortality	N	Mean	Sd	t	p
Troponin at admission	yes	6	11.467	10,650	-2.146	0.243
	no	58	5.671	5,763		
	Mortality	N	Mean	Sd	t	p
Troponin 24 hours before operation	yes	6	3.077	5.870	0.091	0.928
	no	58	2.726	9.205		

Table 4: The relationship between troponin and other parameters

		Age	ICU stay	Discharge from hospital	Troponin at admission	Troponin 24 hours before operation
Age	r	1.000				
	p	0.000				
ICU stay	r	0.189	1.000			
	p	0.131	0.000			
Discharge from hospital	r	-0.170	0.317*	1.000		
	p	0.180	0.011	0.000		
Troponin at admission	r	-0.016	0.249*	0.312*	1.000	
	p	0.900	0.045	0.012	0.000	
Troponin 24 hours before operation	r	0.066	-0.022	-0.068	0.049	1.000
	p	0.602	0.862	0.594	0.697	0.000

ICU: intensive care unit

Discussion

Nowadays coronary angiography is conducted for an increasing number of patients following a recent AMI. The number of patients referred for CABG after a failed angioplasty or due to left main/multi-vessel disease is increasing. Surgeons therefore now face the difficult decision of the optimal timing of CABG operations for clinically stable patients that have had a recent AMI. Even with improvements in myocardial protection and anesthetic management, however, patients with a recent AMI still have a high mortality rate after CABG operations. A retrospective examination shows that CABG operations should be postponed whenever possible for at least three days after the onset of the AMI [8]. In our study, the median time from arrival to CABG for AMI patients was approximately 170 hours (about seven days). Risk of mortality and postoperative complications may be detectable with the extent of myocardial necrosis, so measuring troponin I before the operation is one noninvasive technique for predicting prognosis after CABG.

Pre-op TnI levels may be useful to guide ICU management of CABG patients after AMI. Troponin

measurement can help identify a high-risk patients suited for additional therapeutic and mechanical interventions (e.g., intra-aortic balloon pump) prior to CABG surgery. In patients with acute coronary syndromes (ACSs), cardiac troponins were revealed as valuable biomarkers for the prognoses. In addition, for PCI, elevated cardiac troponins are related to an increased risk of mortality [9].

Cardiac troponins were also studied in several non-cardiac [10] and cardiac [11,12] surgeries. Most of these studies showed a relationship between postoperative troponin elevations and short- or long-term outcomes. After noncardiac surgery, preoperative cTnT concentrations were significantly associated with postoperative MI and long-term mortality [13].

Carrier et al. reported that patients undergoing elective CABG with preoperative positive >0.02 ng/L serum levels of cTnI were more likely to experience postoperative complications and postoperative MI [14]. Thielman et al. [15] reported that higher rates of mortality and higher incidence of major adverse cardiac events depend on preoperative cTnI serum elevation. Montgomery et al. [16] reported increased mortality rates after open-heart surgery in infants with higher preoperative cTnI concentrations. An increased risk of short-term mortality and morbidity after major vascular surgery is associated with elevated cTnI levels [17]. Patients with postoperative cTnI levels greater than 1.5 ng/mL have six times the mortality risk of patients with levels below 1.5 ng/mL.

Several studies also have reported that increased troponin release after cardiac surgery is associated with mortality and adverse outcomes [18,19]. This relationship between elevated cTnI and adverse outcomes may be explained by more severe and unstable coronary artery stenosis. In our study, pre-operative cTnI values were not significantly associated with a higher incidence of low cardiac output syndrome, intra-aortic balloon pump necessity, mechanical ventilation >72 hours, acute renal failure, or in-hospital mortality. Several studies have reported that CABG performed soon after an AMI carries a higher risk of postoperative mortality and morbidity than an operation performed at a later date [20]. A retrospective multicenter analysis of 44,365 patients who underwent CABG after a transmural or nontransmural AMI revealed that in-hospital mortality decreased in all patients that had increased the waiting time between their AMI and surgery. They reported similar postoperative outcomes in patients with both transmural and non-transmural but when CABG was performed within seven days following an AMI, the mortality rate was higher in patients that had had a transmural AMI [21].

Weiss and colleagues [20] broadcasted the results of 40,159 patients hospitalized for AMI who underwent subsequent CABG. Patients were stratified by the timing of CABG into "early" (<2 days from AMI) and "late" (>3 days from AMI) groups. Mortality rates were higher in the early-group patients therefore indicating that CABG ought to be postponed in nonurgent patients for at least three days after an AMI.

Braxton et al. [22] evaluated the timing of CABG after non-Q wave myocardial infarction (MI) and reported that perioperative MI was greater in the non-Q wave MI group when surgery was performed less than 48 hours from admission. Parikh et al. [23] reported that late CABG patients received more red blood cell transfusions and had longer hospital stays. We also found a significant poor positive correlation between admission troponin and ICU stay and the duration of discharge. Paparella et al. [24] reported that those patients with cTnI >0.15 ng/ml at the time of surgery had more complications and worse survival rates than patients with cTnI <0.15 ng/ml.

In the ACTION Registry–GWTG, they reported no difference in ischemic outcomes, including death between patients with NonST MI undergoing CABG early (≤48 hours) vs late (>48 hours). On the other hand, delaying surgery in patients with NonST MI might increase resource use and increase the risk of recurrent ischemia/MI in those waiting for surgical revascularization [21].

Preoperative cardiac troponin levels are more accurate than days for the evaluation of surgery timing. In our study, we performed CABG when troponin levels decreased if a patient's vital signs were stable. This generally took one week. In cases with mortality troponin was not statistically significant, although it was high.

As we described above, if clinical conditions or coronary anatomy of a patient with elevated cTnI values require CABG operation, then surgeons ought to be aware that these patients may be under a higher risk of perioperative myocardial damage and, a higher risk of postoperative adverse events

In contrast to the literature, in our study we could not find any statistically significant relationship between troponin and mortality and postoperative complications. First of all, it can be because of the small numbers of our patient group. And in our clinic, we wait until the troponin decreases if the patient situation is stable.

Therefore, in this study there were no really high values of troponin. There was no statistically significant difference between the number of bypasses and troponin at admission. We only found that there is a significant poor positive correlation between admission troponin and ICU stay and the duration of discharge.

The main limitations of our study were its retrospective design and small numbers of patient group. Therefore, the generalizability of our findings may not extend to all of the clinical centers performing CABG surgery. For clinical decision-making, relative cut-off level and the usefulness of troponin need to be established by large-scale prospective studies.

Finally, patients in our clinic were followed up until troponin levels decreased as low as possible and then operated. There was no correlation between mortality and postoperative complications with troponins. Although there was no significant correlation, troponin elevation was present in those with mortality Therefore, we believe that these results are due to the fact that normalization of cTnI values before CABG operations seems the way for best postoperative results.

Acknowledgement

We acknowledge the medical writing assistance provided by American manuscript editors (www.americanmanuscripteditors.com) for the final draft of the manuscript.

References

1. Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined -a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol. 2000;36:959-69.
2. The Joint European Society of Cardiology/American College of Cardiology Committee. Myocardial infarction redefined—a consensus document of the Joint European Society of Cardiology/ American College of Cardiology Committee for the redefinition ofmyocardial infarction. Eur Heart J 2000;21:1502–13.
3. Adam JE, Bodor GS, Davila-Roman VG, Delmez JA, Apple FS, Ladenson JH, et al. Cardiac troponin I: a marker with big specificity for cardiac injury. Circulation. 1993;88:101-6.
4. Nesher N, Alghamdi AA, Singh SK, Sever JY, Christakis GT, Goldman BS, et al. Troponin after cardiac surgery: apredictor or a phenomenon? Ann Thorac Surg. 2008;85:1348–54.
5. Wu AH, Apple FS, Gibler WB, Jesse RL, Warshaw MM, Valdes R Jr. National Academy of Clinical Biochemistry Standards of Laboratory Practice: recommendations for the use of cardiac markers in coronary artery diseases. Clin Chem. 1999;45:1104 –21.
6. Caputo M, Dihmis W, Birdi I, Reeves B, Suleiman MS, Angelini GD, et al. Cardiac Troponin T and Troponin I release duringcoronary artery surgery using cold crystalloid and cold blood cardio-plegia. Eur J Cardio-thorac Surg. 1997;12:254-60.
7. Tu JV, Jaglal SB, Naylor CD. Multicenter validation of a riskindex for mortality, intensive care unit stay, and overall hospital length of stay after cardiac surgery. Circulation. 1995;91:677-84.
8. Paparella D, Scrascia G, Paramythiotis A, Guida P, Magari V, Malvindi PG, et al. Preoperative Cardiac Troponin I to Assess Midterm Risks of Coronary Bypass Grafting Operations in Patients With Recent Myocardial Infarction. Ann Thorac Surg. 2010;89:696–703.
9. Giannitsis E, Muller-Bardorff M, Lehrke S, Wiegand U, Tölg R, Weidtmann B, et al. Admission troponin T level predicts clinical outcomes, TIMI flow, and myocardial tissue perfusion after primary percutaneous intervention for acute ST-segment elevation myocardial infarction. Circulation. 2001; 104:630–35.
10. Landesberg G, Shatz V, Akopnik I, Wolf YG, Mayer M, Berlatzky Y, et al. Association of cardiac troponin, CK-MB and postoperative myocardial ischemia with long-term survival after major vascular surgery. J Am Coll Cardiol. 2003;42:1547–54.
11. Lehrke S, Steen H, Sievers HH, Peters H, Opitz A, Müller-Bardorff M, et al. Cardiac troponin T for prediction of short- and long-term morbidity and mortality after elective openheart surgery. Clin Chem. 2004;50:1560–7.
12. Thielmann M, Massoudy P, Marggraf G, Knipp S, Schmermund A, Piotrowski J, et al.Role of troponin I, myoglobin, and creatine kinase for the detection of early graft failure following coronary artery bypass grafting. Eur J Cardio-Thorac Surg. 2004;26:102–9.
13. Nagele P, Brown F, Gage BF, Gibson DW, Miller JP, Jaffe AS, et al. High-sensitivity cardiac troponin T in prediction and diagnosis of myocardial infarction and long-term mortality after noncardiac surgery. Am Heart J. 2013;166(2):325-32.
14. Carrier M, Pelletier LC, Martineau R, Pellerin M, Solymoss BC. In elective coronary artery bypass grafting, preoperative troponin T level predicts the risk of myocardial infarction. J Thorac Cardiovasc Surg. 1998;115:1328–34.
15. Thielmann M, Massoudy P ,NeuhauserM, Knipp S, Kamler M, Piotrowski J, et al. Prognostic Value of Preoperative Cardiac Troponin I in Patients With Non–ST-Segment Elevation Acute Coronary Syndromes Undergoing Coronary Artery Bypass Surgery. Chest. 2005; 128:3526-36.
16. Montgomery VL, Sullivan JE, Buchino JJ. Prognostic value of pre-and postoperative cardiac troponin I measurement in childrenhaving cardiac surgery. Pediatr Dev Pathol. 2000;3:53– 60.
17. Kim LJ, Martinez EA, Faraday N, Dorman T, Fleisher LA, Perler BA, et al. Cardiac Troponin I Predicts Short-Term Mortality in Vascular Surgery Patients. Circulation. 2002; 106(18):2366-71.
18. Onorati F, De Feo M, Mastroroberto P, Cristodoro L, Pezzo F, Renzulli A, et al. Determinants and prognosis of myocardial damage after coronary artery bypass grafting. Ann Thorac Surg. 2005;79:837–45.
19. Adabag AS, Rector T, Mithani S, Harmala J, Ward HB, Kelly RF, et al. Prognostic significance of elevated cardiac troponin I after heart surgery. Ann Thorac Surg. 2007;83:1744–50.
20. Weiss ES, Chang DD, Joyce DL, Nwakanma LU, Yuh DD.. Optimal timing of coronary artery bypass after acute myocardial infarction: a review of California discharge data. J Thorac Cardiovasc Surg. 2008;135:503–11.
21. Lee DC, Oz MC, Weinberg AD, Lin SX, Ting W. Optimal timing of revascularization: transmural versus nontransmural acute myocardial infarction. Ann Thorac Surg. 2001;71:198–204.
22. Braxton JH, Hammond GL, Letsou GV, Braxton JH, Hammond GL, Letsou GV, et al. Optimal timing of coronary artery bypass graft surgery after acutemyocardial infarction. Circulation. 1995;92:66–8.
23. Parikh SV, de Lemos JA, Jessen ME, Brilakis ES, Ohman EM, Chen AY, et al. Timing of in-hospitalcoronary artery bypass graft surgery for non- ST segment elevation myocardial infarction patients: Results From theNational Cardiovascular Data Registry ACTION Registry–GWTG (Acute CoronaryTreatment and Intervention Outcomes Network Registry–Get With The Guidelines). JACC Cardiovasc Interv. 2010;3:419–27.
24. Paparella D, Scrascia G, Paramythiotis A, Guida P, Magari V, Malvindi PG, et al. Preoperative cardiac troponin I to assess midterm risks of coronary bypass grafting operations in patients with recent myocardial infarction. Ann Thorac Surg. 2010;89:696–702.

J Surg Med. 2018;2(3):233-235.
DOI: 10.28982/josam.418229

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

The demographic and clinical characteristics of patients with cerebral palsy: A retrospective, single center, observational study

Serebral palsi'li hastalarda demografik ve klinik özellikler: Retrospektif tek merkezli gözlemsel çalışma

Yılmaz İnanç [1], Tuba Tülay Koca [2]

[1] Kahramanmaraş Sütçüimam University, School of Medicine, Department of Neurology, Turkey.
[2] Kahramanmaraş Sütçüimam University, School of Medicine, Department of Physical Therapy and Rehabilitation, Turkey

ORCID ID of the authors:
Yİ: 0000-0002-0423-0941
TTK: 0000-0002-4596-858X

Corresponding author / Sorumlu yazar:
Yılmaz İnanç
Address / Adres: Kahramanmaraş Sütçüimam Üniversitesi, Nöroloji Bölümü, Kahramanmaraş, Türkiye
E-mail: drinancc@gmail.com

Ethics Committee Approval: Ethics committee approval was received from local ethical committee.
Etik Kurul Onayı: Etik kurul onayı local etik kuruldan alınmıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 24.04.2018
Accepted / Kabul Tarihi: 04.06.2018
Published / Yayın Tarihi: 05.06.2018

Abstract

Aim: Cerebral palsy (CP) is a disorder of movement, muscle tone or posture that is caused by damage that occurs to the immature, developing brain, most often before birth.

A good definition of the disease will help for early diagnosis and treatment. The aim of this study was to evaluate the sociodemographic, clinical and radiologic characteristics of patients who were followed up as CP diagnosis.

Methods: Our study was designed as a retrospective, cross-sectional and descriptive. Forty-six patients with CP were included in the study. The age, sex, type of CP, accompanying clinical findings, presence of mental retardation, and cranial magnetic resonance imaging (MRI) data were recorded in the patient files.

Results: The types of CP were determined as spastic hemiparesis in 12 (26.1%) patients, spastic paraparesis in 9 (19.6%), spastic tetraparesis in 17 (37.0%, most frequently)), ataxic in 3 (6.5%), hypotonic in 1 (2.2%), extrapyramidal in 2 (4.4%) and mixed type in 2 (4.4%). In the MRI findings, arachnoid cyst was observed in 4 (11.4%) patients, basal ganglion intensity in 8 (20.2%), encephalomalacia in 8 (20.2%), frontogliotic area in 30 (80.7%, mostly frequently), cortical atrophy in 6 (17.1%), megacisterna in 5 (14.3%), and centrum semiovale hyperintensity in 8 (20.2%). Findings of hypoxic ischemic brain injury were determined in 32 (91.4%) patients.

Conclusion: As CP is a group of diseases for which diagnosis may be difficult but early diagnosis can be beneficial, children at high-risk from birth must be closely monitored, the families must be warned, and if necessary early neuro-imaging tests should be requested. In the long-term follow-up process, in respect of both rehabilitation and the follow-up of comorbidities such as epilepsy, the treatment and follow-up of patients must be applied by a multidisciplinary team to be able to reach maximum physical capacity.

Keywords: Cerebral palsy, Clinical characteristics, Magnetic resonance imaging

Öz

Amaç: Serebral palsi (CP) genellikle doğumdan önce, olgunlaşmamış, gelişmekte olan beyinde meydana gelen hasarın neden olduğu bir hareket, kas tonusu veya postür bozukluğudur. Hastalığın iyi bir tanımlanması erken teşhis ve tedavi için yardımcı olacaktır. Burada CP tanısı ile takipli hastaların sosyodemografik, klinik ve radyolojik özelliklerinin değerlendirilmesini amaçladık.

Yöntemler: Çalışmamız retrospektif, kesitsel, tanımlayıcı olarak dizayn edildi. CP tanılı 46 hasta çalışmaya dahil edildi. Hasta dosyalarındaki yaş, cinsiyet, CP türü, eşlik eden klinik bulgular, mental retardasyon varlığı ve kraniyal magnetik rezonans görüntüleme (MRI) bulguları kayıt edildi.

Bulgular: CP tiplerinden 12 hasta (%26.1) spastik hemiparezik, 9 hasta (%19,6) spastik paraparezik, 17 hasta (%37.0, en sık) spastik tetraparezik, 3 hasta (%6,5) ataksik, 1 hasta (%2,2) hipotonik, 2 hasta (%4,4) ekstrapiramidal, 2 hasta (%4,4) mikst tipte idi. MRI bulgularından araknoid kist 4 hastada (%11.4), bazal ganglion intensitesi 8 hastada (%20,2), ensefalomalazik alan 8 hastada (%20,2), frontogliotik alan 30 hastada (%80,7, en sık), kortikal atrofi 6 hastada (%17,1), megasisterna 5 hastada (%14.3), sentrum semiovale hiperintensitesi 8 hastada (%20,2), ensefalomalazi 8 hastada (%20,2) gözlendi. Hipoksik iskemik beyin hasarı bulguları hastaların 32 (%91.4)'ünde saptandı.

Sonuç: CP tanısı güç koyulabilen fakat erken tanı konulması durumunda daha faydalı olunabilen bir grup hastalık olduğundan özellikle riskli doğan çocuklar yakın takip edilmeli, aileleri uyarılmalı, gerekli görülürse erken dönemde nörogörüntüleme tetkikleri istenmelidir. İleri dönem takip sürecinde hem epilepsi gibi eşlik eden durumların takibi hem de rehabilitasyon açısından hastanın maksimum fiziksel kapasitesine ulaşması için multidisipliner bir ekip tarafından tedavi ve takibinin yapılması gerekmektedir.

Anahtar kelimeler: Serebral palsi, Klinik karakteristikler, Manyetik rezonans görüntüleme

How to cite / Atıf için: İnanç Y, Koca TT. The demographic and clinical characteristics of patients with cerebral palsy: A retrospective, single center, observational study. J Surg Med. 2018;2(3):233-235.

Introduction

The syndrome of Cerebral Palsy (CP) encompasses a large group of childhood movement and posture disorders. It is defined as static encephalopathy which is formed in either the prenatal, perinatal or postnatal period. Severity, patterns of motor involvement, and associated impairments such as those of communication, intellectual ability, and epilepsy vary widely [1].

Incidence has been reported as 1.5-2.5/1,000 live births. In a multi-center, cross-sectional study conducted in Turkey in 1996, 50,000 children in the 0-16 year age group were examined in respect of chronic diseases in childhood and CP prevalence was found to be 0.2%. Several factors are implicated in cerebral palsy etiology. Risk factors include prenatal maternal infection, trauma, brain lesions, asphyxia and trauma at birth, premature birth and very low birth weight. In the etiology of cerebral palsy, prenatal risk factors are 70-80%, postnatal and postnatal risk factors are 20%. The most important risk factors are prematurity and low birth weight. There may be inadequate cognitive functions, epilepsy, emotional problems or musculoskeletal system problems that develop secondary to hearing and sight problems [1-3].

The clinical manifestations of CP vary greatly in the type of movement disorder, the degree of functional ability and limitation and the affected parts of the body. There is currently no cure, but progress is being made in both the prevention and the amelioration of the brain injury. Although the disorder affects individuals throughout their lifetime, most cerebral palsy research efforts and management strategies currently focus on the needs of children [4,5].

The aim of this study was to evaluate the sociodemographic, clinical and radiologic characteristics of CP patients in our center.

Materials and methods

Our study was designed as a retrospective, cross-sectional and descriptive. Forty-six (N=46) patients with CP were included in the study. The age, sex, type of CP, accompanying clinical findings, presence of mental retardation, and cranial magnetic resonance imaging (MRI) data were recorded in the patient files. The age, gender, CP type, concomitant clinical findings (epilepsy, hearing and sight impairments, joint deformities), the presence of mental retardation and MRI findings (conventional T1, T2 sequences) were recorded from the patient data.

Statistical Analysis

SPSS 17 (SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc, USA) was used for statistical analysis. The normal distribution of the data was evaluated using Kolmogorov–Smirnov test. Some descriptive tests were used for the descriptive data. For each parameter, a comparison was done between the two groups. The t test was used for the groups that showed normal distribution. The Mann–Whitney U test was used for the groups that did not show normal distribution. A P value <0.05 was considered statistically significant. The study has been done in accordance with the prıncıples of Helsınkı declaratıon. Approval for the study was granted by the local ethics committee.

Results

The study included 46 patients, comprising 33 (71.7%) males and 13 (28.3%) females with a mean age of 22.5 ± 8.1 years. The types of CP were determined as spastic hemiparesis in 12 (26.1%, patients, spastic paraparesis in 9 (19.6%), spastic tetraparesis in 17 (37.0%, most frequently)), ataxic in 3 (6.5%), hypotonic in 1 (2.2%), extrapyramidal in 2 (4.4%) and mixed type in 2 (4.4%). Epilepsy was determined in 10 (23.9%) patients, sight impairments in 5 (10.9%), hearing impairment in 1 (2.2%), and joint deformities in 17 (37.4%, most frequently). In 16 (34.7%) patients, mental retardation was determined (Table 1). MRI findings were available for 35 (76%) patients. In the MRI findings, arachnoid cyst was observed in 4 (11.4%) patients, basal ganglion intensity in 8 (20.2%), encephalomalacia in 8 (20.2%), frontogliotic area in 30 (80.7%, most frequently), cortical atrophy in 6 (17.1%), megacisterna in 5 (14.3%), and centrum semiovale hyperintensity in 8 (20.2%). Findings of hypoxic ischemic brain injury were determined in 32 (91.4%) patients (Table 2).

Table 1: Distribution of clinical types of patients and associated comorbid pathologies

Patients	Total n=46 (%)
Age (yrs)	22.5
Clinical types of patients	
Spastic hemiparesis	12 (26.1%)
Spastic paraparesis	9 (19.6%)
Spastic tetraparesis	17 (37.0%)
Ataxic	3 (6.5%)
Hypotonic	1 (2.2%)
Extrapyramidal	2 (4.4%)
Mixed	2 (4.4%)
Comorbidities	
Epilepsy	10 (23.9)
Defect of vision	5 (10.9)
Hearing impairment	1 (2.2)
Joint deformities	17 (37.4)
Mental retardation	16 (34.7)

Table 2: Magnetic resonance imaging findings

Patients	Total n=35 (%)
Arachnoid cyst	4 (11.4)
Basal ganglion intensities	8 (20.2)
Encephalomalacic area	8 (20.2)
Frontogliotic area	30 (80.7)
Cortical atrophy	6 (17.1)
Megasisterna magna	5 (14.3)
Sentrum semiovale hyperintensity	8 (20.2)
Encephalomalacia	8 (20.2)

Discussion

Patients with CP at our center were mostly males at 20 years of age. The most common type was spastic tetraparesis type. The most common joint problems were accompanied. Epilepsy was observed in one quadrant of the cases. We have seen the most commonly frontogliotic region on MRI. A third of the cases were mental retarded. Almost all have hypoxic ischemic brain lesions.

Cerebral palsy (CP) develops secondary to lesions in the immature brain and is a non-progressive disease including tonus of varying severity and impairments in posture and movements. Brain development continues until the age of 6-8 years.

Therefore, the clinical table and all kinds of cerebral damage occurring in the first 6-8 years of life that do not show progression are accepted as CP. However, the American Academy for Cerebral Palsy and Developmental Medicine has reported that injury occurring in the central nervous system up to the age of 5 years is valid in the diagnosis of CP [4]. This is one of the reasons for significant morbidity and mortality in short and long-term results. Hypoxic ischemic injury in CP occurs at a high rate in the prenatal period and especially in the third trimester, and perinatal events are responsible at a lower rate [5,6]. In most epidemiological studies, CP has been reported more in males than females [7]. In the current study, 71.7% of the patients were male. The determination of the clinical situation in CP, which is basically a motor disorder, can be made according to the location of the lesion in the brain, changes in tonus, the type of movement impairments and the number of extremities affected [8,9]. Sigurdardottir et al. [8] reported spastic type CP in 87% of patients. Consistent with these findings in literature, spastic type CP was determined at 82% in the current study and the vast majority of these (37%) had tetraparetic involvement.

Although the basic clinical table in children with CP is formed of movement and posture impairments, mental retardation, seizures, ophthalmological problems (e.g., homogeneous hemianopsy, strabismus), asterognosis, proprioception impairments and hearing defects may also be present currently [10]. These accompanying situations cause a significant decrease in the quality of life of patients and can be a significant obstacle to acquiring psychomotor skills. Management strategies include enhancing neurological function during early development; managing medical co-morbidities, weakness and hypertonia; using rehabilitation technologies to enhance motor function; and preventing secondary musculoskeletal problems. Meeting the needs of people with CP in resource-poor settings is particularly challenging [4,5].

In the current study, visual impairment was determined in 10.9% of the patients, hearing impairment in 2.2% and joint deformities in 37.4%. Epileptic seizures may be seen at rates of up to 50% according to the clinical sub-group. These are more frequent in hemiplegic and tetraplegic types in particular [11-14]. Epilepsy was present in 23.9% of the current study patients. Mental status changes ranging from mild to severe are observed at 35%-57%, depending on the area of brain involvement, with a greater likelihood in severe tetraplegic cases. Mental retardation was determined in 34.7% of patients in the current study [15].

Magnetic resonance imaging (MRI) must be a part of the routine clinical and laboratory evaluations of CP patients, and is an important diagnostic method in the determination of pathological changes in cerebral tissue. Abnormal MRI findings were reported at the rate of 86% in a study by Reid et al. [16] and at 93% by Piovesana et al. [17]. Consistent with these findings in literature, findings of hypoxic ischemic injury were determined in 91.4% of the patients in the current study.

Our study has some limitations. The low number of cases and the presence of data from a single center are limitations to the generalization of the results.

Conclusion

As CP is a group of diseases for which diagnosis may be difficult but early diagnosis can be beneficial, children at high-risk from birth must be closely monitored, the families must be warned, and if necessary early neuro-imaging tests should be requested. In the long-term follow-up process, in respect of both rehabilitation and the follow-up of comorbidities such as epilepsy, the treatment and follow-up of patients must be applied by a multidisciplinary team to be able to reach maximum physical capacity.

References

1. Colver A, Fairhurst C, Pharoah PO. Cerebral palsy. Lancet. 2014;383(9924):1240-9. doi: 10.1016/S0140-6736(13)61835-8.
2. MacLennan AH, Thompson SC, Gecz J. Cerebral palsy: causes, pathways, and the role of genetic variants. Am Jour Obst Gynecol. 2015; 213(6):779-88.
3. Richards CL, Malouin F. Cerebral palsy: definition, assessment and rehabilitation. Handb Clin Neurol. 2013;111:183-95.
4. Graham HK, Rosenbaum P, Paneth N, Dan B, Lin JP, Damiano DL, et al. Cerebral palsy. Nat Rev Dis Primers. 2016;2:15082. doi: 10.1038/nrdp.2015.82.
5. Winter L, Colditz PB, Sanders MR, Boyd RN, Pritchard M, Gray PH, et al. Depression, posttraumatic stress and relationship distress in parents of very preterm infants. Arch Womens Ment Health. 2018 Mar 3. doi: 10.1007/s00737-018-0821-6.
6. Yöneyman F, Gürvit G, Yusuf M. Ro-CODEC Screening of the frequency of chronic diseases in children 1997;83-84.
7. Umphred DA. Neurological Rehabilitation. Mosby Inc. 2001;259-86.
8. Sigurdardottir S, Thorkelsson T, Halldorsdottir M, Thorarensen O, Vik T. Trends in prevalence and characteristics of cerebral palsy among Icelandic children born 1990 to 2003. Dev Med Child Neurol. 2009;51(5):356-63.
9. Pereira A, Lopes S, Magalhães P, Sampaio A, Chaleta E, Rosário P. How Executive Functions Are Evaluated in Children and Adolescents with Cerebral Palsy? A Systematic Review. Frontiers in Psychology. 2018;9:21.
10. O'Callaghan ME, MacLennan AH, Gibson CS, et al. Epidemiologic associations with cerebral palsy. Obstet Gynecol. 2011;118:576-82.
11. Oğuz H, Dursun E, Dursun N. Medical Rehabilitation. Istanbul, Nobel Medicine Publisher 2004;957-74.
12. Weir FW, Hatch JL, McRackan TR, Wallace SA, Meyer TA. Hearing loss in pediatric patients with cerebral palsy. Oto & Neur. 2018;39(1):59-64.
13. Yalçın S, Özaras N, Dormans J. Cerebral Palsy Treatment and Rehabilitation. Mas Printing. 2000;13-31:51-6.
14. Downs J, Blackmore AM, Epstein A, Skoss R, Langdon K, Jacoby P at al. The prevalence of mental health disorders and symptoms in children and adolescents with cerebral palsy: a systematic review and meta-analysis. Develop Med & Child Neur. 2018;60(1):30-8.
15. Rosenbaum P, Paneth N, Leviton A, Goldstein M, Bax M, Damiano D at al. Dev Med Child Neurol Suppl. 2007;109:8-14.
16. Reid SM, Dagia CD, Ditchfield MR, Carlin JB, Reddihough DS. Population-based studies of brain imaging patterns in cerebral palsy. Develop Med & Child Neur. 2014;56(3):222-32.
17. Piovesana AM, De Moura-Ribeiro MV, Zanardi VA, Gonçalves VM. Hemiparetic cerebral palsy etiological risk factors and neuroimaging. Arq Neuropsiquiatr 2001;59:29-34.

J Surg Med. 2018;2(3):236-238.
DOI: 10.28982/josam.422797

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

General surgery service with limited feasibility in a rural hospital: Retrospective cohort study

Kırsal hastanede sınırlı fizibilite ile genel cerrahi uygulamaları: Retrospektif kohort çalışma

Fatih Başak [1]

[1] **Department of General Surgery, Health Science University, Umraniye Education and Research Hospital, Istanbul, Turkey**

ORCID ID of the authors
FB: 0000-0003-1854-7437

Abstract

Aim: Many residents living in rural areas have access to health services more difficult than those living in urban areas. Although 20% of the US population lives in rural areas, only 9% of physicians work in these areas, and in particular general surgeons appear to be inadequate in small rural towns. This study was planned in order to determine the applications made from the general surgery in the district state hospital.

Methods: The study was carried out at the Bozkır State Hospital with 25 beds located approximately 150 km away from the center of Konya. In 2009, patient files were reviewed for general surgery polyclinic. Elective and urgent (major and minor) operations were recorded. The results are examined.

Results: During the study period, 4312 patients were seen in the outpatient clinic. The total number of working days in 2009 is 224 and the average number of patients per day is 22. During the study period, 35 major operations were performed. Twelve appendectomies, 15 inguinal hernias, six pilonidal sinus, one goiter and one intestinal resection in a case with strangulated inguinal hernia were performed.

Conclusion: The experience we have in our hospital may be related to the social structure and needs of our region. A rural surgeon, like third-line hospital services, may need experienced teams and adequate infrastructure to confront patients and meet their needs.

Keywords: Rural hospital, Surgery service, Cohort

Öz

Amaç: Kırsal alanda yaşayan birçok sakin, sağlık hizmetlerine erişimleri, kent dışı bölgelerde yaşayanlara göre daha zordur. ABD nüfusunun %20'sinin kırsal bölgelerde yaşıyor olmasına rağmen, hekimlerin sadece %9'u bu alanlarda çalışıyor ve özellikle genel cerrahlar küçük kırsal kasabalarda yetersiz kalmış gibi görünüyor. Bu çalışma ilçe devlet hastanesinde genel cerrahi açıdan yapılan uygulamaların tespiti amacıyla planlandı.

Yöntemler: Çalışma Konya il merkezinden yaklaşık 150 km uzakta bulunan 25 yataklı Bozkır Devlet Hastanesinde gerçekleştirildi. 2009 yılında genel cerrahi polikliniğine başvuran hasta dosyaları incelendi. Elektif ve acil uygulanan major ve minor ameliyatlar kayıt edildi ve sonuçları irdelendi.

Bulgular: Çalışma süresince 4312 hasta poliklinikte görüldü. 2009 yılı toplam çalışılan gün sayısı 224 olup ortalama gün başına 22 hasta düşmektedir. Çalışma süresi içerisinde 35 adet major ameliyat yapıldı. On iki apendektomi, 15 adet kasık fıtığı, altı adet pilonidal sinus, bir guatr ve bir adet boğulmuş herni vakasında barsak rezeksiyonu ve herni onarımı ameliyatı yapıldı.

Sonuç: Hastanemizde edindiğimiz deneyim, bölgemizin sosyal yapısı ve ihtiyaçları ile ilgili olabilir. Kırsal kesimde çalışan cerrah, üçüncü basamak hastane hizmetleri gibi, hastalarla yüzleşmek ve gereksinimleri karşılamak için deneyimli ekiplere ve yeterli altyapıya ihtiyaç duyabilmektedir.

Anahtar kelimeler: Kırsal hastane, Cerrahi uygulamalar, Kohort

Corresponding author / Sorumlu yazar:
Fatih Başak
Address / Adres: Genel Cerrahi Kliniği, Ümraniye Eğitim ve Araştırma Hastanesi, İstanbul, Türkiye
E-mail: fatihbasak@gmail.com

Ethics Committee Approval: Ethics committee approval was not received for this study because of retrospective design.
Etik Kurul Onayı: Etik kurul onayı çalışmanın retrospektif doğasından dolayı alınmamıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 11.05.2018
Accepted / Kabul Tarihi: 05.06.2018
Published / Yayın Tarihi: 05.06.2018

How to cite / Atıf için: Başak F. General surgery service with limited feasibility in a rural hospital; Retrospective cohort study. J Surg Med. 2018;2(3):236-238.

Introduction

Rural areas of developing countries especially suffer from inadequate and irregular distribution of human resources for health [1-4]. Although 50% of the population resides in rural settings, however they have less than 25% of required doctors and 38% of nurses in these areas [5]. This vertical and inequality distribution of health care workers exacerbates health inequalities in rural areas [6-8].

Health worker attrition is a major reported problem in rural areas. In 2010, the World Health Organization proposed policies for keeping attractions, recruitment and health care workers in rural settings. Recommendations include employing health officials with a rural background, including rural health needs in the curriculum, and the use of compulsory rural services [5].

It has been determined that healthcare workers are sufficiently rural in order to improve management, rational distribution, fair distribution and protection of health care workers [8].

Human resources for the health program are registered, mostly doctors, who abandon rural hospitals to attend residential programs in urban settings for special education. In a rural area of Konya, we know little about the health worker attrition, our work rates and individual factors were assessed for attrition in a rural area hospital setting human resources for a two-year mandatory service and health program.

Materials and methods

Descriptive retrospective cohort study is designed, and the universal principles of the 1964 Declaration of Helsinki and its later amendments were applied. Informed consent was not received due to the retrospective nature of the study. This research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects".

Patients who admit to general surgery clinic of Bozkır state hospital of Konya in 2009 are enrolled into this study. Performed all operations, major or other minor local surgeries, were recorded. This rural hospital has 25 beds capacity at study time, and was 150 km and 1.5 hours away from province of Konya. There was a solo general surgeon but no anesthesiologist was present in that year. Blood bank and most of radiological studies also were not available. Hospital had an emergency service 7/24 hours. The surgeon attended to hospital emergency service if needed, and some minor emergent surgeries could be done, but some other has been transferred to larger hospitals. In this study non-trauma general surgery clinical admissions and outcomes will be presented. Trauma records of general surgery clinic of our hospital had been reported in another study last year [9].

Statistical analysis

Variables are expressed as mean ± standard deviations (SD) or as medians (range) depending on their distribution. Categorical variables were expressed as frequencies and percentages.

Results

During the study period, 4312 patients admitted to the outpatient clinic. The total number of working days in 2009 is 224 and the average number of patients per day is 22. During one year study period, 35 patients with major operations were included in the study. Mean age of the patients was 46.7±13.1, and male/female ratio was 1.5 (21/14). Twelve appendectomies, 15 groin hernia repairs, six pilonidal sinuses, one goiter operation and one intestinal resection in a case with strangulated hernia were performed. General anesthesia was used in 14 cases, and local anesthesia was used in the rest. In most of pathologies that requiring surgery, due to patient's preference he/she was transferred to main hospitals in Konya providence.

In addition, 121 minor surgeries, e.g. excisional biopsy of subcutaneous mass were performed. All excised specimens were sent to another hospital with a pathology clinic in Konya providence. No malign pathology is determined in any of specimens.

Discussion

Our findings show that surgery in rural areas might be a vital component of the health care services, but it is limited due to shortage of acceptable availabilities. In our hospital a surgeon had performed only 35 major and 121 minor operations in one year because of deficiency of surgical instruments with new technology such as endoscopy and laparoscopy, lack of blood bank and patient's preference as not choosing the hospital. Most hospital views the ability to provide surgical services as crucial to their rural hospital. However their ability to do so is limited because of current and projected shortages of surgeons and adequate facilities.

It creates the impression that countless are experiencing issues enlisting or potentially holding a specialist to rehearse in their group and this undermines their capacity to offer surgical care. Regarding the rustic surgical workforce, the expanding period of specialists joined with the way that less broad surgery occupants are honing in provincial territories proposes that the lack will just intensify in coming years [10,11]. Given that rustic inhabitants are additionally maturing and that the rate and seriousness of injury in country settings is higher than in urban zones, the requirement for provincial general specialists will probably increment while the supply diminishes [12,13].

One of the principle reasons why there are less specialists honing in rustic healing facilities is that the workforce is maturing and more specialists are resigning without somebody to supplant them. Some future specialists may be picked not to rehearse rustically to some degree since they feel deficiently arranged to go up against the various caseloads that numerous provincial specialists experience in their training [14,15]. A general specialist is regularly the endoscopist, injury specialist, and basic care supplier in a little provincial doctor's facility. Surgical residency preparing, in any case, is ending up more particular as Residency Review Committee for Surgery inhabitant case log information demonstrate that the quantity of gynecologic, orthopedic, and urological methods performed by general surgical occupants declined forcefully in the vicinity of 1999 and 2005 [16].

Moreover, there are not very many preparing programs that are either situated in rustic zones or offer a provincial preparing track [17]. Projects that prepare inhabitants in rustic settings have been appeared to create essential care doctors who will probably rehearse in country regions [18]. This feasible is on account of they give introduction to and involvement in overseeing run of the mill cases seen in provincial practice and enable them to create of a feeling of what it resembles to hone and live in a rustic group. Expanding the quantity of general surgery residency programs that offer rustic preparing knowledge is one means for tending to the country surgery workforce lack; in any case, more activity is expected to create other imaginative approaches to address this expanding issue.

Most by far of provincial clinics studied depend vigorously on the capacity to give surgical administrations as 83% of chairmen in this investigation expressed they would be compelled to decrease administrations on the off chance that they lost their surgical program. While a part of the diminishment in administrations estimated by directors in the present study would be an immediate aftereffect of not performing surgical cases, considerably more pernicious would be the loss of downstream income from related administrations, for example, radiology and drug store. Common health problem among the elderly population in rural area is pain, and these patients get other problems with not applying health-care. Also, patients who leave their neighborhood look for mind at a bigger inaccessible doctor's facility may get other social insurance benefits there too, adding to encourage misfortunes for the littler nearby rustic healing center [19,20].

There are a few potential answers for the issue of surgical staffing in little provincial doctor's facilities incorporating changes out in the open arrangement, surgical preparing, and the structure of surgical practice. Given that free market standards work in our social insurance framework, money related motivating forces would likely offer assistance. Reinforcing the monetary state of little clinics would enable them to give more money related motivators to specialists. What's more, payer repayment incongruities could be acclimated to give better remuneration to surgical administrations in rustic regions. As to surgical preparing, the techniques by which specialists are right now prepared could be acclimated to keep the end of general surgery. This could incorporate building up a general surgery "sub-claim to fame" enveloping more extensive preparing in the fluctuated surgical methods that little country doctor's facilities require their specialists to give. At long last, provincial healing facilities could create imaginative synergistic connections between their specialists and tertiary care focuses to help enhance the issue of expert seclusion [21].

The study has a number of possible limitations. Our data contains only cases that refer to the Bozkır State Hospital. Patients who were brought to the hospital but could not be operated due to technical insufficiency were not included in the study. In addition, it may not be applicable to all rural areas because it is the only one hospital based data. Also, we could not obtain sufficient data about the clinical status of patients who were admitted to hospital, except for the fact that they were discharged.

In conclusion, the experience we have in our hospital is related to the social structure of our region. The rural surgeon needs experienced teams and adequate infrastructure to face patients, such as tertiary hospital services.

References

1. Lehmann U, Dieleman M, Martineau T. Staffing remote rural areas in middle- and low-income countries: a literature review of attraction and retention. BMC Health Serv Res. 2008;8:19.
2. Dolea C, Stormont L, Braichet J. Evaluated strategies to increase attraction and retention of health workers in remote and rural areas. Bull World Health Organ. 2010;88(5):379-85.
3. Chankova S, Muchiri S, Kombe G. Health workforce attrition in the public sector in Kenya: a look at the reasons. Hum Resour Health. 2009;7:58.
4. Appiagyei A, Kiriinya RN, Gross JM, Wambua DN, Oywer EO, Kamenju AK, et al. Informing the scale-up of Kenya's nursing workforce: a mixed methods study of factors affecting pre-service training capacity and production. Hum Resour Health. 2014;12(47):1-10.
5. World Health Organization. Increasing access to health workers in remote and rural areas through improved retention: Global Policy Recommendations. 2010 Accessed April 22 2015
6. Serneels P, Montalvo JG, Pettersson G, Lievens T, Butera JD, Kidanu A. Who wants to work in a rural health post? The role of intrinsic motivation, rural background and faith-based institutions in Ethiopia and Rwanda. Bull World Health Organ. 2010 May;88(5):342-9.
7. Binagwaho A, Kyamanywa P, Farmer PE, Nuthulaganti T, Umubyeyi B, Nyemazi JP et al. The Human Resources for Health Program in Rwanda – A New Partnership. The New England Journal of Medicine. 2013;369(21):2054-9.
8. Buchan J. Reviewing the benefits of health workforce stability. Human Resources for Health. 2010;8:29.
9. Basak F. Addition of a general surgeon without addition of appropriate support is inadequate to improve outcomes of trauma patients in a rural setting: a cohort study of 1962 consecutive patients. Eur J Trauma Emerg Surg. 2017 Dec;43(6):835-9.
10. Thompson MJ, Lynge DC, Larson EH, Tachawachira P, Hart LG. Characterizing the general surgery workforce in rural America. Arch Surg. 2005;140:74-9.
11. Zuckerman R, Doty B, Gold M, Bordley J, Dietz P, Jenkins P, Heneghan S. General surgery programs in small rural New York State hospitals: A pilot survey of hospital administrators. J Rural Health 2006;22:339-42.
12. Kwakwa F, Jonasson O. The general surgery workforce. Am J Surg. 1997;173:59-62.
13. Jonasson O, Kwakwa F, Sheldon GF. Calculating the workforce in general surgery. JAMA. 1995;274:731-4.
14. Ritchie WP, Rhodes RS, Biester TW. Workloads and practice patterns of general surgeons in the United States, 1995-1997: A report from the American Board of Surgery. Ann Surg. 1999;230:533-43.
15. Landercasper J, Bintz M, Cogbil TH, Bierman SL, Buan RR, Callaghan JP, et al. Spectrum of general surgery in rural America. Arch Surg. 1997;132:494-7.
16. Accreditation Council for Graduate Medical Education. Residency Review Committee for Surgery Case Log Statistical Reports. Available at: http://www.acgme.org/residentdatacollection/documentation/statistical_reports.asp. Accessed on August 20, 2007.
17. Wurie HR, Samai M and Witter S. Retention of health workers in rural Sierra Leone: findings from life histories. Hum Resour Health. 2016;14(3):1-15.
18. Brooks RG, Walsh M, Mardon RE, Lewis M, Clawson A. The roles of nature and nurture in the recruitment and retention of primary care physicians in rural areas: A review of the literature. Acad Med. 2002;77:790-8.
19. Öksüz A, Atadağ Y, Aydın A, Kaya D. The frequency of analgesic drug use in 65 years and above diseases and their causes; an experience of family medicine unit. J Surg Med. 2017;1(1):12-4.
20. Aydın A, Atadağ Y, Kaya D, Köşker HD, Başak F, Uçak S. Aile Hekimliği Uygulamasının Bir Eğitim ve Araştırma Hastanesine Ayaktan Hasta Başvurularındaki Etkisi.. Arch Clin Exp Med. 2017;2(3):74-8.
21. American Hospital Association and The Lewin Group. Challenges facing rural hospitals. Trend Watch. 2002;4:1.

J Surg Med. 2018;2(3):239-243.
DOI: 10.28982/josam.417843

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Impact of a program of induced stress therapy on the motor and functional recovery of the upper limb of hemiplegic patients in Kinshasa, Democratic Republic of Congo

Demokratik Kongo Cumhuriyeti, Kinshasa'da endüklenmiş stres terapisi programının hemiplejik hastaların üst ekstremitesinin fonksiyonel ve motor olarak iyileşmesi üzerindeki etkisi

Teddy Bofosa [1], Eric Kam [1], François Njimbu [1], Ponce Mpefi [1], Tharcis Kayembe [2], Betty Miagindula [1]

[1] Department of Physical Medicine and Rehabilitation, Faculty of Medicine, University of Kinshasa, University of Kinshasa, Democratic Republic of Congo
[2] Neuro Psychological and Psychiatric Center, Faculty of Medicine, University of Kinshasa, Democratic Republic of Congo

ORCID ID of the authors

TB: 0000-0002-9878-4995
EK: 0000-0002-8408-7160
FN: 0000-0003-3085-5117
PM: 0000-0002-8355-5102
TK: 0000-0003-4382-6382
BM: 0000-0003-0881-866X

Corresponding author / Sorumlu yazar:
Teddy Bofosa
Address / Adres: Department of Physical Medicine and Rehabilitation, Faculty of Medicine, University of Kinshasa, University of Kinshasa, Democratic Republic of Congo
Tel: +243 850143232
E-mail: bofosa.linkoko@unikin.ac.cd

Ethical consideration: All hemiplegic subjects had consented in writing to participate in the study according to the Helsinki Declarations. The information collected from hemiplegic subjects was kept confidential.
Etik durum: Hemiplejik deneklerin tümü, Helsinki Deklarasyonlarına göre çalışmaya katılmak için yazılı olarak kabul etmişlerdir. Hemiplejik deneklerden toplanan bilgiler gizli tutuldu.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 24.04.2018
Accepted / Kabul Tarihi: 06.06.2018
Published / Yayın Tarihi: 06.06.2018

Abstract

Aim: Stroke is a major cause of disability. As a result of rehabilitation, 80% of hemiplegic patients recover in particular, whereas only 28% to 57% recover the grip. Aim of this study is to evaluate the effects of induced stress therapy on motor and functional recovery of the hemiplegic upper limb, to compare the pace of recovery and upper limb autonomy between hemiplegics subjected to induced stress therapy and not subject to induced stress therapy and evaluate the impact of this therapy in the prevention of upper limb neuromuscular complications and disorders.

Methods: This is an interventional study conducted in 30 hemiplegic vascular patients followed at the University Clinics of Kinshasa and at the General Reference Hospital of Kinshasa for 6 months. The pace of recovery was evaluated by the motor index of Demeurisse. We used Pearson's chi - square to compare the results. The significance level was considered for the value of $p \leq 0.05$.

Results: The mean age of these patients was 57.5±10.5 years, with a male predominance (63.3%). The majority of these patients were civil servants (23.3%), traders (16.7%) and teachers (16.7%), trades making frequent use of the upper limb. After 6 months of re-education, there was no significant increase in tone in patients undergoing stress-induced therapy (p=0.34), whereas, for the comparison group, the increase in tone was very significant (p=0.01); a very significant improvement in motor function (p=0.000) was observed for the group of induced stress therapy, and significant (p=0.05) for the comparison group. The progression of pain was good for the group of induced stress therapy (p=0.02), and negative for patients not subjected to induced stress therapy (p=0.5).

Conclusion: In the course of this study, it was found that induced stress therapy is effective in the functional recovery and prevention of neuro-motor disorders of the upper limb of the vascular hemiplegic.

Keywords: Stroke, Hemiplegia, Upper limb, Induced stress therapy

Öz

Amaç: İnme, önemli bir sakatlık sebebidir. Rehabilitasyonun bir sonucu olarak, hemiplejik hastaların %80'i özellikle iyileşmektedir, oysa sadece %28 ila %57'lik oranlarda kavrama iyileşmektedir. Bu çalışmanın amacı: indüklenmiş stres tedavisinin hemiplejik üst ekstremitenin motor ve fonksiyonel geri kazanım üzerindeki etkilerini değerlendirmek, indüklenmiş stres terapisine tabi tutulan hemiplejikler arasında iyileşme hızını ve üst ekstremite otonomisini karşılaştırmak ve stres terapisine maruz kalmamak ve üst ekstremite nöromüsküler komplikasyonların ve bozuklukların önlenmesinde bu tedavinin etkisini değerlendirmektir.

Yöntemler: Bu, Kinshasa Üniversitesi Kliniklerinde ve 6 ay boyunca Kinshasa Genel Referans Hastanesi'nde takip edilen 30 hemiplejik vasküler hastada yapılan girişimsel bir çalışmadır. İyileşme hızı Demeurisse motor indeksi ile değerlendirildi. Sonuçları karşılaştırmak için Pearson'un ki - kare değerini kullandık. Anlamlılık düzeyi $p \leq 0,05$ değeri için kabul edildi.

Bulgular: Olguların yaş ortalaması 57,5±10,5 yıldı ve erkek ağırlığı %63,3 idi. Bu hastaların çoğunluğu memur (%23,3), tüccar (%16,7) ve öğretmen (%16,7), üst ekstremiteyi sık kullanan esnaflardır. 6 aylık yeniden eğitimden sonra, strese bağlı tedavi uygulanan hastalarda tonda belirgin bir artış görülmezken (p=0,34), karşılaştırma grubunda tonus artışı çok anlamlıydı (p=0,01); İndüklenmiş stres tedavisi grubunda motor fonksiyonda çok önemli bir iyileşme (p=0,001) ve karşılaştırma grubu için anlamlı (p=0,05) bir artış gözlendi. Ağrının ilerlemesi, indüklenmiş stres tedavisi grubuna (p=0,02) ve indüklenmiş stres tedavisine maruz kalmayan hastalar için negatif idi (p=0,5).

Sonuç: Bu çalışmanın sonucunda, vasküler hemiplejik üst ekstremitede nöro-motor bozuklukların fonksiyonel iyileşmesinde ve önlenmesinde indüklenmiş stres tedavisinin etkili olduğu bulunmuştur.

Anahtar kelimeler: İnme, Hemipleji, Üst ekstremite, İndüklenmiş stres tedavisi

How to cite / Atıf için: Bofosa T, Kam E, Njimbu F, Mpefi P, Kayembe T, Miagindula B. Impact of a program of induced stress therapy on the motor and functional recovery of the upper limb of hemiplegic patients in Kinshasa, Democratic Republic of Congo. J Surg Med. 2018;2(3):239-243.

Introduction

Stroke is a major cause of disability and the third leading cause of death after myocardial infarction and cancer in the West [1,2]. The disability related to hemiplegia partially or totally depends on the patient in performing activities of daily life post-stroke. Yesterday apparently absent from sub-Saharan Africa [3], cardiovascular diseases including stroke are now emerging and constitute a major public health problem [4,5]. In the Democratic Republic of Congo (DRC) hospital admissions for stroke occupy the first place among the conditions treated in internal medicine in Kinshasa [6]. Stroke is an acute condition that requires emergency treatment and chronic disease that leads to disabling sequelae requiring long-term management [7]. Numerous studies have shown the effectiveness of rehabilitation in both acute and chronic phase. There are several methods (Perfetti, Bobath ...) used for the rehabilitation of hemiplegic patients, but no study has demonstrated their effectiveness [8], and the results obtained are not always satisfactory

Thus, following a reeducation, there is in particular greater difficulty in obtaining a recovery of the function of the upper limb relative to the lower limb. While 80% of hemiplegic patients recover walking, only 28% to 57% recover the grip [9].

Neuromotor disorders of the upper limb after a stroke make it difficult to perform the various tasks, such as extending the bottom, grabbing and manipulating an object. This situation disrupts the daily activities of life, such as showering, dressing, eating, or bathing.

In order to improve the management of the upper limb of the vascular hemiplegic, new techniques have emerged in recent years, such as mirror therapy, mental imagery, induced stress therapy, etc. [10].

The latter approach is beginning to be integrated more and more in the treatment of hemiplegics followed in the rehabilitation services of the city of Kinshasa province, in the Democratic Republic of Congo. However, we did not find any scientific studies proving its effectiveness; hence the motivation of this study.

Materials and methods

Framework and period of study

The University Clinics of Kinshasa (CUK) and the Kinshasa Provincial Reference General Hospital (HGPRK) were chosen as study framework during the period from 01 August 2017 to 01 January 2018. This choice was justified by the high frequency of admission of patients for cerebrovascular accident.

Study population

It is made of vascular hemiplegic patients outside the acute phase and admitted to rehabilitation. The selected patients met the following criteria: Patients who have agreed to participate in the program, Not having started re-education sessions elsewhere (for the experimental group), Who did 3 months of rehabilitation (for the comparison group), Patient with a motor score of Demeurisse <40 and a modified Ashworth ≤ 2 on the upper limb. Also included were the records of patients undergoing rehabilitation, who formed the comparator group. Anyone who did not meet the above criteria was excluded.

Type of study

This is an experimental study that has demonstrated the effectiveness of stress therapy induced in the rehabilitation of the upper limb of hemiplegic patients in post stroke.

The clinical results obtained with induced stress therapy (IDT) were compared to those of patients rehabilitated by other methods commonly used in our environment.

Method of data collection

Data was collected from patients and medical records using a pre-established form. For TCI patients, clinical evaluations at the beginning and end of the program were conducted. These evaluations concerned the pain assessment (EVA), the spasticity and the motor level of the patients. In patients in the comparison group, we collected clinical data at 3 months of rehabilitation. In medical files, we collected information related to socio-demographic, diagnostic and therapeutic aspects.

Study variables

- Sociodemographic variables: Age (in years), Sex (male or female), Occupation / occupation
- Clinical variables: Duration of hospitalization (in days), Type of stroke (ischemic or hemorrhagic), Spasticity by the modified Ashworth scale, Presence of pain (EVA), Motor level (by the Demeurisse motor index)

Sampling

We took a convenience sample based on the patients available for rehab. We had received a total of 38 patients and, after selection, we selected 30 patients who constituted our sample, including 15 for the group followed by TCI and 15 others who had followed another program.

Operational Definitions

Demeurisse Motor Index: This is a validated motor assessment scale specifically developed for the evaluation of vascular hemiplegics. It stems from muscle testing. This is a simple, validated and recommended evaluation for hemiplegic patients. This scale refers to shoulder abduction, elbow flexion, thumb-index end-to-end grip, hip flexion, knee extension, and dorsiflexion of the foot. The evaluation gives a motor score of 100 for the upper limb and 100 for the lower limb; we divide each of these scores by 2 and we obtain an overall score out of 100. For our series, we only considered the score of the upper limb side to 100 and assigned the following scores:

- From 0 to 9: no motor activity;
- From 10 to 39: low motor activity;
- From 40 to 59: Average motor activity;
- From 60 to 79: acceptable motor activity
- From 80 to 100: good motor activity

Modified Ashworth scale: it is a non-linear but validated and reproducible scale evaluating the resistance of a muscle (spasticity) during its passive elongation (passive movement).

It goes from 0 to 4:

0: no increase in muscle tone

1: a discreet increase in tone manifested by a jump followed by a relaxation or by a minimal resistance at the end of the movement.

1+: a discreet increase in muscle tone manifested by a jump followed by a minimal resistance perceived on less than half of the range of motion.

2: more marked increase in muscle tone affecting most of the range of motion. The joint can be mobilized easily.

3: a significant increase in muscle tone making passive mobilization difficult.

4: the affected joint is fixed in flexion or extension (abduction or adduction)

EVA: Visual analogue scale, it gives an estimate of the intensity (quantification) of the pain ranging from the absence of pain (zero) to the intense pain (ten), a scale ranging from 0 to 10.

Good evolution

Was considered to have a good evolution, the patient of which:

• The modified Ashworth scale was rated less than or equal to 1

• EVA less than 3

• Demeurisse motor index greater than or equal to 60.

Course of the program

Induced stress therapy is one of the new approaches to the rehabilitation of the upper limb of the hemiplegic patient.

It consists in blocking the healthy limb of the patient to force him to use his sick member. Its effectiveness, largely based on the fight against the phenomenon of "non-use acquired", is highlighted in many studies.

After a therapeutic education that consisted in explaining to the patient what induced stress therapy was, we started the program.

Evaluation

We conducted two evaluations during our program. The first at the beginning, the second at the end of the program. These two evaluations consisted of examining the patient in a general way, but more particularly the following aspects:

- Tone appearance using the modified Ashworth scale to highlight the presence or absence of spasticity.

- Pain aspect, consisted of evaluating the intensity of the pain in these patients.

- Motor aspect consisted in evaluating the motor level of the upper limb of the patient, using the motor index of Demeurisse.

Treatment proper

The principles of treatment consisted of:

- Respect the fatigability of the patient
- Fight against spasticity and avoid strengthening it
- Fight against syncinesies
- Adapt the exercises to the patient's abilities
- Allow the patient to do his activities of daily living (ADL) within his capacity.
- The healthy limb being immobilized by an immobilization vest, an immobilization scarf or a velpo band, and the patient had to perform the different tasks or activities of daily life with the sick member. Different objects and toys were used to perform various tasks such as showering, combing hair, eating, writing, moving an object, etc. We also used other exercises involving the cognitive abilities of the patient (concentration, memorization, intention of movement), using different objects (hoops, pads, rings ...) and their characteristics (shape, size, color, weight ...), and adapting the instruction to obtain a movement allowing the stretching of the spastic muscle. For example, we use 3 studs and 3 hoops of different colors. We ask the patient to place a colored pad in the hoop of the same color, which is arranged in such a way that it prompts the patient to spread and stretch his arm to stretch his large pectoral and biceps. The first step is to perform the movement with open eyes, then memorize the location of the different hoops to place each cone in the corresponding hoop with closed eyes.

Statistical analysis

The data was entered by Excel, exported and analyzed with SPSS software version 15.0 for Windows. We used Pearson's chi - square to compare the results. The materiality threshold was considered for the value of $p \leq 0.05$. Quantitative variables were presented as mean and standard deviation and qualitative variables as proportion and absolute value. The results were presented in the form of tables and figures.

Results

The average age of these patients is 57.5±10.5 years, with extremes of 19 years and 83 years, and a higher frequency between 55 years and 60 years (Figure 1).

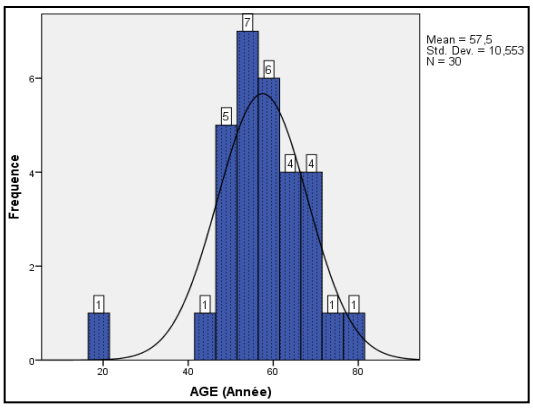


Figure 1: Age distribution of patients

Table 1 shows a male predominance (63.3%) for both the experience group and the comparator group.

Table 1: Distribution of patients by sex

Sex	Group of study				Total	
	Experience group		Comparison group			
	N	%	N	%	N	%
Male	10	33,3	9	30,0	19	63,3
Female	5	16,7	6	20,0	11	26,7
Total	15	50	15	50	30	100

In figure 2, it appears that the majority of these patients are civil servants (23.3%), followed by traders (16.7%) and teachers (16.7%).

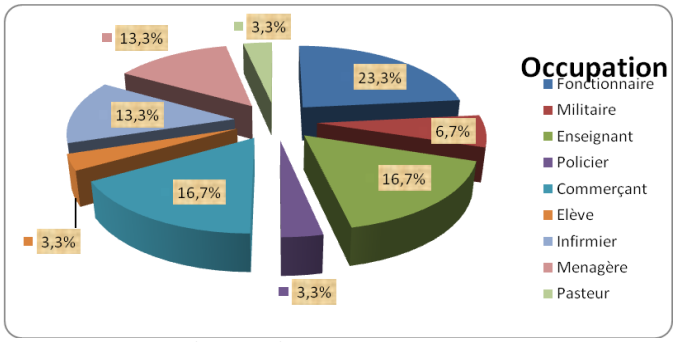


Figure 2: Distribution of patients from two groups according to their occupational occupation

Table 2 gives information on the evolution of spasticity evaluated after 6 months of reeducation by induced stress; it

appears that in this group there was no increase in tone in these patients.

Table 2: Evolution of spasticity level at the end of the program for TCI patients

Level of spasticity (ashworth modified)	Evaluation period			
	Start program		End program	
	N	%	N	%
No spastic hypertonia	8	53,3	8	53,3
Midle hypertonia	5	33,3	7	46,7
Moderate hypertonia	2	13,3	0	0
Total	15	100	15	100

For this group of patients, an increase in tone is observed; patients who had moderate hypertonia at the beginning of the program (33.3%) increased to 66.7% after 6 months, with a significant difference (p=0.01) (Table 3).

Table 3: Evolution of spasticity level at the end of the program for patients not subject to IDD

Level of spasticity (ashworth modified)	Evaluation period			
	Start program		End program	
	N	%	N	%
No spastic hypertonia	7	46,7	0	0
Midle hypertonia	3	20	5	33,3
Moderate hypertonia	5	33,3	10	66,7
Total	15	100	15	100

Evolution of the level of motor skills

Table 4 shows a very significant improvement in the level of motor skills for this group (p=0.000); patients with low motor skills (73.4%) increased to 0% after 6 months of TCI, those with an acceptable level are 0% of patients at 20%.

Table 4: Evolution of motor skills after six months of TCI

Niveau de motricite (index moteur de deumerisse)	Evaluation period			
	Start program		End program	
	N	%	N	%
No motor skills	2	13,3	0	0
Low level of motor skills	11	73,4	0	0
Average level of motor skills	2	13,3	10	66,7
Acceptable level of motor skills	0	0	3	20
Good level of motor skills	0	0	2	13,3
Total	15	100	15	100

Table 5 shows that patients in this group had either low motor skills (46.7%) or moderate motor activity (46.7%); a significant difference (p=0.05) was observed for this parameter, between the initial level and that after 6 months.

Table 5: Evolution of the level of motor skills after 6 months of rehabilitation by other techniques

Level of motricity (deumerisse motor index)	Evaluation period			
	Start program		End program	
	N	%	N	%
No motor skills	4	26,7	0	0
Low level of motor skills	11	73,3	7	46,7
Acceptable level of motor skills	0	0	7	46,7
Good level of motor skills	0	0	1	6,6
Total	15	100	15	100

Evolution of pain

Table 6 shows a good evolution of the pain (p=0.02), the patients who had no pain at the beginning went from 46.6% to 80% after 6 months of TCI, those with Early moderate pain (40%) dropped to 0% by the end of the program.

Table 6: Evolution of pain after 6 months of TCI

Intensity of pain	Evaluation period			
	Start program		End program	
	N	%	N	%
No pain	7	46,6	12	80
Light pain	1	6,7	3	20
Moderate pain	6	40	0	0
Intense pain	1	6,7	0	0
Total	15	100	15	100

Table 7 shows a negative evolution of the intensity of the pain in the patients of this group but with a non-significant difference (p=0.5); those who had not had any pain at first (40%) dropped to 26.7% after 6 months.

Table 7: Evolution of pain after 6 months of rehabilitation by other techniques

Intensity of pain	Evaluation period			
	Start program		End program	
	N	%	N	%
No pain	6	40	4	26,7
Light pain	3	20	5	33,3
Moderate pain	5	33,3	6	40
Intense pain	1	6,7	0	0
Total	15	100	15	100

Discussion

This study was devoted to the evaluation of the effects of stress therapy induced in the rehabilitation of the hemiplegic upper limb. We selected 30 patients among whom 15 were treated by induced stress and the other 15 by other techniques of rehabilitation.

Our sample had a total of 63.3% men versus 36.7% women, with an average age of 57.5±10.5 years, with 19-year and 83-year higher between 55 and 60 years.

In the Daviet et al. study [11], the mean age of the patients was 72 years and corresponded to the age usually reported in the other studies in Europe which is 72 years for the London registry and 74 years for the register of Dijon. This difference with our series can be explained by the fact that the European population is older than ours.

In addition, according to some epidemiological studies, intracerebral hemorrhage occurs mainly after age 50 and concerns more men [12]. This goes in the direction of our series.

The majority of these patients were civil servants (23.3%), followed by traders (16.7%) and teachers (16.7%).

It is then found that in carrying out the aforementioned professional activities, the use of the upper limb is essential, especially to hold the pen and chalk. Hence the need for a good evaluation that will lead to better management, especially involving therapy that does not often require inadvertent manipulation of the hemiplegic upper limb which is in most cases fragile.

From the muscular tonus point of view, we found that the two groups were homogeneous at the beginning of the program, there was no significant difference between them (p=0.3). In addition, most of these patients (53.4% for the TCI group, 56.7% for the comparison group) did not have spasticity at the beginning of the program.

There is no significant difference (p=0.7) between the two groups in relation to the intensity of the pain; most patients had no pain (46% of the cases for the TCI group versus 40% of the cases for the comparison group), followed by those with moderate pain (40% for the TCI group against 33, 3% of cases for the comparison group).

The majority of these patients had a low level of motor skills (73.4% of cases for each group) at the beginning of the program; and there was no significant difference between the two groups with respect to the Deumerisse motor index (p=0.2).

In evaluating the rehabilitation techniques used in the treatment of patients in the comparison group, massage proved to be the most used technique (86.7%), followed by Bobath and Kabath techniques (66.7%) and infrared thermotherapy (66.7%).

In a study conducted at University Clinics in Kinshasa, mobilizations (76%), massage (60%), Bobath technique (60%) and Kabat technique (52%) were reported to be the most commonly used. rehabilitation of patients in post stroke (13); and

those electro-physiotherapy techniques were more dominated by infrared irradiation (28%).

Moreover, it is currently reported that re-education gives back its place to the asset; Robertson and Regnaux [13] synthesized the main studies validating the principles of motor learning insisting on active patient participation, the need for repeated gestures, in an intense and task-oriented way.

Regarding the assessment of the evolution of spasticity in our patients, made by the modified Ashworth scale, we found that after 6 months of stress-induced rehabilitation there was no significant increase (p=0.34) in patients with TCI. Patients who did not present hypertonia at the beginning of the program (53.3%) kept their level until the end (53.3%), slight hypertonia went from 33.3% of patients to 46.3% of patients, 7% and moderate hypertonia from 13.3% to 0% of patients.

On the other hand, for the group of non-TCI patients, an increase in tone is observed; patients who had moderate hypertonia at baseline (33.3%) increased to 66.7% after six months, with a significant difference (p=0.01).

Around the world, approximately 2,000 individuals per million are affected each year by stroke. Of these, just under 40% continue to have spasticity a year later [14]. This percentage of 66.7% of patients with spasticity in our series after 6 months of rehabilitation is high and may be due to an inappropriate treatment that favors manual manipulation (which increases the stretch reflex) to more active rehabilitation.

In another study it was reported that post-stroke spasticity affected just under a quarter of patients. Thus techniques that can increase the stretch reflex should be avoided because spasticity can have a devastating effect on function, comfort, delivery of care; it can lead to musculoskeletal complications, leading in most cases to a reduction in the extent of movement and poor positioning, often accompanied by pain [15].

In relation to motor skills, a very significant improvement (p=0.000) was observed for the group of patients submitted to TCI at the end of the program; patients with a low level of motor skills (73.4%) increased to 0% after 6 months of TCI, those who had an acceptable level went from 0% of patients to 20%.

In the comparison group, patients were found to have either a low motor level (73.3%) or a nil motor activity (26.7%); In addition, patients who had either an average level (46.7%) or a good level of motor skills (6.6%) all switched to the lower level, with a significant regression (p=0.05).

This good motor development observed after induced stress finds its justification in the sense that by its intensive nature, it significantly improves the quality and speed of movement in patients who practice it. These findings have been demonstrated in the Wolf et al randomized EXCITE study published in 2006 [16].

With regard to the evolution of pain, a good evolution of pain is observed (p=0.02); patients who had no initial pain went from 46.6% to 80% after 6 months of TCI, those with moderate early pain (40%) increased to 0% at the end of the program.

On the other hand, there was a negative change in the intensity of pain in non-TCI patients, but with no significant difference (p=0.5); those who had no initial pain (40%) tipped to 26.7% after 6 months and those who had moderate early pain (33.3%) increased to 40% after treatment.

Indeed, some unconstrained reeducations obtain very satisfactory results but seem less effective in time compared to those who practice the constraint [17].

Conclusion

TCI has been found to have not only positive effects in the functional recovery of the upper hemiplegic limb, but also in the reduction of certain disorders that may follow the improper handling of other rehabilitation techniques.

It is therefore necessary that the induced stress therapy is introduced in the protocol for the management of vascular hemiplegia because its effects are beneficial.

Acknowledgement

Our thanks go to the authorities of the University Clinics of Kinshasa and the General Hospital of Provincial Reference of Kinshasa for allowing us to conduct our research within this institution and the hemiplegic subjects to have agreed to work with us.

References

1. Gillume R. Cardiovascular disease in the United States: An epidemiologic overview, In: Elijah Sounders, Cardiovascular Diseases in blacks; F.A. Davis Company 1991:pp 3-16.
2. Zuber M. Prise en charge de l'accident vasculaire cérébral ischémique constitué au transitoire, Rév. Praticien 1997, Tome 11 n°397 : pp 24-30 ;
3. Turpin V. Pourquoi, quand, comment traiter les dyslipoprotéinémies? Nouvelle edition 1991; p 18.
4. Donnison CP. Blood pressure in the African native: It's bearing upon the aetiology of hyperpression and arterial sclerosis. Lancet 1929;1:6-7.
5. WORLD HEALTH ORGANIZATION. Non-communicable diseases: a strategy for the African region who regional office for Africa, Harare 2000.
6. Beevers DG, Prince JC. Hypertension: an emerging problem in Hospital countries royal. Trop Med. 1991;85:324-6.
7. Tambwe M, Mbala-mukendi M, Dikassa LN, M'buyamba-kabangu JR, Morbidity and mortality in hospitalized Zairean adults, South Afr J Med. 1995;85:74.
8. Nicolas P, Pélissier M, Bénaim Ch, Villy J, Hérisson E. les techniques d'inhibition de la spasticité : Concepts, Méthodes et analyse critique, in Perrenou D, Brussel B., Pélissier J., la spasticité, 2001; P.63-69.
9. Kouassi B, Renambo TJ, Piquemal M. Accidents vasculaires cérébraux en Côte-d'Ivoire, CR 60 sens. Inst Cardiol d'Abidjan, Trop cardiol 1992 (n°SPI);154.
10. Brugerolle B. Les accidents vasculaires cérébraux, institut régional de réadaptation de Nancy, centre de réadaptation et de pré orientation. Ann Readapt. 2013;73-89.
11. Cynthia MC, Stein JN. Cardiovascular diseases and the aging woman: overcoming barriers to lifestyle changes, current women's. Health reports 2002;2:366-72.
12. Xhardez Y. Vade-mecum de Kinésithérapie et de rééducation fonctionnelle. Maloine, Paris. 2002; p. 482-489.
13. Isabelle M, Didier M. Prise en charge initiale des accidents vasculaires cérébraux Service de neurologie A, hôpital GUI de Chauliac 2, www. Urgence pratique.com/2 articles/medic/artmedica l9.htm
14. Diela B. Prise en charge rééducative post accident vasculaire cérébral aux Cliniques Universitaires de Kinshasa: Mémoire de fin d'études UNIKIN, 2013; P33.
15. Partridge C J. Physiotherapy approaches to the treatment of neurological physiotherapy, A problem-solving approach, NEW YORK: Churchill – Livingstone. 1996; P.3-14.
16. Wolf S. Effect of Constraint-Induced Movement Therapy on upper extremity function 3 to 9 months after stroke. The EXCITE randomized clinical trial, American medical association, 2006.
17. Simon O. Rééducation par contrainte induite, in Yelnik A, Daniel F, Griffon A, Actualités dans la prise en charge de l'AVC, 2010; p. 89-95.

J Surg Med. 2018;2(3):244-248.
DOI: 10.28982/josam.421768

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

B-Mode ultrasound assessment of intima-media thickness of common carotid, internal carotid, brachial, femoral arteries and abdominal aorta in patients with cardiovascular risk factor

Kardiyovasküler risk faktörü olan hastalarda ana karotid, internal karotid, brakiyal, femoral arterler ve abdominal aorta intima-media kalınlığının B-Mod ultrasonografi ile değerlendirilmesi

Ayşe Selcan Koç [1], Burçak Çakır Peköz [1]

[1] Department of Radiology, University of Health Sciences, Adana Health Practice and Research Center, Adana, Turkey

ORCID ID of the authors:
ASK: 0000-0003-1973-0719
BÇP: 0000-0002-7286-5535

Abstract

Aim: The aim of the present study was to assess the association between common carotid intima-media thickness (IMT) and vascular IMT values measured from different anatomic regions.

Methods: We prospectively included 256 patients. The IMT values of the common carotid and internal carotid, brachial and femoral artery and abdominal aorta were measured by B-mode ultrasound (CC-IMT, IC-IMT, B-IMT, F-IMT and A-IMT). Patients were divided into two groups as increased and normal CC-IMT.

Results: Increased CC-IMT was detected in 55 of 256 patients (21.5%). All IMT variables showed a positive correlation with CC-IMT. Femoral IMT was independently associated with increased CC-IMT. In regression model, each 0.1 mm increase in F-IMT increased the risk of increased CC-IMT by 70.2%. When F-IMT value 1.1 mm was accepted as a cut-off value for the prediction of increased CC-IMT, sensitivity and specificity were 96.4% and 90%, respectively. In ROC curve analyses, the area under curve was calculated as 0.936.

Conclusions: Another vascular IMT location presenting increased CC-IMT best is F-IMT. The limit value for increased F-IMT >1.1mm may be used in practice. The CC-IMT measurement is closely and positively associated with all other vascular IMT measurements.

Keywords: Intima-media thickness, Common carotid artery, Femoral artery

Öz

Amaç: Bu çalışmada, farklı anatomik bölgelerden ölçülen intima-media kalınlığı (IMT) ile ana karotid IMT arasındaki ilişkiyi değerlendirmeyi amaçladık.

Yöntemler: 256 hasta prospektif olarak incelendi. B-mod ultrasound ile ana karotid, internal karotid, brakiyal ve femoral arter ile abdominal aort IMT değerleri ölçüldü (CC-IMT, IC-IMT, B-IMT, F-IMT ve A-IMT). Hastalar normal ve artmış CC- IMT değerlerine göre iki gruba ayrıldı.

Bulgular: 256 hastanın 55'inde (%21,5) artmış CC-IMT tespit edildi. Tüm IMT değerleri CC-IMT ile pozitif olarak korelasyon göstermekteydi. Femoral IMT bağımsız olarak artmış CC-IMT ile ilişkiliydi. Regresyon analizine göre F-IMT'deki her 0,1 mm'lik artış, artmış CC-IMT riskini % 70,2 artırmaktaydı. F-IMT cut-off değeri 1,1 mm olarak kabul edildiğinde artmış CC-IMT varlığını %96,4 duyarlılık ve %90 özgüllük ile tespit etmekteydi. ROC eğri analizinde, eğri altında kalan alan değeri 0,936 olarak ölçüldü.

Sonuç: Artmış CC-IMT'i en iyi belirleyen diğer IMT bölgesi F-IMT olduğu bulundu. Klinik pratikte F-IMT sınır değeri olarak >1,1 mm kullanılabilir. CC-IMT ölçümü tüm diğer vasküler IMT ölçümü ile yakın ve pozitif olarak ilişkilidir.

Anahtar kelimeler: İntima-media kalınlığı, Ana karotid arter, Femoral arter

Corresponding author / Sorumlu yazar:
Ayşe Selcan Koç
Address / Adres: Radyoloji Kliniği, Sağlık Bilimleri Üniversitesi, Adana Sağlık Uygulama ve Araştırma Merkezi, Adana, Türkiye
E-mail: drayseselcankoc@gmail.com

Ethics Committee Approval: The study was approved by Ethics Committee of Cukurova University, School of Medicine in 2017.
Etik Kurul Onayı: Çalışma 2017 yılında Çukurova Üniversitesi, Tıp Fakültesi Etik Kurulundan onay alınmıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 07.05.2018
Accepted / Kabul Tarihi: 19.06.2018
Published / Yayın Tarihi: 22.06.2018

Introduction

The intima-media thickness (IMT) of the common carotid artery was found increased in the patients with hypertension (HT), diabetes mellitus (DM), stroke, myocardial infarction and coronary artery disease (CAD); therefore it is recommended as a routine examination [1-6]. The studies that examine the presence of subclinical target organ damage by another vascular IMT except common carotid IMT (CC-IMT) are limited [7-12]. The most important reasons for using CC-IMT when compared with other vascular IMT, the localization of the carotid artery on the neck is superficial, easy to view and it can be examined in high resolution regardless of probe frequencies.

How to cite / Atıf için: Koç AS, Peköz BÇ. B-Mode ultrasound assessment of intima-media thickness of common carotid, internal carotid, brachial, femoral arteries and abdominal aorta in patients with cardiovascular risk factor. J Surg Med. 2018;2(3):244-248.

There are limited numbers of studies comparing IMT values in different regions in the literature. Such limited number of studies reported that increase of IMT is similar in all vascular system and all vascular IMT values are positively associated with each other [7, 13]. The aim of the present study was to determine the association between vascular IMT value measured from different anatomic regions and CC-IMT as well as the IMT location which would detect the increased CC-IMT best.

Materials and methods

We prospectively included 256 patients (mean age: 53.7±9.8 years, male/female: 88/168) with at least one cardiovascular risk factor, including HT, dyslipidemia, DM and smoking. Patients were categorized into two main groups: patient with increased CC-IMT (>0.9 mm) or normal CC-IMT (≤0.9 mm). Patients with secondary or malignant HT, congestive heart failure, cerebrovascular disease, severe heart valve disease, inflammatory disorders, hematologic disorders, cancer and pregnancy were excluded from the study. The Local Ethics Committee approved the study protocol, and each participant provided written informed consent. After assessment of detailed medical history and a complete physical examination, the baseline characteristics of patients including age, sex, HT, current smoking status, family history of CAD, hyperlipidemia, presence of CAD and stroke, body mass index (BMI) were recorded for all patients.

Left and right CC-IMT and internal carotid IMT (IC-IMT), brachial artery IMT (B-IMT), common femoral artery IMT (F-IMT) and abdominal aorta IMT (A-IMT) were examined with a high-resolution ultrasound (USG) Doppler system (Philips EPİQ 7), equipped with a 5-12 MHz high-resolution convex and linear transducer (Philips Health Care, Bothell, WA, USA). Ultrasound scanner setting was made to be useful for every patient for all B-mode USG examination (gain [55–75 dB]; penetration depth [2.5–8cm]). All arteries were studied in both longitudinal and transversal sections. All arteries were scanned longitudinally to visualize the IMT in the posterior or far wall of artery. All measurements were made on frozen images. Two images of the best quality were chosen for analysis in each study subject. The IMT is defined as the distance from the front edge of the first echogenic line to the anterior margin of the second line. The first line represents the intima-lumen interface and the second line represents the collagen-containing top layer of the adventitia. Vascular IMT was measured using ultrasonic calipers in case by 2 independent and blinded observers. All IMT values were calculated as averages of six measurements.

Subjects were examined at supine position. Patients' head were turned 45° from the site being scanned for carotid artery. Carotid IMT was measured from the far wall of the right and left carotid artery within 10 mm proximal (for common) and after (for internal) to bifurcation on two-dimensional ultrasound images (Figure 1a). Brachial artery was assessed and B-IMT was obtained level of the antecubital fossa and 1-2 cm proximal from bifurcation (Figure 1b). Common femoral artery was assessed and F-IMT was obtained 1-2 cm proximal from the bifurcation (Figure 1c). Abdominal A-IMT was examined midway between the origins of the celiac truncus (tripod) and iliac arteries (Figure 1d). Increased IMT was accepted for A-IMT, CC-IMT, IC-IMT, F-IMT and B-IMT as higher than 2.99 mm, 0.90 mm, 0.90 mm, 1.3 mm and 0.35 mm, respectively [1-2,14-15].

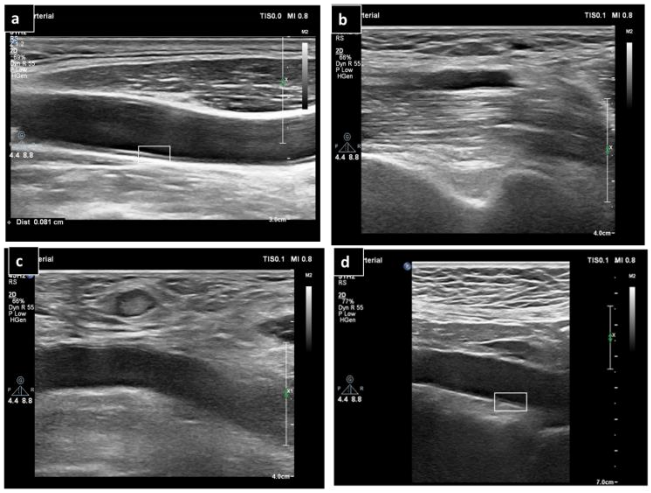


Figure 1: IMT measurements with B-mode ultrasound from different vascular regions a) CC-IMT b) B-IMT c) F-IMT d) A-IMT

Statistical analysis

All analyses were performed through SPSS 20.0 statistical software package (SPSS for Windows 20.0, Chicago, IL, USA). Continuous parameters in the group data were specified as mean ± standard deviation. Categorical parameters were presented in numbers and percentage. Continuous parameters that showed normal distribution were compared using the t test, whereas the Mann-Whitney U test used for non-normally distributed samples. Chi-Square test was used for comparison of categorical variables. Multivariate, stepwise forward conditional logistic regression analysis was used to determine the independent predictors of increased CC-IMT. As results of such analysis, increase or decrease of the significant variables were presented by Odds Ratio according to the unit increase. All significant parameters in the univariate analysis were selected in the multivariate model. A receiver operator characteristic (ROC) curve analysis was carried out to identify the optimal cut-off point of F-IMT to detect increased CC-IMT. The value of the area under the curve was calculated as a measure of the accuracy of the test. The statistical significance level was accepted as $p<0.05$.

Results

We detected the CC-IMT increased in 55 patients (21.5%). Patients were categorized into two main groups: patient with increased CC-IMT or normal CC-IMT. Comparison of the baseline clinical and demographics were shown in Table 1. Besides the age, BMI and presence of CAD, there was not any statistically significant difference in clinical and demographics parameters ($p>0.05$). Advanced age and presence of CAD was higher in patients with increased CC-IMT group. CC-IMT group had to smaller BMI than normal group (Table 1). Patients with increased CC-IMT presented a significantly higher IC-IMT, A-IMT, F-IMT and B-IMT (Table 2). All IMT variables showed a positive correlation with CC-IMT as determined by B-mode USG (Table 3).

Table 1: Baseline characteristics

	Increased CC-IMT n=55	Normal CC-IMT n=201	p
Age (year)	55.6±10.9	53.1±9.4	0.033
Gender (female)	33	135	0.175
Heart rate (beat/min)	79.2±12.1	78.5±10.8	0.804
Systolic blood pressure (mmHg)	84.5±15.9	82.6±15.3	0.712
Diastolic blood pressure (mmHg)	137.1±9.3	136.7±9.1	0.082
Body mass index (kg/m^2)	27.5±2.8	28.4±2.6	0.002
Hypertension, n (%)	82 (74.5%)	271 (67.4%)	0.093
Smoking, n (%)	22 (14.5%)	84 (20.9%)	0.808
Diabetes mellitus, n (%)	20 (18.2%)	70 (17.4%)	0.888
Hypercholesterolemia, n (%)	24 (21.8%)	70 (17.4%)	0.330
Family history, n (%)	36 (32.7%)	140 (34.8%)	0.855
Coronary artery disease, n (%)	12 (10.9%)	18 (4.5%)	0.019
Cerebrovascular disease (n, %)	4 (3.6%)	8 (2%)	0.684

CC-IMT: Common carotid intima-media thickness

Table 2: Vascular ultrasound finding in patients with increased CC-IMT and normal CC-IMT

	Increased CC-IMT n=55	Normal CC-IMT n=201	p
Internal carotid IMT (mm)	0.95±0.10	0.72±0.16	<0.001
Abdominal aortic IMT (mm)	2.53±0.37	1.25±0.64	<0.001
Femoral IMT (mm)	1.25±0.20	0.78±0.22	<0.001
Brachial IMT (mm)	0.43±0.10	0.38±0.08	<0.001
Increased internal carotid IMT (n, %)	42 (38.2%)	82 (20.4%)	<0.001
Increased abdominal aortic IMT (n, %)	54 (49.1%)	56 (13.9)	<0.001
Increased femoral IMT (n, %)	42 (38.2%)	40 (10%)	<0.001
Increased brachial IMT (n, %)	42 (%38.2)	102 (25.4%)	<0.001

CC-IMT: Common carotid intima-media thickness

Table 3: Correlation analysis of B-mode ultrasound variables in relation to the variables in CC-IMT

	p value	Coefficient of Correlation
Internal carotid IMT (mm)	<0.001	0.693
Abdominal aortic IMT (mm)	<0.001	0.544
Femoral IMT (mm)	<0.001	0.437
Brachial IMT (mm)	<0.001	0.282

IMT: Intima-media thickness

Multivariate linear regression analysis showed that IC-IMT and A-IMT most important variables in predicting CC-IMT (β level 0.562, p<0.001 and β level 0.280, p=0.017, respectively). The only independent predictor of increased CC-IMT was the F-IMT (p<0.001). Logistic regression analysis showed that every 0.1 mm increase in F-IMT caused a 70.2% increase in the risk of increased CC-IMT (Table 4). Receiver operating characteristic (ROC) curve analysis also showed that when F-IMT value 1.1 mm was accepted as a cut-off value for the prediction of increased CC-IMT, sensitivity and specificity were 96.4% and 90%, respectively. The area under ROC was calculated as 0.936 (0.915–0.956), which indicates good discriminatory power.

Table 4: Independent risk factors for occurrence of increased CC-IMT

	Odds Ratio	95% Confidence Interval	p
Femoral IMT (0.1 mm)	1.702	1.506 – 1.894	<0.001

IMT: Intima-media thickness

Discussion

The most important outcome of the present study was to detect a close, positive association between CC-IMT and all other vascular IMT measurements. An independent relation exists between CC-IMT and F-IMT values. Furthermore, the F-IMT ≥1.1 mm independently detects increased CC-IMT.

The increase in CC-IMT is closely associated with subclinical organ damage and atherosclerosis; and it is recommended as a routine examination [1]. The CC-IMT detected by B-mode USG is known as a feasible and repeatable evaluation in the patients with HT [2]. CC-IMT is closely associated with presence and severity of CAD; and stroke and myocardial infarction [3-6].The most important causes of CC-IMT as target IMT include superficial location on the neck, easy imaging and easy access because of open location of such area and number of CC-IMT data in the literature. However, some studies were conducted with IMT in other anatomic regions [2, 9,16,17].

There are studies focusing on subclinical target organ damage through examination of abdominal A-IMT in HT patients [11,12]. However, since evaluation of A-IMT is more difficult than CC-IMT and there is not any device enabling sufficient tissue penetration, it is not a routine test for monitoring of the patients with HT. Measurement of A-IMT was considered as a better parameter to detect subclinical target organ damage during early stages of CV diseases, especially in pediatric and adolescent children group. Only a limited number of studies reported availability of descending thoracic A-IMT measurement through transesophageal echocardiography (TEE) [2,9,10]. Belhassen et al. [2] reported that the increase of descending A-IMT (≥ 3 mm) detected by TEE determined presence of CAD independently. In a recent study including middle-aged patients group diagnosed with sporadic idiopathic hypoparathyroidism found a close association between A-IMT and CC-IMT. In addition to the close correlation detected in the previous studies, we also found a close and independent association between CC-IMT and A-IMT in regression analysis.

A close association exists between the atherosclerosis detected in the brachial artery by autopsy and atherosclerosis of coronary and carotid arteries [18]. In a study conducted on the individuals with CV risk factor, a close association was found between CC-IMT and B-IMT [15]. In the aforesaid study, the patents with risk factor for CV disease could be detected when limit value for B-IMT is taken as 0.28 mm [15]. Another study assessing the B-IMT reported average B-IMT of the patients with CV mortality as 0.37 mm [19]. However, several studies conducted showed a poor association between B-IMT and CC-IMT [20,21]. A close association was detected between B-IMT and CC-IMT in the present study; however, such association was poorer than the association between CC-IMT and F-IMT as well as A-IMT.

It was shown that the increase in F-IMT is a determinant for increased vascular hypertrophy [16] and associated with early atherosclerosis formation and increased CC-IMT [13,17]. CC-IMT is related to peripheral artery disease as well as other vascular diseases such as atherosclerosis. Kirhmajer MV et al. [22] reported in their study that a close association exists between F-IMT and severity of CAD; and F-IMT may be used as a novel determinant for CV risk factor such as CC-IMT. Another study conducted demonstrated that formation of atherosclerotic plaque is more in common femoral artery when compared with carotid artery; and F-IMT is thicker than CC-IMT [23]. Similarly, we detected that thickness of F-IMT is more than CC-IMT in the patients with CV risk factors. As a result of our study, use of F-IMT measurement was considered as a determinant to indicate subclinical target involvement such as CC-IMT.

The studies conducted reported the normal F-IMT thickness as 0.562±0.074 mm for males and 0.543±0.063 mm for females [24]. However, as much as we searched, there is not any limit value for increased F-IMT. Although the average F-IMT value was found in the patients with CAD was found 1.3 mm,

this does not reflect increased F-IMT [14]. Similar to the aforesaid study, the F-IMT value in the patients with increased CC-IMT was found 1.25±0.20 mm. Furthermore, in addition, the limit value of F-IMT was found 1.1mm for prediction of increased CC-IMT in ROC analysis.

There are limited numbers of studies in the literature comparing the IMT values in at least 4 different regions mentioned above. Furthermore, there is not any study measuring CC-IMT, IC-IMT, B-IMT, F-IMT and A-IMT simultaneously with vascular ultrasound in adult patients. Only a study conducted on middle aged patient group with congenital adrenal hyperplasia measured IMT of 4 different vascular regions including common carotid, carotid bulbus, femoral and abdominal aorta. In such study, IMT increase was detected in all vascular system of the patients with congenital adrenal hyperplasia [7]. Neiva Neto et al. [13] reported in their study that A-IMT values of the carotid, vertebral, femoral and abdominal arteries are positively and significantly associated with each other and detection the IMT increase in any of these arteries would be sufficient. A recent and similar study evaluated the association between internal, external and common carotid arteries, vertebral artery and femoral artery and abdominal aorta IMT [13]. A positive association was found between all vascular IMT measurements in such study conducted with fewer patients [13]. Results of the present study are consistent with previous studies and all vascular IMT levels are associated with each other.

Although there are data for IMT measurement from vascular regions other than CC-IMT, the studies conducted for CC-IMT are wider and multi-centered; and increase of CC-IMT was included in the guidelines. However, the actual objective of our study was to detect the vascular IMT region which is closest to CC-IMT. The most ideal measurement for IMT increase in peripheral vascular system should continue to be carotid IMT. However, inclusion of vascular IMT values into the ultrasound report during upper limb Doppler and abdominal USG scans may be useful for the clinician. It was concluded that the patients with F-IMT of ≥1.1 mm should be specified.

There are same limitations in our study. In a study measuring CC-IMT and F-IMT in the patients with CAD showed higher values and a close association between both IMT value and severity of CAD [14]. However, presence and severity of CAD was not assessed in the present study. CAD was detected more in the patients with increased CC-IMT; however severity of CAD was not examined. It was shown that the treatments used for atherosclerosis, in particular, regress IMT [25]. However, we did not review the effect of medical treatments on IMT in the present study. Our study is not a follow-up study and therefore no disease control CC-IMT and other IMT assessments have been performed [26]. Automatic measurement especially removes operator dependence and is more useful for repetitive measurements. However, our high-resolution device did not have this software program so we could not make this evaluation.

In conclusions, as a result of the present study and review of the previous studies, it was concluded that evaluation of vascular IMT which is a determinant for initiation of atherosclerosis as well as subclinical target organ damage should be performed on carotid and femoral arteries. The limit value for CC-IMT is used as >0.9 mm according to the guidelines whereas it may be >1.1 mm for F-IMT according to the result of the present study.

References

1. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J. 2013 Jul;34(28):2159-219.
2. Belhassen L, Carville C, Pelle G, Monin JL, Teiger E, Duval-Moulin AM, et al. Evaluation of carotid artery and aortic intima-media thickness measurements for exclusion of significant coronary atherosclerosis in patients scheduled for heart valve surgery. J Am Coll Cardiol. 2002;39:1139-44.
3. Handa N, Matsumoto M, Maeda H, Hougaku H, Ogawa S, Fukunaga R, et al. Ultrasonic evaluation of early carotid atherosclerosis. Stroke. 1990;21:1567–72.
4. Heiss G, Sharrett AR, Barnes R, Chambless LE, Szklo M, Alzola C. Carotid atherosclerosis measured by B-mode ultrasound in populations: associations with cardiovascular risk factors in the ARIC study. Am J Epidemiol. 1991;134:250–6.
5. Wofford JL, Kahl FR, Howard GR, McKinney WM, Toole JF, Crouse JR 3rd. Relation of extent of extracranial carotid artery atherosclerosis as measured by B-mode ultrasound to the extent of coronary atherosclerosis. Arterioscler Thromb. 1991;11:1786–94.
6. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK, Jr., the Cardiovascular Health Study Collaborative Research Group. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. N Engl J Med. 1999;340:14–22.
7. Sartorato P, Zulian E, Benedini S, Mariniello B, Schiavi F, Bilora F, et al. Cardiovascular risk factors and ultrasound evaluation of intima-media thickness at common carotids, carotid bulbs, and femoral and abdominal aorta arteries in patients with classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency. J Clin Endocrinol Metab. 2007;92:1015-8.
8. Belhassen L, Carville C, Pelle G, Monin JL, Teiger E, Duval-Moulin AM, et al. Evaluation of carotid artery and aortic intima-media thickness measurements for exclusion of significant coronary atherosclerosis in patients scheduled for heart valve surgery. J Am Coll Cardiol. 2002;39:1139-44.
9. Kallizaros JE, Tsioufis CP, Stefanadis CI, Pitsavos CE, Toutouzas PK. Close relation between carotid and ascending aortic atherosclerosis in cardiac patients. Circulation. 2000;102:263–8.
10. Tomochika Y, Tanaka N, Ono S, Murata K, Muro A, Yamamura T, et al. Assessment by transesophageal echography of atherosclerosis of the descending thoracic aorta in patients with hypercholesterolemia. Am J Cardiol. 1999;83:703–9.
11. Labropoulos N, Zarge J, Mansour MA, Kang SS, Baker WH. Compensatory arterial enlargement is a common pathobiologic response in early atherosclerosis. Am J Surg. 1998;176:140–3.
12. Meena D, Prakash M, Gupta Y, Bhadada SK, Khandelwal N. Carotid, aorta and renal arteries intima-media thickness in patients with sporadic idiopathic hypoparathyroidism. Indian J Endocrinol Metab. 2015;19:262-6.
13. Neiva Neto EC, Piatto MJ, Paschôa AF, Godoy Ide B, Schlaad SW, Van Bellen B. Intima-media thickness: correlation between carotids, vertebral artery, aorta and femoral arteries. Int Angiol. 2015;34:269-75.
14. Lisowska A, Musiał WJ, Knapp M, Prokop J, Dobrzycki S. Carotid and femoral atherosclerotic lesions in patients with coronary heart disease confirmed by angiography. Kardiol Pol. 2005;63:636-42.
15. Iwamoto Y, Maruhashi T, Fujii Y, Idei N, Fujimura N, Mikami S, et al. Intima-media thickness of brachial artery, vascular function, and cardiovascular risk factors. Arterioscler Thromb Vasc Biol. 2012;32:2295-303.
16. Cheng KS, Mikhailidis DP, Hamilton G, Seifalian AM. A review of the carotid and femoral intima-media thickness as an indicator of the presence of peripheral vascular disease and cardiovascular risk factors. Cardiovasc Res. 2002;54:528-38.
17. Kirhmajer MV, Banfic L, Vojkovic M, Strozzi M, Bulum J, Miovski Z. Correlation of femoral intima-media thickness and the severity of coronary artery disease. Angiology. 2011;62:134-9.

18. Sorensen KE, Kristensen IB, Celermajer DS. Atherosclerosis in the human brachial artery. J Am Coll Cardiol. 1997;29:318-22.
19. Hafner F, Kieninger A, Meinitzer A, Gary T, Froehlich H, Haas E, et al. Endothelial dysfunction and brachial intima-media thickness: long term cardiovascular risk with claudication related to peripheral arterial disease: a prospective analysis. PLoS One. 2014;9:e93357.
20. Agewall S, Henareh L, Jogestrand T. Intima-media complex of both the brachial artery and the common carotid artery are associated with left ventricular hypertrophy in patients with previous myocardial infarction. J Hypertens. 2005;23:119-25.
21. Koyoshi R, Miura S, Kumagai N, Shiga Y, Mitsutake R, Saku K. Clinical significance of flow-mediated dilation, brachial intima-media thickness and pulse wave velocity in patients with and without coronary artery disease. Circ J. 2012;76:1469-75.
22. Kirhmajer MV, Banfic L, Vojkovic M, Strozzi M, Bulum J, Miovski Z. Correlation of femoral intima-media thickness and the severity of coronary artery disease. Angiology. 2011;62:134-9.
23. Lucatelli P, Fagnani C, Tarnoki AD, Tarnoki DL, Stazi MA, Salemi M, et al. Femoral Artery Ultrasound Examination. Angiology. 2017;68:257-65.
24. Depairon M, Tutta P, van Melle G, Hayoz D, Kappenberger L, Darioli R. Reference values of intima-medial thickness of carotid and femoral arteries in subjects aged 20 to 60 years and without cardiovascular risk factors. Arch Mal Coeur Vaiss. 2000;93:721-6.
25. Cheng KS, Mikhailidis DP, Hamilton G, Seifalian AM. A review of the carotid and femoral intima-media thickness as an indicator of the presence of peripheral vascular disease and cardiovascular risk factors. Cardiovasc Res. 2002;54:528-38.
26. Mita T, Katakami N, Shiraiwa T, Yoshii H, Gosho M, Shimomura I, et al. Dose-Dependent Effect of Sitagliptin on Carotid Atherosclerosis in Patients with Type 2 Diabetes Mellitus Receiving Insulin Treatment: A Post Hoc Analysis. Diabetes Ther. 2017;8:1135-46.

J Surg Med. 2018;2(3):249-252.
DOI: 10.28982/josam.424450

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Effects of peri-operative administration of steroids on the blood glucose levels of patients with and without diabetes undergoing laparoscopic cholecystectomy

Laparoskopik kolesistektomide peroperatif uygulanan steroidin diyabetik ve diyabetik olmayan hastaların kan şekeri üzerine etkileri

Duygu Demiriz Gülmez [1], Asu Özger Özgültekin [2], Osman Ekinci [2], Mehmet Gülmez [3]

[1] Department of Anesthesiology, Op. Dr. Ergun Özdemir Görele State Hospital, Giresun, Turkey
[2] Department of Anesthesiology, University of Health Science, Haydarpasa Numune Education and Research Hospital, Istanbul, Turkey
[3] Department of General Surgery, Op. Dr. Ergun Özdemir Görele State Hospital, Giresun, Turkey

ORCID ID of the authors
DDG: 0000-0002-0874-7067
AÖÖ: 0000-0003-4307-9604
OE: 0000-0002-7891-1774
MG: 0000-0001-8803-6160

Corresponding author / Sorumlu yazar:
Duygu Demiriz Gülmez
Address / Adres: Op. Dr. Ergun Özdemir Görele Devlet Hastanesi, Anestezi Kliniği, Giresun, Türkiye
E-mail: duygudemiriz@hotmail.com

Ethics Committee Approval: The study was approved by Ethics committee of the Haydarpasa Numune Education and Research Hospital (approval No. HNEAH-KAEK 2014/KK/65).
Etik Kurul Onayı: Çalışma için etik kurul onayı Haydarpaşa Numune Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulundan (Karar No: HNEAH- KAEK 2014/KK/65) alınmıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 17.05.2018
Accepted / Kabul Tarihi: 10.06.2018
Published / Yayın Tarihi: 22.06.2018

Abstract

Aim: To examine blood glucose levels in patients with and without diabetes undergoing laparoscopic cholecystectomy under general anesthesia following intravenous administration of 8 mg dexamethasone to minimize postoperative complications.

Methods: Hundred patients, 50 patients with diabetes and 50 without diabetes, who underwent laparoscopic cholecystectomy and met the inclusion criteria, were divided into 2 groups. After administration of 8 mg dexamethasone, blood glucose values were observed at the 30th and 120th min and compared between the groups.

Results: Increase in blood glucose levels at the 30- and 120-min marks were statistically significant relative to the pre-induction blood glucose levels ($p=0.002$ and $p<0.001$, respectively) in the non-diabetic group. On comparing blood glucose levels at the 30- and 120-min marks, a statistically significant increase was seen to have occurred over time ($p<0.001$).

Conclusion: Results of the current study showed that dexamethasone caused hyperglycemia in patients with and without diabetes the 12 h after surgery. We recommend that after administration of dexamethasone, tight monitoring of blood glucose levels should be considered.

Keywords: Blood Glucose, Diabetes, Steroid

Öz

Amaç: Genel anestezi altında laparoskopik kolesistektomi yapılan diyabetik ve diyabetik olmayan hastalara postoperatif dönemde oluşabilecek komplikasyonları önlemek amacıyla uygulanan 8 mg deksametazonun kan şekeri üzerine etkilerini gözlemlemek.

Yöntemler: Laparoskopik kolesitektomi planlanan, çalışmaya katılma kriterlerini karşılayan 100 hasta, 50 diyabetik olmayan ve 50 diyabetik hasta olmak üzere iki gruba ayrıldı. 8 mg deksametazon uygulanmasından sonra 30. ve 120. dk kan şekeri değerleri ölçüldü ve gruplar arasında karşılaştırıldı.

Bulgular: Diyabetik olmayan grupta kan şekerindeki 30. ve 120. dk değerlerindeki artış indüksiyon öncesi kan şekeri değerlerine göre istatistiksel olarak anlamlı idi ($p=0.002$ ve $p<0.001$). Kan şekeri seviyelerinin 30. ve 120. dk değerleri karşılaştırıldığında, zaman ilerledikçe istatistiksel olarak anlamlı bir artış olduğu tespit edildi ($p<0.001$).

Sonuç: Çalışmamızın sonuçlarına göre deksametazon diyabetik ve diyabetik olmayan hastalarda cerrahiden 12 saat sonra hiperglisemiye yol açmaktadır. Bu sebeple deksametazon uygulanmasından sonra kan şekerinin sıkı bir şekilde izlenmesi gerektiğini önermekteyiz.

Anahtar kelimeler: Kan şekeri, Diyabet, Steroid

Introduction

Diabetes is a chronic metabolic disease that requires continuous medical care. It is characterized by insulin deficiency or related defects that lead to incomplete metabolism of carbohydrates, fats, and proteins. The prevalence of diabetes mellitus (DM) is rising globally, with the number of patients with diabetes expected to increase to 366 million by 2030 [1]. Currently, there are 2.6 million patients with diabetes in Turkey, of which approximately 0.8 million were unaware of the disease [2].

How to cite / Atıf için: Gülmez DD, Özgültekin AÖ, Ekinci O, Gülmez M. Effects of peri-operative administration of steroids on the blood glucose levels of patients with and without diabetes undergoing laparoscopic cholecystectomy. J Surg Med. 2018;2(3):249-252.

Regulation of blood glucose levels is a crucial issue in individuals undergoing surgical treatment as the associated stress can produce hyperglycemia in both patients with and without diabetes. Although no definite blood glucose values have been established thus far, it is clinically accepted that insulin treatment is necessary if the blood glucose levels rise above 180 mg/dl [3-5]. However, peri-operative hunger, long-acting insulin, or oral anti-diabetic drugs administered prior to surgery can cause hypoglycemia. Infections and myocardial infarctions are also common complications associated with DM, with the risk of infection during the postoperative period being dependent on the peri-operative blood glucose levels rather than the HbA1c values [6,7]. Specifically, the risk of postoperative infection increases by 30% with every 40 mg/dL increase in blood glucose levels during surgery [8].

The risk of hyperglycemia can be minimized by selecting minimally invasive surgical procedures and neuroaxial anesthesia, both of which are associated with less surgical stress [9-11]. During general anesthesia, volatile anesthetics may increase blood glucose levels by promoting hepatic glucose production [3].

Administration of glucocorticoids during the peri-operative period can reduce the inflammatory, hormonal, and immunological effects of surgical stress, and prevent complications such as postoperative nausea, vomiting, and laryngeal edema. Additionally, these corticosteroids can also reduce peripheral and hepatic insulin sensitivity by affecting the post-receptor mechanisms, and increase the blood glucose levels by promoting gluconeogenesis or, in other words, the production of glucose from amino acids and fats. This effect may impair blood glucose regulation in both patients with and without diabetes, and previous studies have shown that even low doses of corticosteroids can lead to hyperglycemia [12].

The current study examined blood glucose levels in patients with and without diabetes undergoing laparoscopic cholecystectomy under general anesthesia following intravenous administration of 8 mg dexamethasone to minimize postoperative complications.

Materials and methods

This prospective, case-control study was conducted at the Department of Anesthesiology, Haydarpasa Numune Education and Research Hospital, Istanbul, Turkey, between August 2015 and August 2016. Ethical approval was obtained from the research ethics committee of the Haydarpasa Numune Education and Research Hospital (approval No. HNEAH-KAEK 2014/KK/65); informed consent was obtained from all patients. This study was conducted in accordance with the tenets of the Declaration of Helsinki.

This study included 110 patients (age: 18–70 years) who were scheduled to undergo laparoscopic cholecystectomy. Of these, 10 patients were excluded from the study as one patient with diabetes and 3 patients without diabetes required additional steroids and 3 patients with diabetes and 3 patients without diabetes required surgical treatment that exceeded 2 h in duration. The final sample thus consisted of 100 patients (50 patients with diabetes and 50 without diabetes).

The exclusion criteria included a history of undergoing radiotherapy or chemotherapy within the last 6 months, body mass index >40 kg/m^2, immunosupression, and surgical durations exceeding 2 h due to associated complications. Patients using inhaled corticosteroids were also ineligible for inclusion as were those > 18 years and pregnant women.

Patients who underwent laparoscopic cholecystectomy at the Haydarpasa Numune Training and Research Hospital and met the inclusion criteria were divided into 2 groups based on the presence or absence of DM. Patients were pre-medicated with 0.5 mg atropine sulfate and 10 mg diazepam 30 min prior to surgery, and were monitored throughout the procedure. The fingertip blood glucose values were also measured using strips at the same time.

In order to check the accuracy of the glucometer devices Accu-Check (Roche Diagnostics, Indianapolis, IN) which were calibrated regularly, the blood glucose values of the first patient with diabetes were measured in the laboratory and compared with the values observed on the devices. Similar studies have previously measured blood glucose levels using a glucometer [13].

In the current study, routine administration of 0.5–1 mcg/kg fentanyl, 2 mg/kg propofol, and 1 mg / kg vecuronium bromide was carried out. Additionally, 8 mg dexamethasone was also delivered intravenously to prevent postoperative nausea and vomiting. Anesthesia was induced by administering 1% sevoflurane, 0.05–0.5 mcg/kg/min remifentanil infusion and 50% O_2 / 50% air. Additionally, 0.9% isotonic NaCl solution was administered throughout the operation, and blood glucose levels were measured using a fingertip strip. The values observed at the 30^{th} and 120^{th} min after dexamethasone administration were compared between the diabetic and non-diabetic (ND) groups.

Statistical analysis

The data have been presented using descriptive statistical methods (frequency, percentage, mean, standard deviation), and the Kolmogorov-Smirnov distribution test was used to examine the distribution of the data. Pearson's Chi-square test and Fisher's Exact test were used to compare categorical variables, and a t-test was used to compare parameters between groups. Repeat measurements of ANOVA were used for intra-group comparisons, and the level of statistical significance was set at p-value <0.05. All statistical analyses were performed using a statistical package, SPSS 21.0.

Results

This study included 100 patients, of which 50 were diagnosed with DM and 50 were without diabetes. Twelve (24.0%) of the patients in the DM group managed their diagnosis using exercise and diet, 30 (60.0%) patients used OAD, and 8 (16.0%) patients used insulin.

The mean age of patients in the DM group was significantly higher (p=0.004) than that of patients in the ND group. No significant differences in weight, height, gender, BMI (body mass index), and duration of surgery were observed between the DM and ND groups (p>0.05).

The pre-induction blood glucose, 30-min blood glucose, and 120-min blood glucose levels were significantly higher in the DM group (p<0.001). The increase in blood glucose levels at

the 30 min mark was not statistically significant relative to the pre-induction blood glucose levels (p=0.287) in this group. However, the increase observed at the 120-min mark was statistically significant relative to the pre-induction blood glucose levels (p<0.001). Moreover, upon comparing the blood glucose levels at the 30- and 120-min marks, a statistically significant increase was seen to have occurred over time (p<0.001).

In the ND group, the increase in blood glucose levels at the 30- and 120-min marks were seen to be statistically significant relative to the pre-induction blood glucose levels (p=0.002 and p<0.001, respectively). Moreover, upon comparing the blood glucose levels at the 30- and 120-min marks, a statistically significant increase was seen to have occurred over time (p<0.001) (Table 1).

Table 1: Binary Pairwise Comparison of Data

Group	(I) measurement	(J) measurement	Mean Difference (I-J)	Std. Error	p	95% Confidence Interval of Difference [1] Lower	Upper
DM	1	2	−6.940	4.083	0.287	−17.062	3.182
		3	−34.860*	5.836	<0.001	−49.327	−20.393
	2	1	6.940	4.083	0.287	−3.182	17.062
		3	−27.920*	5.043	<0.001	−40.421	−15.419
	3	1	34.860*	5.836	<0.001	20.393	49.327
		2	27.920*	5.043	<0.001	15.419	40.421
ND	1	2	−10.380*	2.889	0.002	−17.541	−3.219
		3	−32.280*	4.720	<0.001	−43.981	−20.579
	2	1	10.380*	2.889	0.002	3.219	17.541
		3	−21.900*	4.456	<0.001	−32.946	−10.854
	3	1	32.280*	4.720	<0.001	20.579	43.981
		2	21.900*	4.456	<0.001	10.854	32.946

DM: Diabetes mellitus, ND: non-diabetic, * indicates p<0.05 and a statistically significant difference between the mean values, [1] Bonferroni multiple comparison test was used.
I and J represent the variable coding assigned by SPSS for the comparison of measurements. The differences between these codings and the mean values of the measurements were determined
1 = pre-induction blood glucose level
2 = blood glucose level at 30 min
3 = blood glucose level at 120 min

Discussion

Surgical stress is known to induce insulin resistance and hyperglycemia in patients with and without diabetes by triggering the secretion of hormones such as the growth factor hormone, glucagon, catecholamine and glucocorticoids. Hyperglycemia is induced within the first hour of surgery, and is seen to persist until the fifth postoperative day, proportionate to the magnitude of the surgical stress.

Glucocorticoids can be used to reduce the inflammatory, hormonal, and immunological effects of surgical stress in the peri-operative period [14]. Preoperative intravenous dexamethasone reduces postoperative inflammation and its associated laryngeal edema [15]. Dexamethasone also prevents postoperative nausea and vomiting [12]. A previous randomized, controlled, double-blinded study conducted by Thue Bisgaard et al. [16] included administration of either 8 mg dexamethasone or a placebo 90 min prior to laparoscopic cholecystectomy treatment. The patients were followed up with for 2 days postoperatively, and the pain, infection, vomiting and respiratory functions scores were recorded. Comparison of the 2 groups exhibited a reduction in these parameters, and the authors suggested that this could be attributed to the anti-inflammatory and immunosuppressive effects of dexamethasone.

Peri-operative steroids have both positive and negative effects, and the most significant adverse effect that may increase the risk of mortality and morbidity is that it increases hyperglycemic activity, even at low doses. Hans et al. [12] measured the blood glucose levels following administration of 10 mg dexamethasone to prevent postoperative nausea and vomiting following abdominal operations in 32 patients without diabetes and 31 patients with diabetes. The blood glucose values were seen to increase in both groups. Moreover, the blood glucose levels peaked at 120 min after dexamethasone administration in both groups, and the rate of elevation of blood glucose was also similar between the groups. These results demonstrated that even doses as low as 8 mg could induce significant elevations in blood glucose levels [12].

Given that surgical stress causes hyperglycemia and steroids administered for various reasons can contribute to this hyperglycemic effect further, peri-operative monitoring of patients with diabetes is essential as the risk of diabetic ketoacidosis or hyperglycemic hyperosmolar syndrome is increased. Delay in wound healing due to hyperglycemia, cerebral ischemia, renal ischemia, endothelial dysfunction, or wound infection may also occur.

These complications can directly affect the risk of postoperative mortality and morbidity, thus leading us to question exactly how much influence peri-operative administration of steroids had on the blood glucose levels of patients with and without diabetes. This study included patients undergoing laparoscopic cholecystectomy instead of open cholecystectomy [9,17] in order to minimize and standardize the effects of surgical stress on blood glucose levels.

Glucocorticoids were administered at various doses (8 mg, 10 mg, and 16 mg) to prevent postoperative nausea and vomiting, and no significant differences in the antiemetic effects were observed. Administration of 8 mg dexamethasone during induction was preferred as this was believed to be the minimum effective dose associated with the least side-effects.

A similar study conducted by Basem et al. [13] examined the effects of low doses of steroids on the blood glucose levels of surgically stressed patients with and without diabetes (n = 185). The authors proposed 2 hypotheses, as follows: a) patients with diabetes were more likely to exhibit an increase in blood glucose levels than those without diabetes, and b) steroid injections would lead to higher blood glucose levels in patients with diabetes than in those without diabetes. Dexamethasone (8 mg) and placebos were administered pre-surgically in 90 and 95 patients, respectively. The results of this study showed that patients with diabetes exhibited higher preoperative blood glucose levels than those without diabetes, and both groups presented with significantly elevated blood glucose levels during the operation. However, patients without diabetes exhibited a significant elevation of blood glucose levels following steroid injection, and this was in contrast to the patients with diabetes whose blood glucose levels were not significantly elevated after steroid injection.

Lunkins et al. [18] included 34 patients without diabetes undergoing craniotomy in their study. Of these, one group of patients received placebos only, one group received preoperative dexamethasone, one group received 10 mg of intravenous dexamethasone, and one group of patients received 4 mg of intravenous dexamethasone 6 h after surgery. All of the patients exhibited an increase in blood glucose levels for a period

of 12 h. The highest increase in blood glucose levels was observed within the first 8–10 h in patients that had received intraoperative dexamethasone.

In our study, although the increase in blood glucose levels observed in patients without diabetes 30 min after induction was statistically significant, measured values were clinically acceptable in both groups (mean value: DM group = 135.6 mg/dl; ND group = 111.14 mg/dL). The increase in blood glucose level 120 min after induction was clinically significant in both patients with and without diabetes. Moreover, the peak blood glucose level was 265 mg/dl in the DM group and 275 mg/dl in the ND group.

Pasternak at al. examined the effects of 10 mg of dexamethasone administered to prevent cerebral edema in patients undergoing craniotomy, and found that the mean blood glucose levels were significantly higher in patients who had received dexamethasone than in those who had received the placebo [19].

The findings of these studies were in agreement with those of the current one, which also observed a clinically significant increase in mean blood glucose levels following glucocorticoid administration.

The study is limited by the fact that all the patients received 8 mg dexamethasone. The effect of dexamethasone should be assessed in comparison with patients who received placebo.

Dexamethasone has anti-inflammatory properties that prevent the adverse effects of surgical stress, affect post-receptor mechanisms, and cause hyperglycemia by reducing peripheral and hepatic insulin sensitivity. In agreement with this, the results of the current study showed that dexamethasone caused hyperglycemia in both patients with and without diabetes in the 12 h after surgery. We recommend that after administration of dexamethasone, tight monitoring of blood glucose levels should be considered.

References

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004;27:1047-53.
2. Satman I, Yilmaz T, Sengül A, Salman S, Salman F, Uygur S, et al. Population-based study of diabetes and risk characteristics in turkey results of the Turkish diabetes epidemiology study (TURDEP). Diabetes Care. 2002;25:1551-6.
3. Smiley DD, Umpierrez GE. Perioperative glucose control in the diabetic or nondiabetic patient. South Med J. 2006;99:580.
4. Juul AB, Wetterslev J, Kofoed-Enevoldsen A. Long-term postoperative mortality in diabetic patients undergoing major non-cardiac surgery. Eur J Anaesthesiol. 2004;21:523-9.
5. Moghissi ES, Korytkowski MT, DiNardo M, Einhorn D, Hellman R, Hirsc h IB, et al. American association of clinical endocrinologists and American diabetes association consensus statement on inpatient glycemic control. Endocr Pract. 2009;15:353-69.
6. Robertshaw HJ, McAnulty GR, Hall GM. Strategies for managing the diabetic patient. Best Pract Res Clin Anaesthesiol. 2004;18:631-43.
7. Latham R, Lancaster AD, Covington JF, Pirolo JS, Thomas CS. The association of diabetes and glucose control with surgical-site infections among cardiothoracic surgery patients. Infect Control. 2001;22:607-12.
8. Ramos M, Khalpey Z, Lipsitz S, Steinberg J, Panizales MT, Zinner M, et al. Relationship of perioperative hyperglycemia and postoperative infections in patients who undergo general and vascular surgery. Ann Surg. 2008;248:585-91.
9. Moitra VK, Meiler SE. The diabetic surgical patient. Curr Opin Anaesthesiol. 2006;19:339-45.
10. Ljungqvist O, Nygren J, Soop M, Thorell A. Metabolic perioperative management: novel concepts. Curr Opin Crit Care. 2005;11:295-9.
11. Thorell A, Nygren J, Ljungqvist O. Insulin resistance: a marker of surgical stress. Curr Opin Clin Nutr Metab Care. 1999;2:69-78.
12. Hans P, Vanthuyne A, Dewandre PY, Brichant JF, Bonhomme V. Blood glucose concentration profile after 10 mg dexamethasone in non-diabetic and type 2 diabetic patients undergoing abdominal surgery. Br J Anaesth. 2006;97:164-70.
13. Abdelmalak BB, Bonilla AM, Yang D, Chowdary HT, Gottlieb A, Lyden SP, et al. The hyperglycemic response to major noncardiac surgery and the added effect of steroid administration in patients with and without diabetes. Anesth Analg. 2013;116:1116-22.
14. Holte K, Kehlet H. Perioperative single-dose glucocorticoid administration: pathophysiologic effects and clinical implications. J Am Coll Surg. 2000;195:186-712.
15. Weber CR, Griffin JM. Evaluation of dexamethasone for reducing postoperative edema and inflammatory response after orthognathic surgery. J Oral Maxillofac Surg. 1994;52:35-9.
16. Bisgaard T, Klarskov B, Kehlet H, Rosenberg J. Preoperative dexamethasone improves surgical outcome after laparoscopic cholecystectomy: a randomized double-blind placebo-controlled trial. Ann Surg. 2003;238:651-60.
17. Ljungqvist O, Nygren J, Soop M, Thorell A. Metabolic perioperative management: novel concepts. Curr Opin Crit Care. 2005;11:295-9.
18. Lukins MB, Manninen PH. Hyperglycemia in patients administered dexamethasone for craniotomy. Anesth Analg. 2005;100:1129-33.
19. Pasternak JJ, McGregor DG, Lanier WL. Effect of single-dose dexamethasone on blood glucose concentration in patients undergoing craniotomy. J Neurosurg Anesthesiol. 2004;16:122-5.

J Surg Med. 2018;2(3):253-256.
DOI: 10.28982/josam.435834

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Can failure of choledochal cannulation in endoscopic retrograde cholangiopancreatography be prevented?

Endoskopik retrograd kolanjiyopankreatografide kanülasyon başarısızlığı önlenebilir mi?

Yahya Kemal Çalışkan [1], Mustafa Uygar Kalaycı [1]

[1] Department of General Surgery, University of Health Science, Kanuni Sultan Suleyman Education and Research Hospital, Istanbul, Turkey

ORCID ID of the authors
YKÇ: 0000-0003-1999-1601
MUK: 0000-0002-2215-0072

Corresponding author / Sorumlu yazar:
Yahya Kemal Çalışkan
Address / Adres: Sağlık Bilimleri Üniversitesi, Kanuni Sultan Süleyman Eğitim ve Araştırma Hastanesi, Genel Cerrahi kliniği, Küçükçekmece, İstanbul, Türkiye
E-mail: yahyakemalc@yahoo.com

Ethics Committee Approval: Ethics committee approval was not received because the study was performed retrospectively.
Etik Kurul Onayı: Çalışmamız retrospektif olması nedeniyle etik kurul onayı alınmamıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 23.06.2018
Accepted / Kabul Tarihi: 25.06.2018
Published / Yayın Tarihi: 25.06.2018

Abstract

Aim: Endoscopic retrograde cholangiopancreatography (ERCP) is frequently used in the diagnosis and treatment of hepatic, biliary and pancreatic diseases. Failure during cannulation, however, requires other interventions. The purpose of this work is to create the parameters that can be used to predict failure during ERCP.

Methods: Case control study planned. ERCP procedures between December 2016 and February 2018 were evaluated. Duplicate attempts and causes, cannulation status were recorded and the factors affecting cannulation were examined. Descriptive analyzes were used for statistical evaluation, chi-square test for categorical data and t-test for continuous data. A p value of 0.05 or less was considered statistically significant in the analysis.

Results: A total of 458 ERCP procedures were performed in 288 patients during the study period. 159 of the patients were female, 129 were male, female / male ratio was 1.2, mean age was 59±17.9 and age range was 17-105. When ERCP indications were evaluated, 258 patients (89.6%) were treated due to choledocholithiasis. In the first procedure, selective choledochal cannulation was successful in 257 (89.3%) patients (229 patients with ERCP catheter and 28 patients with assisted methods), and these patients constituted study group. The remaining patients who cannulation was failed included in control group. There were no age and gender differences in the patients who failed cannulation (p: 0.270, 0.256, respectively). In failed cases, the duodenal diverticulum and pancreas head tumor were seen. In the first operation, 264 patients, mainly choledocholithiasis (n: 214), could be diagnosed.

Conclusion: It has been shown that the gender and age of the patient and structural differences such as the duodenal diverticulum do not affect the success of cannulation during ERCP. Upper abdominal operations like Billroth II and Roux-en-Y gastrojejunostomy reduce the success rate of cannulation. It is thought that the correlation between experience level of endoscopist and cannulation success.

Keywords: Endoscopic retrograde cholangiopancreatography, Choledochal cannulation, Prevention

Öz

Amaç: Endoskopik retrograd kolanjiyopankreatografi (ERCP) sıklıkla hepatik, safra yolları ve pankreatik hastalıkların tanı ve tedavisinde kullanılır. Bununla birlikte, kanülasyon sırasında başarısızlık diğer müdahaleleri gerektirir. Bu çalışmanın amacı, ERCP sırasında başarısızlığı öngörmek için kullanılabilecek parametreleri oluşturmaktır.

Yöntemler: Olgu kontrol çalışması planlandı. Aralık 2016 - Şubat 2018 tarihleri arasında gerçekleştirilen ERCP işlemleri değerlendirildi. Hastalarda gerçekleştirilen mükerrer girişimler ve nedenleri, kanülasyon durumları kayıt edildi ve kanülasyonu etkileyen faktörler incelendi. İstatistik değerlendirmede tanımlayıcı analizler, kategorik veriler için Ki-kare testi ve sürekli veriler için t-testi testi kullanıldı. Analizlerde p değerinin 0,05 ve daha düşük olması istatistiksel olarak anlamlı kabul edildi.

Bulgular: Çalışma döneminde 288 hastaya uygulanan toplam 458 ERCP işlemi uygulandı. Hastaların 159'u kadın, 129'u erkek, kadın/erkek oranı 1,2, yaş ortalaması 59±17,9 ve yaş aralığı 17-105'di. ERCP endikasyonu değerlendirildiğinde 258 (%89,6) hastada koledokolityazis nedeniyle işlemin gerçekleştirildiği görüldü. İlk işlemde 229 hastada ERCP kateteri ile ve 28 hastada yardımcı yöntemler ile olmak üzere 257 (%89,3) hastada selektif koledok kanülasyonu başarılı oldu. 236 hastada 15 dakikadan az süre içinde kanülasyon başarılı oldu. 31 (%10,7) hastada kanülasyon ilk işlemde başarısız oldu. Başarısız olan hastalarda yaş ve cinsiyet açısından fark saptanmadı (sırasıyla p: 0,270, 0,256). Başarısızlık sebebi olarak geçirilmiş mide-duodenum ameliyatları, duodenum içi divertikül, pankreas başı tümörü görüldü. İlk işlemde başlıca koledokolityazis (n:214) olmak üzere 264 hastaya tanı konulabildi.

Sonuç: Hastanın cinsiyeti, yaşı ve duodenal divertikülü gibi yapısal farklılıkları ERCP sırasında kanülasyonun başarısını etkilemediği gösterildi. Billroth II ve Roux-en-Y gastrojejunostomi gibi üst karın ameliyatlarının kanülasyon başarı oranını düşürdüğü görüldü. Endoskopistlerin tecrübe seviyeleri ile kanülasyon başarısı arasında korelasyon olduğu düşünülmektedir.

Anahtar kelimeler: Endoskopik retrograd kolanjiyopankreatografi, Koledok kanülasyonu, Önleme

How to cite / Atıf için: Çalışkan YK, Kalaycı MU. Can failure of choledochal cannulation in endoscopic retrograde cholangiopancreatography be prevented? J Surg Med. 2018;2(3):253-256.

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a complex endoscopic procedure with complications. It is widely used in the diagnosis and treatment of pancreatic and biliary system diseases. Recently, the use of non-invasive imaging methods such as computerized tomography, magnetic resonance cholangiopancreatography, and the positive contribution they have made to diagnosis, the use of ERCP for diagnostic purposes, and the use of therapeutic procedures, especially endoscopic sphincterotomy (ES), have increased. Diagnostic ERCP related complications are common; complications such as bleeding, perforation and pancreatitis are more due to ES. It has been shown that a large number of parameters originating from the patient, endoscopist, and procedure are effective on ERCP complications [1,2].

The achievement of ERCP includes the cannulation of the biliary tract and acquiring a cholangiogram on the grounds that cannulation is the initial step for both symptomatic and restorative mediations [3]. Disappointment amid cannulation renders the ERCP unsuccessful and offers ascend to different results, including cholangitis and pancreatitis, which may require mediations, for example, percutaneous transhepatic cholangiography (PTC) and medical procedure, with higher morbidities [4].

In this study, we aimed to determine factors associated with cannulation failure of ERCP intervention.

Materials and methods

Case-control study was planned, and Helsinki Declaration principles about study of Human subjects were applied through the study. Between December 2016 and February 2018, 288 consecutive patients scheduled for ERCP were included in the study. All ERCP procedures were performed by the same endoscopist (YKC). All of the patients were informed about the procedure and the risks to be done and the confirmation form was taken. Comprehensive anamnesis was obtained from all patients before the procedure and physical examination was performed. Complete blood count, hemostasis tests, blood urea, electrolyte, glucose, ALT, AST, alkaline phosphatase, gamma glutamic transpeptidase and bilirubin levels were measured. Electrocardiography, pulmonary and direct abdominal graphs were recorded. All of the patients started prophylactic antibiotics. Olympus and Pentax duodenoscopes with a working channel of 2.8 mm were used for ERCP. As the electrosurgical unit, manually operated Erbe 200 S electro-cautery was used. All cases were sedated with pharyngeal anesthesia with lidocaine spray and midazolam as needed. Hypocine N-butyl bromide (Buscopan ampule, Eczacıbaşı İlaç San. ve Tic. AŞ) was used as antiperistaltic drug. The cannulation was started with the standard ERCP catheter and tapered catheter, sphincterotomy and guidewire were used respectively in cases that cannulation could not be done. If the cannulation could not be achieved with these, the precut was applied. The incidence of periampullary diverticulum during perforation, papilline appearance, number of interventions applied to the papilla for cannulation and duration of cannulation, which accession was performed with the accession, precut incision, number of pancreas cannulation, number of pancreas drainage after pancreatic drainage, bleeding occurred, clot development, obstruction state, ERCP diagnosis, therapeutic procedures, complete or partial success or failure of the procedure, buscopan amount used and sedation applied and amount of application were recorded. After the procedure is over, the patients are supine; perforation, drainage of the pancreatic duct, abdominal and mediastinal regions in terms of residual stone and biliary drainage were examined by fluoroscopy. The principle basis for the achievement of ERCP was the cannulation of the biliary tract.

Statistical analysis

Statistics were performed with Statistics Package for Social Sciences (IBM SPSS statistics version 23, IBM Corporation, USA). Variables are expressed as mean ± standard deviations (SD) or as medians (range) depending on distribution. Categorical variables were expressed as frequencies and percentages. The Chi-square and Fisher's exact tests were used for comparison of continuous parametric variables. Normality was assessed by means of the Kolmogorov–Smirnov test. The t-test was used for comparison of parametric variables with normal distribution. The statistical results were presented with a 95% confidence interval (CI). The differences were considered statistically significant if the p-value was less than 0.05.

Results

Of the 288 patients studied, 129 were male and 159 were female (female / male ratio: 1.2). The mean age was 59±17.9 years and ranged from 17 to 105 years. Selective choledochal cannulation was successful at 257 (89.3%) patients in first attempt. 28 of these cannulation were possible by the help of assisted methods, and these patients constituted study group. In the first procedure, the cannulation was failed in 31 (10.7%) patients, and these patients included in control group. There were no age and gender differences between groups (p=0.270, 0.256, respectively).

The mean duration of choledochal cannulation was 7.2 minutes, and the mean total procedure time was 26 minutes. In 236 patients, the cannulation was successful in less than 15 minutes.

In ERCP diagnosis, there were 214 cases of choledocholithiasis, 19 cases of malignant biliary stricture, 6 cases of benign biliary stricture, 8 cases of postoperative bilateral fistula, 7 cases of biliary obstruction, and 7 cases of biliary pancreatitis. Some of the patients had more than one pathology. Therapeutic procedures were ES in 196 patients, stone removal in 140 patients, and biliary stent in 56 patients.

A diverticulum was detected in 34 (11.8%) patients. A precut incision was performed in 54 (18.7%) patients. At the point when the impact of duodenal diverticula on the cannulation achievement rate was assessed, it was discovered that cannulation was effective in 31 (91.2%) of the patients who have a diverticulum. A factual examination demonstrated that duodenal diverticula does not impact the cannulation achievement rate (p=0.356).

A total of 34 (11.8%) patients previously had a history of upper abdominal surgery. Of the 34 patients with an upper abdominal surgery, the ampulla was cannulated in 30 (88.2%)

cases. The cannulation achievement rate in patients with a past upper abdominal surgery was lower (p=0.031).

Discussion

In most prospective studies, the rate of early complication due to ERCP and / or sphincterotomy is 5% -10% [2-4]. ERCP-related death is rare (<0.5%) and is often associated with cardiopulmonary complications [5,6]. Advanced age is generally considered an important factor, but multivariate analyzes do not support it [6]. The underlying disease and operation are the most important factors. In previous studies, ERCP bleeding rate was 20% [7], but in recent studies this rate decreased to 1-2% [8-11]. Bleeding usually results in endoscopic sphincterotomy (ES) and is usually seen early. Bleeding ranges from 0.9% to 2.3% in the literature [4,5], which is 3.1% higher than reported in the literature. ES-linked bleeding is due to precut incision, needle-tipped sphincterotome pre-incision, and pulsed shear flow. Actually precut incision may increase the cannulation but can increase the complications [11].

Accomplishment amid ERCP suggests the cannulation of the biliary tract and acquiring the cholangiogram on the grounds that cannulation is the initial step for both demonstrative and, if vital, remedial mediations [3]. It ought to likewise be noticed that cannulation disappointment renders ERCP unsuccessful and may prompt genuine consequences. These incorporate cholangitis and pancreatitis and may require intercessions with higher morbidities, for example, PTC and medical procedure [4].

There are few examinations in the restorative writing with respect to age and cannulation achievement rates amid ERCP. Lobo et al. [12] demonstrated that the recurrence of periampullary diverticula increments fundamentally in patients more than 75 years old, and they found that cannulation achievement rates diminish altogether because of diverticula that expansion with age. While assessing our information, age was not observed to be a hazard factor for effective cannulation in the single-variable examination. In the numerous variable investigation, the disappointment rate was found to have expanded by 1.01-overlay for every one-year increment in the patient's age.

There is additionally no information with respect to the effect of sex on the cannulation achievement rate. In a Japanese report by Fukatsu et al., the accomplishment of ERCP was accounted for to be bring down in ladies [3]. In spite of the fact that the cannulation achievement rate was observed to be altogether lower in the single-variable examination in our arrangement, sex was not observed to be a factor impacting the disappointment of ERCP in the numerous variable investigation.

The connection between duodenal diverticula and the cannulation achievement rate has been explored in detail. There are distinctive perspectives with respect to the impact of duodenal diverticula on cannulation. Lobo et al. [12] confirmed that the recurrence of duodenal diverticula increments with age and declines the cannulation achievement rate. They found that the accomplishment of treating intradiverticular papillas was essentially lower than that of juxtadiverticular papillas. In an examination directed on 400 patients, Boix et al. [13] recognized periampullary diverticula in 131 (32.8%) patients. Fukatsu et al. [3] found a 15% recurrence of duodenal diverticula in their arrangement, and they didn't view this as a factor affecting the cannulation achievement rate. In our study, duodenal diverticula were distinguished in 11.8% of the patients. Investigation proposed that the nearness of duodenal diverticula does not impact the cannulation achievement rate.

In the arrangement by Choudari et al. [14], Billroth I or II arrangement, Roux-en-Y gastrojejunostomy, gastric outlet block, and narrowing of the duodenum have been recorded as purposes behind ERCP disappointment. In an investigation by Baron et al. [15], Billroth II medical procedure, gastrojejunostomy, hepaticojejunostomy, Whipple procedure, and gastrointestinal impediments or narrowing were accounted for to cause ERCP failure. In our study, previous upper abdominal surgery was found as related with cannulation failure.

The risk factors for failure of ERCP cannulation may vary depending on the parameters used in the studies and the number of patients. It is possible and necessary to know the technical risk factors involved, including the endoscopist's experience, and they should be minimized as possible.

In conclusion, gender and age of the patient do not have any influence on the cannulation success rate during ERCP. Also we detected that anatomical changes like duodenal diverticula does not affect cannulation success. However, previous upper abdominal surgery has a negative effect on the cannulation success rate during ERCP. In addition, experience of endoscopist may effect on cannulation success.

References

1. Cheng CL, Sherman S, Watkins JL, Barnett B, et al. Risk Factors for Post-ERCP Pancreatitis: A Prospective Multicenter Study. Am J Gastroenterol. 2006;101:139-47.
2. Freeman ML, DiSario JA, Nelson DB, Fennerty MB, et al. Risk factors for post-ERCP pancreatitis: a prospective, multicenter study. Gastrointest Endosc. 2001;54:425-34.
3. Fukatsu H, Kawamoto H, Kato H, et al. Evaluation of needleknife precut papillotomy after unsuccessful biliary cannulation, especially with regard to postoperative anatomic factors. Surgical Endoscopy and Other Interventional Techniques. 2008;22(3):717–23.
4. Perdue DG, Freeman ML. ERCOST Study Group. Failed biliary ERCP: a prospective multicenter study of risk factors, complications and resource utilization. Gastrointestinal Endoscopy. 2004;59(5):192.
5. Freeman ML. Adverse outcomes of endoscopic retrograde cholangiopancreatography. Rev Gastroenterol Dis. 2002;2:147-68.
6. Freeman ML. Adverse outcomes of ERCP. Gastrointest Endosc. 2002;56:273-82.
7. Sherman S, Lehman GA. Complications of endoscopic retrograde cholangiopancreatography and endoscopic sphincterotomy. In: Barkin J, O'Phelan CA, eds. Advanced Therapeutic Endoscopy New York: Raven Press 1990:201-10.
8. Masci E, Toti G, Mariani A, et al. Complications of diagnostic and therapeutic ERCP: a prospective multicenter study. Am J Gastroenterol. 2001;96:417-23.
9. Freeman ML, Nelson DB, Sherman S, et al. Complications of endoscopic biliary sphincterotomy. N Engl J Med. 1996;335:909-18.
10. Freeman ML, Nelson DB, Sherman S, et al. Same-day discharge after endoscopic biliary sphincterotomy: observations from a prospective multicenter complications study. Gastrointest Endosc. 1999;49:580-6.
11. Leung JWC, Chan FKL, Sung JJY, Chung S. Endoscopic sphincterotomy-induced hemorrhage: a study of risk factors and the role of epinephrine injection. Gastrointest Endosc. 1995;42:550-4.
12. Lobo DN, Balfour TW, Iftikhar SY. Periampullary diverticula: consequences of failed ERCP. Annals of the Royal College of Surgeons of England. 1998;80(5):326–31.

13. Boix J, Lorenzo-Z´u˜niga V, A˜na˜nos F, Dom`enech E, Morillas RM, Gassull MA. Impact of periampullary duodenal diverticula at endoscopic retrograde cholangiopancreatography: a proposed classification of periampullary duodenal diverticula. Surgical Laparoscopy, Endoscopy and Percutaneous Techniques. 2006;16(4).208–11.
14. Choudari CP, Sherman S, Fogel EL, et al. Success of ERCP at a referral center after a previously unsuccessful attempt. Gastrointestinal Endoscopy. 2000;52(4):478–83.
15. Baron TH, Petersen BT, Mergener K, et al. Quality indicators for endoscopic retrograde cholangiopancreatography. American Journal of Gastroenterology. 2006;101(4): 892–97.

J Surg Med. 2018;2(3):257-261.
DOI: 10.28982/josam.420428

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Assessment of regional cerebral blood flow in patients with early and late onset alcohol dependence: SPECT study

Erken ve geç başlangıçlı alkol bağımlılarında bölgesel beyin kan akımının değerlendirilmesi: SPECT çalışması

Esin Erdoğan [1], Erdal Vardar [2], Gülay Durmuş Altun [3], Mehmet Fatih Fırat [4]

[1] Department of Psychiatry, University of Health Sciences, Izmir Bozyaka Training and Research Hospital, Izmir, Turkey
[2] Department of Psychiatry, Trakya University, School of Medicine, Edirne, Turkey
[3] Department Nuclear Medicine, Trakya University, School of Medicine, Edirne, Turkey
[4] Department Nuclear Medicine, Dr Siyami Ersek Thorasic and Cardiovascular Surgery Training and Research Hospital, Istanbul, Turkey

ORCID ID of the authors
EE: 0000-0003-0100-652X
EV: 0000-0002-5836-6174
GDA: 0000-0001-9340-1476
MFF: 0000-0002-9029-8773

Corresponding author / Sorumlu yazar:
Esin Erdoğan
Address / Adres: Sağlık Bilimleri Üniversitesi, İzmir Bozyaka Eğitim ve Araştırma Hastanesi, Psikiyatri Bölümü, Saim Çıkrıkçı Cad. No:59, Karabağlar, İzmir, Türkiye
E-mail: dresinerdogan@gmail.com

Ethics Committee Approval: Ethics committee approval was obtained from the ethics committee of Trakya University Medical Faculty.
Etik Kurul Onayı: Etik kurul onayı Trakya Üniversitesi, Tıp Fakültesi etik kurulundan alınmıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 02.05.2018
Accepted / Kabul Tarihi: 26.06.2018
Published / Yayın Tarihi: 27.06.2018

Abstract

Aim: Alcohol dependence has negative effects on the structure and functionality of the brain. The age of onset of alcohol is an important parameter in the grouping of alcoholics. The aim of this study is to compare whether regional cerebral blood flow (r-CBF) values differ between early (EO) versus late onset (LO) alcoholic patients.

Methods: A total of 33 male patients with alcohol dependence as per DSM-IV criteria and 13 healthy controls were enrolled for the study. Regional measures of cortical cerebral blood flow were assessed using a high resolution Tc-99m-HMPAO single photon emission computed tomography (SPECT). Alcoholic subjects were divided into two groups according to onset of problematic alcohol drinking age.

Results: When three groups were compared, r-CBF differences were obtained in inferior frontal, inferior temporal, inferior left occipital and middle left frontal regions. Decreased r-CBF values were found in LO group when they compared to controls in both lower frontal and temporal regions ($p<0.05$). LO group showed significant reduced r-CBF values in regions of inferior frontal and temporal, inferior left occipital and middle left frontal when compared with EO.

Conclusion: Our findings revealed that, there were differences in r-CBF values in EO and LO alcoholics at early abstinence period. These findings suggest that frontal lobes have a key role in alcoholism neurobiology, as noted in previous studies. Repeating the measurements after a long-term abstinence will be useful in revealing differences among the alcoholic groups.

Keywords: Alcoholism, SPECT, Cerebral blood flow

Öz

Amaç: Alkol bağımlılığının beynin yapısı ve işlevselliği üzerinde olumsuz etkileri vardır. Alkole başlangıç yaşı, alkol bağımlılarının gruplandırılmasında önemli bir parametredir. Bu çalışmanın amacı erken (EB) ve geç başlangıçlı (GB) alkol bağımlılarında bölgesel beyin kan akımı (b-BKA) değerlerlerinin farklılık gösterip göstermediğini karşılaştırmaktır.

Yöntemler: DSM-IV ölçütlerine gore alkol bağımlılğı tanısı olan 33 erkek hasta ve 13 sağlıklı control çalışmaya alınmıştır. Kortikal serebral kan akımının bölgesel değerleri yüksek çözünürlüklü Tc-99m-HMPA tek foton emisyon bilgisayarlı tomografi kullanılarak değerlendirilmiştir. Alkolik olgular sorunlu alkol başlangıç yaşına göre iki gruba ayrılmıştır.

Bulgular: Üç grup karşılaştırıldığında alt frontal, alt temporal, alt sol oksipital ve orta sol frontal bölgelerde b-BKA farklılıkları saptanmıştır ($p<0.05$). GB grupta control grubuna göre her iki alt frontal ve temporal bölgede azalmış b-BKA değerleri bulunmuştur ($p<0.005$). GB grup EB grupla karşılaştırıldığında, alt frontal ve temporal, alt sol oksipital ve orta sol frontal bölgelerde anlamlı derecede azalmış b-BKA değerleri göstermiştir ($p<0.05$).

Sonuç: Bulgularımız erken ayıklık dönemindeki EB ve GB alkol bağımlılarında b-BKA'nda farklılıklar olduğunu ortaya koymuştur. Bu bulgular daha önceki çalışmalarda da belirtildiği üzere frontal lobun alkolizmin nörobiyolojisinde kilit role sahip olduğuna işaret etmektedir. Uzun sureli ayıklık döneminden sonra ölçümlerin tekrarlanması alkol bağımlısı gruplar arasındaki farklılıkların ortaya konmasında yararlı olacaktır.

Anahtar kelimeler: Alkolizm, SPECT, Serebral kan akımı

How to cite / Atıf için: Erdoğan E, Vardar E, Altun GD, Fırat MF. Assessment of regional cerebral blood flow in patients with early and late onset alcohol dependence: SPECT study. J Surg Med. 2018;2(3):257-261.

Introduction

Alcoholism is a major public health problem in the world from both social and economic points of view. The adverse effects of alcohol abuse on human brain morphology, blood flow, metabolism, and neurocognition are well documented in the medical literature [1]. Functional neuroimaging studies in alcoholics have shown that global cerebral metabolic or perfusion defects mainly in the frontal regions without neurological diseases [2-5]. Among many significant findings from the literature studies on regional cerebral bood flow (r-CBF) of alcoholics, the most consistent one seems to be frontal hypoperfusion, although other cortical regions are also affected [3,6-9]. Whether these changes developed as a result of alcohol use or they have existed from the beginning has been discussed. Widespread bilateral reductions in white matter integrity were observed in abstinent alcoholics. The left inferior frontal gyrus was associated with drinking severity [10]. Binge drinking and withdrawal symptoms have been associated with the greatest neural abnormalities, particularly in frontal, parietal, and temporal regions [11]. Some studies have also reported that brain metabolism is increased during withdrawal period from alcohol [7,12]. There are also studies reporting that cerebral hypoperfusion improves in long-term abstinent alcoholics [13].

Advances of neuroimaging technology have allowed neurobiological theories and clinical heterogeneity of alcoholism to become better understood. Efforts to distinguish alcoholic patients into different subtypes are not new in the clinical field [14]. The classification system of Cloninger et al. and Knorring et al. are most approval and similar however have some differences [15-17]. Cloninger et al. suggested the existence of Type 1 and 2 alcoholism as different alcoholism subtypes [15]. Type 1 alcoholic patient's characteristics are late onset, moderate drinking behavior, less psychosocial problems and good prognosis. In contrast, type 2 alcoholics have more alcohol related problems, early onset of alcohol abuse (before twenties), family history of alcoholism, antisocial personality trait, affective disorder, genetic predisposition and poor psychosocial functioning [17]. The age of onset of alcohol abuse was the most significant finding in several classification studies [17,18]. The aim of the present study was to examine a possible differentiating pattern of regional cerebral blood flow (r-CBF) in patients with early and late onset alcoholism. In doing this, we intended to assess whether subdivisions of alcoholic populations based on age of onset to alcohol abuse is accompanied by different cerebral blood blow changes.

Materials and methods

The study was approved by local Ethics Committee (5.28.2012/007.2002). Subjects signed a written informed consent form. Thirty-three male patients of DSM-IV diagnosis of alcohol dependence and 13 healthy individuals were included in the study. Patients who had a severe physical illness, history of psychotic disorder, any evidence of an organic mental disorder, history of substance abuse (apart from nicotine) in the year before their admission to the hospital, or symptoms of any major affective disorder were excluded from the study. Lifetime severity of drinking problems was assessed by the Michigan Alcoholism Screening Test (MAST) [19]. Depression and anxiety levels were measured with Hamilton Depression Rating Scale (HDRS) and Hamilton Anxiety Rating Scale (HARS) [20,21]. The patients who started alcohol abuse before 20 years of age were classified as 'early onset' (EO, n=18) while those who began alcohol abuse after the age of 20 were grouped as 'late onset' (LO, n=15). In addition, at least two instances of social complications of alcoholism had to have been reported for the time before the age of 20 (such as job loss, alcohol related absence from school or work, arrest for intoxicated behavior, or violence while intoxicated). For the control group, 13 healthy males were selected on similarity to the patients in age, handedness and gender. Exclusion criteria comprised of neurologic/psychiatric illnesses, history of cardiovascular or endocrinological disorders and history of severe head trauma.

r-CBF measurement

r-CBF images were obtained by Single Photon Emission Computed Tomography (SPECT) using Tc-99m-HMPAO (hexamethyl propylene amine oxide). The measurements of r-CBF were performed at the end of a seven-day drug-free period and at the sixth and seven weeks of admission to the hospital. SPECT scans were enumerated randomly, and the clinical information was prepared by a blinded nuclear medicine expert. High-resolution SPECT was performed with double-capped Siemens e-cam camera (Siemens, Gerfahldt, Germany). The radioactivity distribution in the brain was recorded in a circular universe as 128 x 128 matrix 60 minutes after the administration of radioactive isotope. Reconstruction procedure was carried out using Butterworth filter (cut-off frequency 0.27 Nyquist, order 7) in Icon (Siemens) computer system, and fixed attenuation correction was performed with Chang method.

Visual analysis

Standard three dimensional cross-sections were examined. Perfusion defect was assessed in accordance with the criteria that contain observing more than 10% of asymmetry, wider reduced perfusion area than one or several sections, and observing the same defect in more than one plan [22].

Semiquantitative analysis:

In the horizontal sections obtained by grounding on orbitomeatal (OM) line, the images that are over approximately 33mm, 49.5 mm and 66 mm of the OM line were used for numerical calculation [23] (Figure 1). Cortex limits in selected cross-sections were determined through semi-automatic program, and the enumerations in the region of interest (ROI) were recorded as average enumeration. 6 pieces of ROI were placed in both sections [24] (Figure 2).

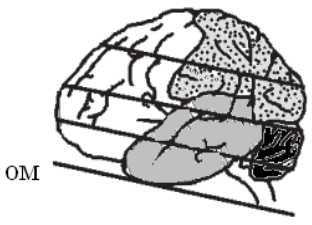


Figure 1: Schematic illustration of transaxial SPECT slices which are parallel to orbitomeatal line

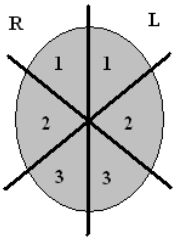


Figure 2: Schematic illustration of the regions of interest over a transaxial slice

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) for Windows, Version 18.0 software. r-CBF compared by one-way analysis of variance and Kruskal-Wallis analysis. Mann-Whitney U test was applied to dually compare the data of EO, LO and the control group with each other. Differences were considered to be significant if $p<0.05$.

Results

There were no statistically significant differences between the study groups in terms of age and gender. The average age of onset of alcohol abuse was 15.5±2.1 years in EO group and 24.8±4.7 years in LO group, the difference between groups was statistically significant (z=-4,790, p<0.001). Differences between groups in terms of total duration of dependence, age of first treatment admission, amount of daily alcohol intake were not statistically significant. There was statistically no significant difference between the MAST scores of the EO and LO alcoholics (z=-1.123, p=0.432). The depression scores of EO and LO groups in the abstinence period were found to be similar (EO=7.5±6.2, LO=6.4±3.2; z=0.000, p=1.000). Anxiety scores of both groups were not different from each other (EO=18,7±5.3; LO=17.5±3.8 z=-1.609, p=0.345). Table 1 shows sociodemographic and clinical characteristics of EO and LO groups.

Table 1: Sociodemographic and clinical characteristics of EO and LO Alcohol Dependents

	EO n:18 mean±SD	LO n=15 mean±SD	z	p
Age	38.9±9.7	43.9±7.6	-1.789	0.067
Education (year)	8.9±3.8	10.6±3.7	-2.046	0.047*
Age of onset of alcohol abuse (year)	15.5±2.1	24.8±4.7	-4.790	<0.001*
Age of first treatment admission (year)	37.2±5.9	43.2±10.8	-2.023	0.53
Daily alcohol intake (standard drink/day)	17.1±4.9	14.7±3.9	-1.890	0.23
Total duration of dependence (year)	14.5±6.4	13.2±4.8	-0.987	0.64
MAST	34.3±5.9	29.7±4.3	-1.123	0.432
HDRS	7.5±6.2	6.4±3.2	0.000	1.000
HARS	18.7±5.3	17.5±3.8	-1.609	0.345

EO: Early onset, LO: Late onset, Mann Whitney U testi, *p<0.05=statistically significant beween groups, SDd: standart deviation, MAST: Michigan Alcoholism Screening Test, HDRS: Hamilton Depression Rating Scale, HARS: Hamiton Anxiety Rating Scale

The relative perfusion rates of the groups are presented in Table 2. There were statistically significant differences in mean r-CBF in inferior frontal and temporal, inferior left occipital and middle left frontal regions. Compared with the results of control subjects, relative perfusion was significantly decreased in inferior frontal and temporal regions in the LO group (x2 =6.016, df=2, p=0.049) (Table 2). Decreased perfusion rates were determined in LO alcoholics in the inferior frontal-temporal-left occipital, middle left frontal regions, in comparison to those of EO group. There were no statistically significant differences in mean r-CBF between EO alcoholics and control group.

Discussion

Our study shows that especially regions of frontal and temporal lobes in both hemispheres are more affected in the early abstinence period. Our results support evidences of frontal system abnormalities in abstinent alcoholic subjects [25,26]. r-CBF values were different among the EO and LO alcoholics in the present study. In the light of these results, problematic drinking age may be a differentiating pattern in grouping alcoholism at the short-term abstinence period. There was no difference in the severity of alcoholism and period of abstinence among the groups in our study, but the early onset group had been exposed to toxic effects of alcohol for a longer period of time. Although there is no difference in terms of alcohol consumption intensity, the doses of benzodiazepines in first weeks of treatment and duration of detoxification period were higher in EO alcoholics than the LO group. Studies with r-CBF values in different alcoholic subgroups revealed inconsistent results. Tutus et al. reported that observed frontal lobe perfusion deficits in neuroimaging studies might be transistory in withdrawal period, but contrast to this suggestion data in long term abstinent alcoholics have shown perfusion defects [7,27].

Table 2: Comparison of r-CBF among three groups

r-CBF		EO n=18 mean±SD			LO n=15 mean±SD			Control n=13 mean±SD			Anova Test Kruskall Wallis x^2	df	P
Inferior slices	Right frontal	110.8	±	28.9	88.6	±	22.5	112.5	±	22.6	8.166	2	0.017* a,b
	Left frontal	109.4	±	28.4	88.0	±	26.4	111.2	±	22.3	7.723	2	0.021* a,b
	Right temporal	115.9	±	31.7	96.2	±	23.1	117.3	±	16.9	7.819	2	0,020* a,b
	Left temporal	115.1	±	28.9	95.6	±	26.0	117.7	±	16.7	7.957	2	0,019* a,b
	Right occipital	118.8	±	29.5	101.1	±	26.9	111.1	±	13.8	4.293	2	0.177
	left occipital	121.1	±	28.9	101.3	±	26.7	111.2	±	13.5	6.531	2	0.038* a
Middle slices	Right frontal	119.6	±	30.1	98.4	±	25.7	107.3	±	16.2	5.901	2	0.052
	Left frontal	118.1	±	28.7	95.2	±	28.0	106.1	±	17.4	6.878	2	0.032*a
	Right parietal	116.6	±	29.6	97.8	±	26.4	107.8	±	18.1	3.718	2	0.156
	Left parietal	117.3	±	29.2	97.5	±	27.7	107.5	±	15.4	5.368	2	0.068
	Right occipital	117.1	±	29.0	99.4	±	27.2	105.1	±	14.4	4.157	2	0.125
	Left occipital	117.1	±	28.2	99.0	±	27.1	106.0	±	15.3	5.644	2	0.059
	Right frontal	114.6	±	28.8	98.0	±	25.4	103.5	±	18.2	4.004	2	0.135
Upper slices	Left frontal	113.0	±	28.2	95.0	±	26.7	104.4	±	14.5	5.274	2	0.072
	Right parietal	109.5	±	27.5	96.2	±	25.2	102.3	±	16.4	2.923	2	0.232
	Left parietal	110.7	±	27.1	94.6	±	26.7	103.3	±	18.1	4.453	2	0.108
	Right posterior parietal	113.6	±	29.2	98.7	±	27.7	106.4	±	18.0	2,667	2	0,264
	Left posterior parietal	113.2	±	27.7	96.8	±	25.3	103.0	±	18.0	4.741	2	0,093

r-CBF: regional Cerebral Blood Flow, SD=standad deviation, *Kruskal wallis test p<0.05=statistically significant difference between three groups.
Post Hoc Test Multiple Comparisons results: a: LO group has statistically significant difference compared to EO (p<0.05), b: LO group has statistically significant difference compared to control (p<0.05)

Demir et al. reported SPECT results of EO versus LO alcoholics were not different each other but r-CBF values of EO and LO alcoholics were statistically different than the control subjects. Perfusion defect was found in left superior frontal region in the EO group by Demir et al [3]. In our study, in contrast to EO alcoholics, LO alcoholics showed inferior occipital brain area perfusion defect. As the LO group is considered to be older, depending on the effect of aging on the brain, hypoperfusion in posterior brain area like cerebellum and occipital lob may occur in alcoholism [28].

Evaluation of changes in the volumes of cerebral tissue and spinal fluid revealed that brain tissue recovery in the first month of the soberness is faster than the following 12 months. [29,30]. The fastest brain tissue recovery was observed in sober individuals with the highest drinking intensity and basal brain reduction. In the rapid return of the brain tissue recovery, sober periods were found to be effective. This can be interpreted as explanatory for the close results of EO group with control group in terms of regional cerebral blood flow at the end of the second month. In another study evaluating alcoholics in the early abstinence period and after 12 months showed that the abstinent subjects and control group are not different from each other in terms of frontal and parietal grey matter perfusion [31].

We have used the age of onset to alcohol abuse as a more significant biological determinant in our study. It is evident from comparative studies that all different classification approaches suffer from potential diagnostic imprecision or overlap problems. In our study, we wonder why LO group could not reach normal r-CBF values in the early abstinence period. Is the older age of this group a factor in terms of neuroplasticity? We think that perfusion deficits of some regions may be a transient finding in abstinence. These changes may reflect a metabolic state related to termination of alcohol, or a general brain metabolic change in chronic alcoholics. The longitudinal literature studies in neuroimaging area did not classify alcoholics into groups according to the age of onset.

It is now well-known that alcohol causes widespread effects on central nervous system. Recent neurophysiological studies show that there is a compensatory re-organization of the brain system in alcoholics balancing the frontal lobe dysfunctions. The alcoholic brain damage is consistently shown to be reversible in both structural and functional studies and latest techniques point out to an active regeneration process in different alcoholic groups which seems to be an important encouraging factor for treatment modalities. Female cases were not included in our study, because these are low in rate in clinical practice. Obtained results should be interpreted as preliminary since the number of cases in both groups is low. In addition, another limitation in our study is the fact that basal cerebral blood flow values of both groups were not measured. The fact that we could not perform longitudinal measurement in the longtime abstinence period is another limitation. Performing neuroimaging studies evaluating brain functions in alcoholics that are long-standing soberness, involving both genders, will be valuable for the scientific literature. In literature, there are no studies on cerebral blood flow apart from the study of Demir et al. which was conducted by classifying the dependents according to the age of onset [3]. In this sense, our study is valuable. The degree of neurobiological anomalies following acute detoxification and the flexibility of recovery during abstinence are not only affected by existing comorbid situations (cigarette, mood disorders, hypertension, etc.), but they are also affected by genotype. The support of multi-dimensional diagrams and classifications with brain imaging and genetic studies will provide support for the endophenotypes that distinguishes alcoholism. We believe that this study will shed light on further clinical studies with larger sampling.

References

1. Oscar-Berman M, Marinkovic K. Alcohol: Effects on neurobehavioral functions and the brain alcoholism and the brain: An overview. Neuropsychol Rev. 2007;17:239–57.
2. Soyka M, Dresel S, Horak M, Ruther T, Tatsch K. PET and SPECT findings in alcohol hallucinosis: Case report and super-brief review of the pathophysiology of this syndrome. World J.Biol.Psychiatry. 2000;1:215-18.
3. Demir B, Ulug B, Lay EE, Erbas B. Regional cerebral blood flow and neuropsychological functioning in early and late onset alcoholism. Psychiatry Res. 2002;115:115-25.
4. Suzuki Y, Oishi M, Mizutani T, Sato Y. Regional cerebral blood flow measured by the resting and vascular reserve (RVR) method in chronic alcoholics. Alcohol Clin.Exp Res. 2002;26:95-9.
5. Kubota M, Nakazaki S, Hirai S, Saeki N, Yamaura A, Kusaka T. Alcohol consumption and frontal lobe shrinkage: Study of 1432 non-alcoholic subjects. J Neurol Neurosurg Psychiatry. 2001;71:104-6.
6. Nicolas JM, Catafau AM, Estruch R, Lomeña FJ, Salamero M, Herranz R, et al. Regional cerebral blood flow-SPECT in chronic alcoholism: relation to neuropsychological testing. J Nucl Med. 1993;34:1452-9.
7. Tutus A, Kugu N, Sofuoglu S, Nardali M, Kugu N, Karaaslan F, et al. Transient frontal hypoperfusion in Tc-99m hexamethylpropyleneamineoxime single photon emission computed tomography imaging during alcohol withdrawal. Biol Psychiatry. 1998;43:923-8.
8. Noel X, Sferrazza R, Van Der LM, Paternot J, Verhas M, Hanak C, et al. Contribution of frontal cerebral blood flow measured by (99m) Tc-Bicisate spect and executive function deficits to predicting treatment outcome in alcohol-dependent patients. Alcohol Alcohol. 2002;37:347-54.
9. Pach D, Hubalewskava DA, Szurkowska Kamenczak A, Targosz D, Gawlikowski T, Huszno B, et al. Evaluation of regional cerebral blood flow using 99m Tc-ECD SPECT in ethanol alcohol dependent patients: pilot study. Przegl Lek. 2007;64(4-5):204-7.
10. Fortier CB, Leritz EC, Salat DH, Lindemer E, Maksimovskiy AL, Shepel J, et al. Widespread effects of alcohol on white matter microstructure. Alcohol Clin Exp Res. 2014;38(12):2925-33.
11. Squeglia LM, Jacobus J, Tapert SF. The effect of alcohol use on human adolescent brain structures and systems. Handb Clin Neurol. 2014;125:501-10.
12. Daglish MR, Nutt DJ. Brain imaging studies in human addicts. Eur Neuropsychopharmacol. 2003;13:453-8.
13. Dupont RM, Rourke SB, Grant I, Lehr PP, Reed RJ, Challakere K, et al. Single photon emission computed tomography with iodoamphetamine-123 and neuropsychological studies in long-term abstinent alcoholics. Psychiatry Res. 1996;67:99-111.
14. Ebstein EE, Labovie E, McCrady B, Jensen NK, Hayaki J. A multi-site study of alcohol subtypes: classification and overlap of unidimensional and multi-dimensional typologies. Addiction. 2002;97:1041-53.
15. Cloninger CR, Bohman M, Sigvardsson S. Inheritance of alcohol abuse. Cross-fostering analysis of adopted men. Arch Gen Psychiatry. 1981;38(8):861-8.
16. Johnson BA, Cloninger CR, Roache JD, Bordnick PS, Ruiz P. Age of onset as a discriminator between alcoholic subtypes in a treatment-seeking outpatient population. Am J Addict. 2000;9:17-27.
17. Buydens-Brachey M, Branchey M, Noumair D. Age of alcoholism onset. Relationship to psychopathology. Arch Gen Psychiatry. 1989;4:225-30.
18. Von Knorring L, Palm V, Anderson H. Relationship between treatment outcome and subtypes of alcoholism in men. J Stud Alcohol. 1985;46:388-91.

19. Selzer M. The Michigan alcoholism screening test: The quest for new diagnostic instrument. Am J Psychiatry. 1971;127:1653-8.
20. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960;23:56-62.
21. Hamilton M. The assessment of anxiety states by rating. British J of Med Psychol. 1959;32:50-5.
22. Chiu NT, Chang YC, Lee BF, Huang CC, Wang ST. Differences in 99mTc-HMPAO brain SPET perfusion imaging between Tourette's syndrome and chronic tic disorder in children. Eur J Nucl Med. 2001;28:183-90.
23. Rubin RT, Villanueva-Meyer J, Ananth J, Trajmar PG, Mena I. Regional xenon 133 cerebral blood flow and cerebral technetium 99m HMPAO uptake in unmedicated patients with obsessive-compulsive disorder and matched normal control subjects. Determination by high-resolution single-photon emission computed tomography. Arch Gen Psychiatry. 1992;49:695-702.
24. Yazici KM, Kapucu O, Erbas B,Varoglu E, Gülec C, Bekdik CF. Assessment of changes in regional cerebral blood flow in patients with major depression using the 99mTc-HMPAO single photon emission tomography method. Eur J Nucl Med. 1992;19:1038-43.
25. Moselhy HF, Georgiou G, Kahn A. Frontal lobe changes in alcoholism: A review of the literature. Alcohol Alcohol. 2001;36:357-68.
26. Clark CP, Brown GG, Eyler LT, Drummond SP, Braun DR, Tapert SF. Decreased perfusion in young alcohol-dependent women as compared with age-matched controls. Am J Drug Alcohol Abuse. 2007;33(1):13-9.
27. Gansler DA, Harris GJ, Oscar-Berman M, Streeter C, Lewis RF, Ahmed I, et al. Hypoperfusion of inferior frontal brain regions in abstinent alcoholics: A pilot SPECT study. J.Stud.Alcohol. 2000;61:32-7.
28. Harris GJ, Oscar-Berman M, Gansler A, Streeter C, Lewis RF, Ahmed I, et al. Hypoperfusion of the cerebellum and aging effects on cerebral cortex blood flow in abstinent alcoholics: A SPECT study. Alcohol Clin.Exp.Res. 1999;23:1219-27.
29. Gazdzinski S, Durazzo TC, Meyerhoff DJ. Temporal dynamics of whole brain tissue volume changes during recovery from alcohol dependence. Drug Alcohol Depend. 2005;78(3):263-73.
30. Gazdzinski S, Durazzo DC, Mon A, Yeh PH, Meyerhoff DJ. Cerebral white matter recovery in abstinent alcoholics-a multimodality magnetic resonance study. Brain. 2010;133:1043-53.
31. Durazzo TC, Gazdzinski S, Mon A, Meyerhoff DJ. Cortical perfusion in alcohol dependent individuals during short-term abstinence: Relationships to resumption of hazardous drinking following treatment. Alcohol. 2010;44(3):201-10.

J Surg Med. 2018;2(3):262-264.
DOI: 10.28982/josam.427084

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

An evaluation of the infection agents and the demographic characteristics of patients followed up on a mechanical ventilator in neurology intensive care: A retrospective, single center, observational study

Nöroloji yoğun bakımda mekanik ventilatörde takip edilen hastaların enfeksiyon etkenleri ve demografik özelliklerinin değerlendirilmesi: Retrospektif tek merkezli gözlemsel çalışma

Yılmaz İnanç [1],Yusuf İnanç [2]

[1] Kahramanmaraş Sütçüimam University, School of Medicine, Department of Neurology, Kahramanmaraş, Turkey
[2] Gaziantep University, School of Medicine, Department of Neurology, Gaziantep, Turkey

ORCID ID of the authors
Yİ: 0000-0002-0423-0941
Yİ: 0000-0003-2652-1157

Corresponding author / Sorumlu yazar:
Yılmaz İnanç
Address / Adres: Kahramanmaraş Sütçüimam Universitesi, Tıp Fakültesi, Nöroloji Bölümü, Kahramanmaraş, Türkiye
E-mail: drinancc@gmail.com

Ethics Committee Approval: Ethics committee approval was obtained from the local ethics committee.
Etik Kurul Onayı: Etik kurul onayı local etik kurulundan alınmıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 25.05.2018
Accepted / Kabul Tarihi: 27.06.2018
Published / Yayın Tarihi: 03.07.2018

Abstract

Aim: The incidence of nosocomial infections is higher than other sites of the hospitals at intensive care units (ICU) because of high frequency of invasive interventions and multidrug resistant microorganism's prevalence. Ventilator-related pneumonia cases have the highest mortality risk among the nosocomial infections. The aim of this study was to evaluate the endotracheal aspirate cultures and the demographic characteristics of patients followed up on mechanical ventilation in Neurology Intensive Care.

Methods: Our study was designed as a retrospective, cross-sectional and descriptive. Retrospective evaluation was made of 51 patients who were attached to a mechanical ventilator in the last 6 months and from whom a tracheal aspirate culture was taken. The endotracheal aspirate samples were taken under sterile conditions using a specifically designed catheter with the method of administering saline into the intubation tube and then aspiration. Blood culture results sent for analysis at the same time as the tracheal aspirate samples were also retrospectively evaluated in patients determined with positive production. A record was made of the demographic characteristics of the patients, diagnosis on admittance to ICU, risk factors, and microbial production in the tracheal aspirate culture.

Results: In the first culture, there was no production in 22 (43.1%) cases, and Acinetobacter baumanii was determined in 14 (27.5%) patients, Pseudomonas aeruginosa in 3 (5.9%), Klebsiella pneumonia in 3 (5.9%), Staphylococcus aureus in 2 (3.9%), Corynebacterium striatum in 2 (3.9%), Acinetobacter baumanii + Pseudomonas aeruginosa in 2 (3.9%), Acinetobacter baumanii + Klebsiella pneumonia in 2 (3.9%), and Acinetobacter baumanii + Escherichia coli in 1 (2.0%). The second culture was taken from patients on the mean 11th day. In 3 (10.7%) patients there was no production in the second culture and in the other patients, Acinetobacter baumanii was determined in 15 (53.6%) patients, Pseudomonas aeruginosa in 3 (10.7%), Klebsiella pneumonia in 2 (7.1%), Escherichia coli in 1 (3.6%), Corynebacterium striatum in 1 (3.6%), and Acinetobacter baumanii + Pseudomonas aeruginosa in 3 (10.7%).

Conclusion: The culture results in this study of patients admitted for neurological reasons were observed to be consistent with findings in literature. The high mortality rate of 64.7% in these ICU patients is due to the majority being ischemic stroke patients. This suggests that both the severe table associated with neurological findings and agents such as Acinetobacter baumanii and Pseudomonas aeruginosa contribute to Neurology ICU patients.

Keywords: Nosocomial infection, Neurological intensive care unit, Mechanical ventilator

Öz

Amaç: Yoğun bakım üniteleri hastane geneline göre invazif girişimlerin daha sık uygulandığı dirençli mikroorganizmaların daha çok izole edildiği yerlerdir ve bu nedenle buralarda hastane enfeksiyonları daha sıktır. Ventilatör ilişkili pnömoniler mortalitesi en yüksek nozokomiyal enfeksiyonlardır. Bu çalışmada nöroloji yoğun bakımda mekanik ventilatörde takip edilen hastaların demografik özellikleri, endotrakeal aspirat kültürleri yönünden değerlendirilmesi amaçlandı.

Yöntemler: Çalışmamız retrospektif, kesitsel, tanımlayıcı olarak dizayn edildi. Son 6 ayda mekanik ventilatöre bağlı ve trakeal aspirat kültürü alınan 51 hasta retrospektif olarak değerlendirildi. Endotrakeal aspirat örnekleri; steril şartlarda, örnek almak için tasarlanmış özel kateterler kullanılarak, entübasyon tüpünün içinden serum fizyolojik verilip aspire edilmesi yöntemiyle elde edildi. Üreme saptanan hastaların trakeal aspirat örnekleri ile eş zamanlı gönderilen kan kültür sonuçları da geriye dönük olarak değerlendirildi. Hastaların demografik özellikleri, yoğun bakıma yatış tanıları, risk faktörleri, trakealaspirat kültür mikrobiyal üremeleri kaydedildi.

Bulgular: İlk kültürde 22 (%43,1) hastada üreme yoktu, 14 (%27,5) hastada Acinetobacter baumanii, 3 (%5,9) hastada Pseudomonas aeruginosa, 3 (%5,9) hastada Klebsiella pneumonia,2 (%3,9) hastada Staphylococcus aureus, 2 (%3,9) hastada Corynebacterium striatum, 2 (%3,9) hastada Acinetobacter baumanii + Pseudomonas aeruginosa, 2 (%3,9) hastada Acinetobacter baumanii + Klebsiella pneumonia, 1 (%2,0) hastada Acinetobacter baumanii+ Escherichia coli saptandı. Hastaların ikinci kültür alınma süresi ortalama 11. gün idi. İkinci kültürde 3 (%10,7) hastada üreme yoktu. 15 (%53,6) hastada Acineto bacterbaumanii, 3 (%10,7) hastada Pseudomonas aeruginosa, 2 (%7,1) hastada Klebsiella pneumonia, 1 (%3,6) hastada Escherichia coli, 1 (%3,6) hastada Corynebacterium striatum, 3(%10,7) hastada Acinetobacter baumanii + Pseudomonas aeruginosa saptandı.

Sonuç: Yaptığımız çalışmada nörolojik nedenlerle yatan hastalarda da literatürle uyumlu olarak benzer kültür sonuçları izlenmiştir. Büyük çoğunluğunu iskemik inmeli hastaların oluşturduğu yoğun bakım hastalarımızda mortalite oranımız %64,7 gibi yüksek oranda idi. Bu duruma hem nöroloji yoğun bakım hastalarının nörolojik bulgularına bağlı ağır tablosunun olması hem de Acinetobacter baumanii ve Pseudomonas aeruginosa gibi etkenlerin birlikte katkısı olduğu düşüncesindeyiz.

Anahtar kelimeler: Nazokomial enfeksiyon, Nörolojik yoğun bakım ünitesi, Mekanik ventilatör

How to cite / Atıf için: İnanç Y, İnanç Y. An evaluation of the infection agents and the demographic characteristics of patients followed up on a mechanical ventilator in neurology intensive care: A retrospective, single center, observational study. J Surg Med. 2018;2(3):262-264.

Introduction

Nosocomial infections are most frequently seen and the greatest cause of mortality in Intensive Care Units (ICU). Serious infections, primarily sepsis, are responsible for 60% of mortality in ICUs and 40% of the costs. Ventilator-associated pneumonia, urinary tract infections, bacteremia and catheter infections and surgical site infections are the most common nosocomial infections in intensive care units [1]. The aim of this study was to evaluate the endotracheal aspirate cultures and the demographic characteristics of patients followed up on mechanical ventilation in Neurology Intensive Care.

Materials and methods

Our study was designed as a retrospective, cross-sectional and descriptive. From a total of 119 patients followed up in the Stroke and Neurology ICU of Gaziantep University Medical Faculty Hospital between January and December 2017, retrospective evaluation was made of 51 patients who were attached to a mechanical ventilator in the last 6 months and from whom a tracheal aspirate culture was taken. The endotracheal aspirate samples were taken under sterile conditions using a specifically designed catheter with the method of administering saline into the intubation tube and then aspiration. Blood culture results sent for analysis at the same time as the tracheal aspirate samples were also retrospectively evaluated in patients determined with positive production. A record was made of the demographic characteristics of the patients, diagnosis on admittance to ICU, risk factors, and microbial production in the tracheal aspirate culture.

Statistical analysis

Statistical evaluation was performed using SPSS 19.0 software (IBM, New York, USA). Descriptive statistics were given as statistical mean, standard deviation, number and percentage values.

Results

The patients comprised 29 (56.9%) females and 22 (43.1%) males with a mean age of 64.1±15.9 years. Diagnoses were determined as ischemic stroke in 34 (66.7%) patients, subarachnoid bleeding in 4 (7.8%), encephalitis in 4 (7.8%), Guillan-Barre syndrome in 3 (5.9%), intracerebral hemorrhage in 3 (5.9%), Parkinson's disease in 1 (2%), myasthenia gravis in 1 (2%) and dementia in 1 (2%). Risk factors were present as hypertension in 40 (78.4%) patients, diabetes in 20 (39.2%), coronary artery disease in 20(39.2%), smoking in 34 (66.7%), heart failure in 8 (15.7%) and chronic obstructive pulmonary disease in 6 (11.8%) (Table 1). The mean time to taking the first culture from the patients was 5 days.

In the first culture, there was no production in 22 (43.1%) cases, and Acinetobacter baumanii was determined in 14 (27.5%) patients, Pseudomonas aeruginosa in 3(5.9%), Klebsiella pneumonia in 3 (5.9%), Staphylococcus aureus in 2(3.9%), Corynebacterium striatum in 2(3.9%), Acinetobacter baumanii + Pseudomonas aeruginosa in 2(3.9%), Acinetobacter baumanii + Klebsiella pneumonia in 2 (3.9%), and Acinetobacter baumanii + Escherichia coli in 1 (2.0%). The second culture was taken from patients on the mean 11th day. In 3 (10.7%) patients there was no production in the second culture and in the other patients, Acinetobacter baumanii was determined in 15 (53.6%) patients, Pseudomonas aeruginosa in 3(10.7%), Klebsiella pneumonia in 2 (7.1%), Escherichia coli in 1 (3.6%), Corynebacterium striatum in 1 (3.6%), and Acinetobacter baumanii + Pseudomonas aeruginosa in 3 (10.7%) (Table 2). 33 (64.7%) patients whose tracheal culture was positive deceased during follow-up.

Table 1: Patient Characteristics

Patients	Total n=51 n (%)
Age (yrs) mean±standard deviation	64.1±15.9
Diagnosis	
Ischemic stroke	34 (66.7%)
Subarachnoid hemorrhage	4 (7.8%)
Encephalitis	4 (7.8%)
Guillain Barre syndrome	3 (5.9%)
Hemorrhagic stroke	1 (2.0%)
Parkinson's disease	2 (1.9%)
Myastenia gravis	1 (2.0%)
Dementia	1 (2.0%)
Risk factors	
Hypertension	40 (78.4)
Diabetes	20 (39.2)
Chronic obstructive pulmonary disease	6 (11.8)
Smoking	34 (66.7)
Heart failure	8 (15.7)
Coronary artery disease	20 (39.2)

Table 2: Causative microorganisms

Causative microorganisms n =51	Initial culture n (%)	Second culture n (%)
A. baumanii	14(27.5)	15(53.6)
P. aeruginosa	3(5.9)	3(10.7)
K. pneumonia	3(5.9)	2(7.1)
S. aureus	2(3.9)	-
Corynebacterium striatum	2(3.9)	1(3.6)
A. baumanii + P. aeruginosa	2(3.9)	3(10.7)
A. baumanii + K. pneumonia	2(3.9)	-
A. baumanii + E. coli	1(2.0)	-
E. coli	-	1(3.6)

A. baumanii: Acinetobacter baumanii, P. aeruginosa: Pseudomonas aeruginosa, E. coli: Escherichia coli, K. pneumonia: Klebsiella pneumonia, S. aureus: Staphylococcus aureus

Discussion

Nosocomial infections are a significant cause of morbidity and mortality throughout the world. ICU is the department where hospital-acquired infections are seen most often and with the highest mortality rates [2]. Infection complications have been reported in 36% of patients staying more than 48 hours in ICU [3].Changes in consciousness in patients in Neurology ICU increase the risk of aspiration pneumonia and other infections with the need for nasogastric catheter and the application of percutaneous endoscopic gastrostomy. Invasive interventions such as the application of mechanical ventilation, tracheostomy and catheter, the use of broad-spectrum antibiotics and the length of stay in ICU are significant reasons for the development of difficult-to-treat infections with resistant pathogens in ICU [4].

Ventilator-associated pneumonia is the most common nosocomial infection with the highest mortality rate in intensive care units. Ventilator-associated pneumonia accounts for 70% of hospital-acquired pneumonia in intensive care units. Mechanical ventilation increases the risk of pneumonia seven times. Mechanical ventilation pneumonia cases constitute about 10-20% of nosocomial infections. When ventilator-associated

pneumonia develops in patients, the mortality ranges from 27 to 76% [5].

In the diagnosis of ventilator-related infections, as the sensitivity and specificity of clinical and radiological findings are low, gram staining and cultures from respiratory tract samples such as endotracheal aspirate, broncho-alveolar lavage and dry-brush samples, are of guidance in diagnosis and treatment. Correct determination of the etiological agent is extremely important for the early initiation of antimicrobial treatment. A 4-8 -hour delay in the start of treatment has been shown to increase mortality. Therefore, empirical antibiotic treatment is started by the clinician without waiting for laboratory results [6,7]. At the same time, early diagnosis and treatment directed at the agent in ventilator-related infections shortens the length of hospital stay, and reduces mortality rates, the rates of resistant strains and costs. Moreover, the determination of the local antibiotic resistant profile contributes to the rational use of antibiotics. Gram-negative, non-fermentative bacteria such as Pseudomonas and Acinetobacter have been reported to be the leading agents resulting in infections in ICU and extremely high rates of morbidity and mortality have been reported in the diseases they cause [2,8].

In the current study, production was determined in the first blood culture in 56.9% of all the patients and the pathogen showing most frequent production was Acinetobacter baumanii at 27.5% followed by Pseudomonas aeruginosa at 5.9%. In the second blood culture, there was production in 89.3% of the patients and again the most common pathogen was Acinetobacter baumanii at 53.6% followed by Pseudomonas aeruginosa at 10.7%. These findings were consistent with previous reports in literature. However, in studies conducted in recent years, there has been observed to be an increase in the frequency of Staphylococcus aureus together with the gram negative bacteria isolated in ICUs [9]. Staphylococcus aureus was determined in 3.9% of the current study patients. The majority of the patient group followed up in ICU in this study comprised ischemic stroke patients. Of the risk factors that play an important role in the prognosis of ischemic stroke, hypertension was determined in 78.4% of the patients and diabetes in 39.2%, the high mortality rate of 64.7% in these ICU patients is due to the majority being ischemic stroke patients. This suggests that both the severe table associated with neurological findings and agents such as Acinetobacter baumanii and Pseudomonas aeruginosa contribute to Neurology ICU patients [10,11].

The low number of cases and the presence of data from a single center are limitations to the generalization of the results.

In conclusion, nosocomial infections are a significant problem in Turkey, just as they are throughout the world. Ventilator-associated pneumonia is the most common nosocomial infection in intensive care units. The culture results in this study of patients admitted for neurological reasons were observed to be consistent with findings in literature. Advanced age, the application of an endotracheal tube and comorbidities in patients requiring follow-up in ICU are reasons that increase mortality rates. The fact that the neurological pattern of the patients is advanced, and the coexistence of the infections increases this rate much more.

References

1. Walaszek M, Rozanska A, Bulanda M, Wojkowska-Mach, J. Epidemiology of healthcare-associated infections in Polish intensive care. A multicenter study based on active surveillance. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2018;72(1):33-44.
2. Küme G, Demirci M. Antimicrobial susceptibilities of nonfermentative gram negative bacteria isolated from lower respiratory tract samples of patients in intensive care units and risk factors associated with lower respiratory tract infection. DEÜ Faculty of Medicine Journal. 2012;26(1):37–4.
3. Hinduja A, Dibu J, Achi E, Patel A, Samant R, Yaghi S. Nosocomial infections in patients with spontaneous intracerebral hemorrhage. American Journal of Critical Care. 2015;24(3):227-31.
4. Inanc Y, Gokce M, Tuncel D, Inanc Y,Ozcekic Demirhan S, Bavli S. Percutaneous endoscopic gastrostomy in neurology intensive care unit. IJSM. 2018;4(1):33-5.
5. Safdar N, Dezfulian C, Collard HR, Saint S. Clinical and economic consequences of ventilatorassociated pneumonia: a systematic review. Critical care med. 2005;33:2184.
6. Nseir S, Martin-Loeches I. Ventilator-associated tracheobronchitis: Where are we now? Rev Bras Ter Intensiva. 2014;26:212–4.
7. Bassetti M, Taramaso L, Giacobbe DR, Pelosi P. Management of ventilator-associated pneumonia: epidemiology, diagnosis and antimicrobial therapy. Expert Rev Anti Infect Ther. 2012;10:1405-23.
8. Houck PM, Bratzler DW, Nsa W, Ma A, Bartlett JG. Timing of antibiotic administration and outcomes for Medicare patients hospitalized with community-acquired pneumonia. Arch Intern Med. 2004;164(6): 637-44.
9. Ray U, Ramasubban S, Chakravarty C, Goswami L, Dutta S. A prospective study of ventilator-associated tracheobronchitis: incidence and etiology in intensive care unit of a tertiary care hospital. Lung India: official organ of Indian Chest Society. 2017;34(3):236.
10. Namıduru M, Güngör G, Karaoğlan I, Dikensoy O. Antibiotic resistance of bacterial ventilator associated pneumonia in surgical intensive care units. J Int Med Res. 2004;32:78-83.
11. Mi H, Li S, Li H, Hu W. The effects of infection on severe stroke patients in the neurological intensive care unit in China. Int J Neurosci. 2018 Aug;128(8):715-20.

J Surg Med. 2018;2(3):265-268.
DOI: 10.28982/josam.422921

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Evaluation of air pollution by PM_{10} and SO_2 levels in Erzurum province, Turkey: Descriptive study

Türkiye Erzurum ilinde havadaki PM_{10} ve SO_2 düzeyleri ile hava kirliliğinin değerlendirilmesi: Gözlemsel çalışma

Zahide Koşan [1], Duygu Kavuncuoğlu [1], Elif Okşan Çalıkoğlu [1], Ezel Bilge Yerli [1]

[1] Department of Public Health, Atatürk University, Erzurum, Turkey

ORCID ID of the authors
ZK: 0000-0002-1429-6207
DK: 0000-0002-0546-5478
EOÇ: 0000-0001-8959-5001
EBY: 0000-0002-0209-0711

Corresponding author / Sorumlu yazar:
Duygu Kavuncuoğlu
Address / Adres: Atatürk Üniversitesi, Tıp Fakültesi, Halk Sağlığı Bölümü, Erzurum, Türkiye
E-mail: duygu_koylu@hotmail.com

Ethics Committee Approval: An approval was obtained from the Clinical Studies Ethics Board of Faculty of Medicine of Ataturk University (Meeting No: 3, Decision No: 15, Date: 15 August 2017) for conducting the study.
Etik Kurul Onayı: Çalışmanın yürütülmesi için Atatürk Üniversitesi Tıp Fakültesi Klinik Araştırmalar Etik Kurulu'ndan (Toplantı No: 3, Karar No: 15, Tarih: 15 Ağustos 2017) onay alındı.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 11.05.2018
Accepted / Kabul Tarihi: 03.07.2018
Published / Yayın Tarihi: 03.07.2018

Abstract

Aim: Air pollution is an important, global, health-threatening environmental risk factor. Air pollution can cause potentially fatal respiratory tract and other diseases. Erzurum is the largest and most developed city in northeast Turkey. The purpose of this study was to determine levels of air pollution in the center of Erzurum province in 2012 and 2017.

Methods: Data for the Erzurum station for July 2012-July 2017 in this cross-sectional descriptive study were obtained from the Turkish Ministry of the Environment and Urban Planning Air Quality Monitoring Stations web site. The data obtained were compared with European Union (EU) Countries, World Health Organization (WHO) and Turkish national threshold values. Descriptive statistics were expressed as median, minimum-maximum value and percentage, Kruskal Wallis and Mann Whitney U tests were used in the analysis.

Results: At the Erzurum station, the PM_{10} (particles less than 10 microns) median value for the years 2012-2017 was 27 (min: 2; max: 443), the SO_2 median value was 6 (min: 0; max: 443).

PM_{10} exceeded the Turkish national limit on 22 days in 2012; 37 in 2013; 23 in 2014; 40 in 2015; 74 in 2016; and 27 in 2017. SO2 did not exceed the Turkish national limit on any days in 5 years. SO_2 (sulfur dioxide) exceeded the WHO limits on 3 days in 2012, 30 in 2013, 42 in 2014, 56 in 2015, 37 in 2016 and none in 2017.

Statistical analysis revealed that PM_{10} and SO_2 values varied significantly by year ($p<0.001$), season ($p<0.001$) and month ($p<0.001$). The values for both parameters were higher in winter, and the highest median values occurred in January.

Conclusion: The problem of air pollution in Erzurum has decreased compared to previous years, but it still not at recommended levels.

Keywords: Air pollution, Particulate matter, Sulfur dioxide

Öz

Amaç: Hava kirliliği, küresel sağlığı tehdit eden önemli bir çevresel risk faktörüdür. Hava kirliliği, ölümcül olabilen solunum yolu hastalıkları ve diğer hastalıklara neden olur. Erzurum, Türkiye'nin kuzeydoğusundaki en büyük ve en gelişmiş şehridir. Bu çalışmada 2012-2017 yılları arasında Erzurum şehir merkezinde havadaki PM_{10} (10 mikrondan küçük partiküller) ve SO_2 (sülfür dioksit) düzeylerinin değerlendirilmesi amaçlanmıştır.

Yöntemler: Kesitsel tanımlayıcı tipte yapılan bu çalışmada T.C. Çevre ve Şehircilik Bakanlığı Hava Kalitesi İzleme İstasyonları Web Sitesinden Temmuz 2012-Temmuz 2017 Erzurum istasyonu verileri edinilmiştir. PM_{10} ve SO_2 ölçümlerinin 24 saatlik ortalamaları belirtilen tarihler için indirilmiş ve Dünya Sağlık Örgütü (DSÖ), Avrupa Birliği (AB) Ülkeleri ve Türkiye ulusal sınır değerleri ile karşılaştırılmıştır. Tanımlayıcı istatistikler ortanca, en küçük-en büyük değer ve yüzde olarak sunulmuş, analizlerde Kruskal Wallis ve Mann Whitney U testleri kullanılmıştır. İstatistiksel anlamlılık düzeyi $p<0,05$ kabul edilmiştir.

Bulgular: Erzurum istasyonunda 2012-2017 yıllarının PM_{10} ortanca değeri 27 (min:2; max:443), SO_2 ortanca değeri 6 (min:0; max: 137)'dır. Yıllara göre PM_{10} Türkiye sınır değerini aşan gün sayısı 2012'de 22; 2013'te 37; 2014'te 23; 2015'te 40; 2016'da 74; 2017'de 27'dir. SO_2 değerleri için Türkiye sınır değeri aşan gün 5 yıl için bulunmamaktadır. SO_2 DSÖ sınır değerini aşan gün sayısı 2012'de 3, 2013'te 30; 2014'te 42; 2015'te 56; 2016'da 37'dir ve 2017'de bulunmamaktadır. Verilerin analizleri sonucunda PM_{10} ve SO_2 değerlerinin yıllara göre ($p<0,001$), mevsimlere göre ($p<0,001$) ve aylara göre ($p<0,001$) aralarındaki farkın istatistiksel olarak anlamlı olduğu bulunmuştur. Kış mevsiminde her iki parametre ortancaları daha yüksek olup, en yüksek ortancalar Ocak ayına aittir.

Sonuç: Erzurum'daki hava kirliliği sorunu önceki yıllara göre azalmıştır, ancak hala hedeflenen edilen seviyelerde değildir.

Anahtar kelimeler: Hava kirliliği, Partiküler madde, Kükürt dioksit

How to cite / Atıf için: Koşan Z, Kavuncuoğlu D, Çalıkoğlu EO, Yerli EB. Evaluation of air pollution by PM_{10} and SO_2 levels in Erzurum province, Turkey: Descriptive study. J Surg Med. 2018;2(3):265-268.

Introduction

Air pollution is an important, global, health-threatening environmental risk factor. Air pollution refers to contamination by any chemical, physical or biological agent that alters the natural atmospheric characteristics of an internal or external space. Important sources of air pollution include fuels used for heating, motorized vehicles, industrial facilities, and forest fires [1]. In 2014, 92% of the world population were living in regions with poor air quality according to World Health Organization (WHO) guidelines [2].

Air pollution can cause potentially fatal respiratory tract and other diseases. Air pollution of the external environment is estimated to have caused 3 million cases of premature death worldwide in 2012. Approximately 72% of these deaths were due to ischemic heart disease and stroke, 14% to chronic obstructive pulmonary disease or acute lower respiratory tract infections, and 14% to lung cancer. Significant inequality exists in exposure to air pollution, with 88% of these deaths occurring in low and moderate income countries [2].

Investigation of air pollution commenced with episodes that occurred in the Meuse Valley in Belgium in 1934, in Donora in the USA in 1947, and in London in 1952 [3]. The London smog of 1952 is regarded as the catalyst for air pollution epidemiology research, with a mortality rate three time higher than normal during this period [4]. Legal measures aimed at controlling air pollution were first implemented in the USA and the UK, and reducing urban air pollution was found to contribute significantly to the elimination of winter fogs [5]. The "Directive on Achieving Savings in Fuel Consumption and Reducing Air Pollution Caused by Heating Facilities in Cities," published by the Turkish Ministry of Energy and Natural Resources in 1972, was the first to directly address the question of air pollution [6]. This directive was subsequently updated over the years, and the Directive on Air Quality Evaluation and Management (DAQEM) entered into effect on 06.06.2008 as a result of harmonization with European Union (EU) regulations. Under the scope of that directive, pollutants such as ozone (O3), carbon monoxide (CO) and nitrogen oxide (NO), and particularly sulfur dioxide (SO2) and particulate matter (PM), are measured at fully automated measurement stations established in all 81 provinces in Turkey. Measurement data collected from these stations are forwarded to the Turkish Ministry of the Environment and Urban Planning Data Processing Center and are simultaneously published on the www.havaizleme.gov.tr web site [7].

Erzurum is the largest and most developed city in northeast Turkey. The city is not an industrial one. It is one of Turkey's highest-altitude cities, and winter temperatures can be as low as -40 C. Air pollution in Erzurum is to a large extent caused by the heating and traffic [8]. In addition, air pollution on windless days represents a serious threat to public health in Erzurum, which is surrounded by mountains 2-3000 m in height to both north and south.

Previous scientific research into air pollution in Erzurum has involved data for 1990-2008, 2003-2004, 2003-2006, and 2009-2012 [8-11]. The purpose of this study was to determine levels of air pollution in the center of Erzurum province in 2012 and 2017, and to assess the current situation compared to that in previous years.

Materials and methods

Our research was designed as a descriptive, cross-sectional study, and was performed between August and December, 2017. PM_{10} (particles less than 10 microns) and SO_2 values constituted the dependent study variables, while winter, summer, month and year represented the independent variables. Winter was defined as the period between 1 October and 31 March, and summer as the period between 1 April and 30 September. Air pollution measurements in Erzurum are performed by fully automated devices installed by the Turkish Ministry of the Environment and Urban Planning, and data are published on the ministry website. Mean 24-h PM_{10} and SO_2 measurements for the Erzurum, Aziziye, Palandöken and Taşhan stations (in the central part of the province) between July 2012 and July 2017 were collected from the Turkish Ministry of the Environment and Urban Planning web site. These data were compared with Turkish national threshold values, and threshold values recommended by EU countries and the World Health Organization (WHO) (Table 1).

Table 1: EU, Turkish and WHO limits for SO_2 and PM_{10}

	EU countries [12]	Turkey (2017) [13]	WHO [14]
SO_2 (sulfur dioxide)	125 μg/m^3 *	175 μg/m^3	20 μg/m^3
PM_{10} (particulate material)	50 μg/m^3**	70 μg/m^3	50 μg/m^3

* not to be exceeded more than 3 times in one year, ** not to be exceeded more than 35 times in one year, EU: European Union, WHO: World Health Organisation

Statistical analysis

Data recording and analysis was performed using SPSS 22.00 software. Normal distribution of variables was examined using the Kolmogorov-Smirnov test. Non-normally distributed data were expressed as median, minimum, maximum, and percentage values. The Kruskal Wallis and Mann Whitney U tests were used for statistical analysis. P values <0.05 were regarded as statistically significant.

Results

PM_{10} was measured on 1707 days (93.4%) and SO_2 on 1507 days (82.5%) in the Erzurum station in 2012-2017. The median PM_{10} value in this five-year period was 27 μg/m^3 (min: 2; max: 443), and the mean SO_2 value was 6 μg/m^3 (min: 0; max: 137). PM_{10} exceeded Turkish national, EU and WHO threshold values on 395 days, representing 21.6% of the days on which measurement was carried out. SO_2 exceeded national and EU threshold limits on 1 day (0.1%) and WHO limits on 168 days (9.2%). Annual SO_2 and PM_{10} levels are shown in Table 2.

Table 2: SO_2 and PM_{10} levels in Erzurum by years

	PM_{10} (μg/m^3)			SO_2 (μg/m^3)		
	Median	Minimum	Maximum	Median	Minimum	Maximum
2012	41	9	336	7	2	36
2013	20	2	305	5	1	82
2014	21	5	249	6	1	116
2015	29	4	237	7	1	137
2016	34	7	443	7	1	118
2017	29,5	5	182	11,5	4	19

PM_{10} values exceeded Turkish threshold limits on 22 days in 2012 (11.9%), 237 in 2013 (10.1%), 23 in 2014 (6.3%), 40 in 2015 (11.0%), 74 in 2016 (20.2%), and 27 in 2017 (14.9%). PM_{10} values exceeded EU country and WHO threshold limits on 53 days in 2012 (28.8%), 56 in 2013 (15.3%), 43 in

2014 (11.8%), 80 in 2015 (21.9%), 116 in 2016 (31.7%), and 47 in 2017 (26.0%) (Figure 1, 2).

SO_2 values did not exceed Turkish threshold limits on any days during the five-year study period, and exceeded EU country limits on only one day, in 2015. However, SO_2 values exceeded WHO limits on 3 days in 2012 (1.6%), 30 in 2013 (8.2%), 42 in 2014 (11.5%), 56 in 2015 (15.3%), 37 in 2016 (10.1%) and none in 2017.

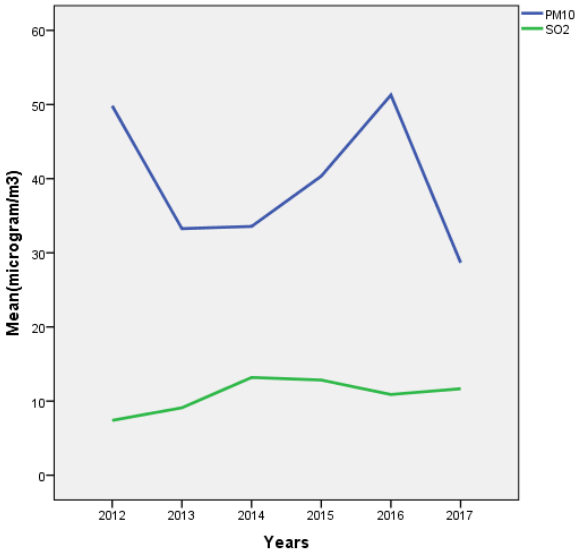


Figure 1: SO_2 and PM_{10} levels in Erzurum by years

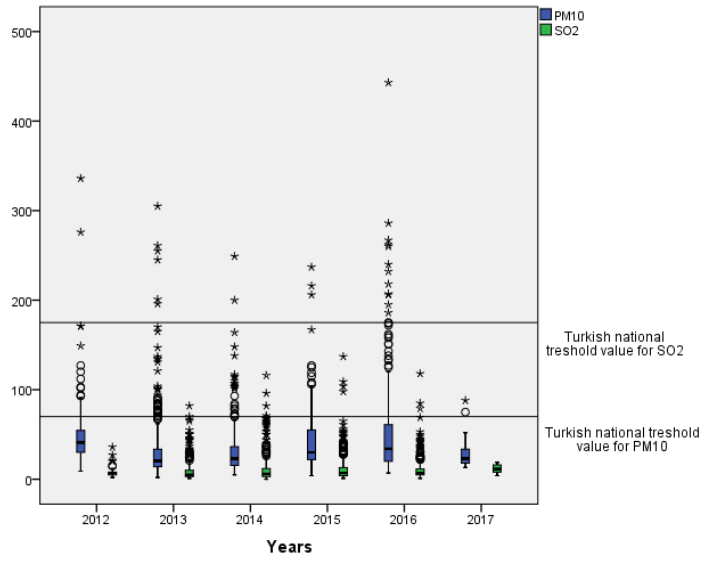


Figure 1: Distribution of SO_2 and PM_{10} parameters by national threshold values

Variation in PM_{10} and SO_2 values by years was statistically significant ($p<0.001$ for both). There was no statistically significant difference in terms of PM_{10} levels between 2013 and 2014, or between 2016 and 2017, but significant decreases were observed in the following years. A significant decrease occurred in SO_2 levels between 2012 and 2013, while a significant increase occurred between 2016 and 2017. SO_2 increased significantly at the end of five years ($p<0.001$).

No statistically significant difference was determined in PM_{10} and SO_2 levels in terms of seasons or months ($p<0.001$ for both). The median PM_{10} winter value was 55.4 (minimum: 2, maximum: 443), and the median SO_2 value was 14.9 (minimum: 1, maximum: 137). Median summer values were 24.1 (minimum: 2, maximum: 106) for PM_{10} and 6.2 (minimum: 1, maximum: 96) for SO2. SO_2 and PM_{10} levels by months are shown in Table 3.

Table 3: SO_2 and PM_{10} levels by months

	PM_{10} ($\mu g/m^3$)			SO_2 ($\mu g/m^3$)		
	Median	Minimum	Maximum	Median	Minimum	Maximum
January	81.09	5	305	22.56	1	116
February	80.63	13	443	20.03	4	118
March	37.13	7	174	8.10	2	31
April	22.60	4	76	7.47	1	19
May	18.26	6	48	4.15	1	18
June	22.10	4	58	3.82	1	13
July	23.52	8	70	8.23	1	96
August	32.23	7	78	4.45	1	9
September	25.87	2	106	8.78	1	69
October	31.14	2	118	7.06	2	29
November	41.54	8	98	14.06	2	137
December	63.37	8	336	18.63	1	82

The highest monthly median values for both air pollution parameters were determined in January, while the highest mean values were recorded in February.

Discussion

Levels of PM_{10} and SO_2, two parameters assessing air pollution in measurements performed in the center of Erzurum province in 2012-2017 significantly exceeded both EU and WHO limits and also Turkish national threshold values. PM_{10} values exceeded the recommended limits for EU countries on more than 35 days a year in this research. SO_2 levels did not exceed EU country limits more than three days in any of the five years. However, SO_2 levels were considerably above the limit recommended by the WHO for a healthy ecosystem.

Turalıoğlu et al. [12] showed that air pollution levels in Erzurum increased significantly in 2003-2004. Beyhun et al. [11] reported that pollution continued to rise in 2003–2006, after which a statistically significant decrease was observed in pollution parameters (particularly SO_2). In particular, the short-term and winter limits determined by the 2006 Directive on the Protection of Air Quality were not exceeded. One study of air pollution in Erzurum between 1990 and 2008 determined a decrease in SO_2 and PM_{10} in the city center [10]. In our own research, while we observed a decrease in PM_{10} levels between 2012 and 2017, SO2 levels increased. Our findings and those of other studies performed in our province indicate that there has been a marked decrease in both parameters compared to previous years. All studies conducted in Erzurum, which is not affected by industrial air pollution, have reported, in agreement with our findings, that air pollution peaks in January, in parallel to increased fuel consumption in winter [10,11].

The Erzurum Air Quality Assessment Report, which evaluated data for the province in 2009-2012, reported that the peak PM_{10} and SO_2 emissions occurred at times of high fuel consumption, that significant increases occurred when ambient temperatures were very low, and that motorized transport emissions occurring at the same times as heating system-based emissions contributed significantly to peaks in air pollution parameters and to intense air pollution lasting many hours [8]. The use of natural gas is a major factor in the gradual decrease observed since 2015 in our province, in which fuels and traffic are the most important pollutants [11]. SO2 levels increased at the end of our five-year study period, an increase that may be attributed to a move away from high-quality fuels, increased traffic, and problems with motorized vehicle exhaust emissions. The results of studies conducted in different provinces of Turkey

have shown that decreases in air pollution parameters can be achieved through actions taken by local administrations [13,14]. Studies conducted at the international level have also shown that air pollution prevention measures and amendments to legislation can overcome various problems, but that air pollution agents continue to represent a threat to health by changing forms over the years [15]. For all these reasons, the adoption of appropriate measures by local administrations will be effective in reducing air pollution. The results of scientific research into air pollution and its causes at the national level must be closely monitored to permit the updating of legislation aimed at air pollution agents.

In its reports into air pollution, the Union of Chambers of Turkish Engineers and Architects regards the province of Iğdır as a region under particular threat from air pollution, and has reported that air pollution has persisted in the province due to a failure to take precautionary measures. PM_{10} limits in the province of Iğdır were exceeded 265 times in 2015 and 242 times in 2016. Inversion deriving from natural geographic conditions prevents the dispersion of pollution [16]. This shows the importance of establishing air corridors through urban areas in order to avoid long-term persistence of the threat caused by air pollution episodes.

The present study also evaluated SO_2 and PM_{10} levels in Erzurum in 2012-2017 in terms of months and seasons. The fact that this descriptive, cross-sectional study was unable to reveal the causes of air pollution represents a limitation. However, the findings are important in terms of assessing the existing position for local administrators and for future research on the subject, and in showing the dimensions of the preventable problem of air pollution with its impacts on public health.

Conclusion

The problem of air pollution in Erzurum has decreased compared to previous years, but it still not at recommended levels. It continues to represent a threat to public health. Local administrations must adopt the requisite precautionary measures to prevent air pollution, particularly in winter; our province has especially harsh winters. Inspections are essential, and the public must be incentivized on the subject of using high-quality fuels.

References

1. Air pollution. 19.07.2017; Available from: http://www.who.int/topics/air_pollution/en/.
2. Ambient (outdoor) air quality and health. 17.07.2017; Available from: http://www.who.int/mediacentre/factsheets/fs313/en/.
3. Filleul L, Medina S, Cassadou S. Urban particulate air pollution: from epidemiology to health impact in public health. Revue d'epidemiologie et de sante publique. 2003;51(5):527-42.
4. Bell ML, Davis DL. Reassessment of the lethal London fog of 1952: novel indicators of acute and chronic consequences of acute exposure to air pollution. Environmental health perspectives. 2001;109(Suppl 3):389.
5. Seaton A, Godden D, Macnee W, Donaldson K. Particulate air pollution and acute health effects. The lancet. 1995;345(8943):176-8.
6. Sümer GÇ. Hava Kirliği Kontrolü: Türkiye'de Hava Kirliliğini Önlemeye Yönelik Yasal Düzenlemele-rin ve Örgütlenmelerin İncelenmesi. Uluslararası İktisadi ve İdari İncelemeler Dergisi. 2014;13(13):37-56.
7. Ulusal Hava Kalitesi İzleme Ağı. 19.07.2017; Available from: http://www.havaizleme.gov.tr/Default.ltr.aspx.
8. Karaca A, Şenol A, Denizli F, Çiçek M, Derman Y. Erzurum Air Quality Assessment Report. 2013, Erzurum: T.R. Environment And Urban Ministry.
9. Kırımhan S, Boyabat N. Erzurum'da hava kirliliği-Son rapor. Atatürk Üniversitesi Çevre Sorunları Sempozyumu–5, Erzurum. 1983;12:6-8.
10. Kopar İ, Zengin M. Coğrafi faktörlere bağlı olarak Erzurum kentinde hava kalitesinin zamansal ve mekânsal değişiminin belirlenmesi. Türk Coğrafya Dergisi. 2009;53:51-68.
11. Beyhun NE, Vançelik S, Acemoğlu H, Koşan Z, Güraksın A. Erzurum İli Kent Merkezinde 2003–2006 Yılları Arasında Hava Kirliliği. TAF, Preventive Medicine Bulletin. 2008;73(3):237-42.
12. Turalioğlu FS. An assessment on variation of sulphur dioxide and particulate matter in Erzurum (Turkey). Environmental Monitoring and Assessment. 2005;104(1-3):119-30.
13. Topbaş M, Çan G, Kapucu M. Effects of local decisions on air polution in Trabzon, Turkey during 1994-2000. Turk J Public Health. 2004;2:80-4.
14. Eğri M. 1996-1997 kış döneminde Malatya il merkezi hava kirliliği parametrelerine meteorolojik koşulların etkisi. İnönü Univ Tip Fak Derg. 1997;4:265-69.
15. Brunekreef B, Holgate ST. Air pollution and health. The lancet. 2002;360(9341):1233-42.
16. Hava Kirliliği Raporu 2016. 2017 11.04.2018; Available from: http://www.cmo.org.tr/resimler/ekler/a941df595b4c831_ek.pdf?tipi=67&turu=H...0.

J Surg Med. 2018;2(3):269-272.
DOI: 10.28982/josam.428632

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

A case-control study on rosacea and vitamin D levels

Rozasea ve D vitamini düzeyleri üzerinde bir vaka kontrol çalışması

Gülhan Gürel [1], Müjgan Karadöl [2], Emine Çölgeçen [1]

[1] Department of Dermatology, Bozok University School of Medicine, Yozgat, Turkey
[2] Department of Biochemistry, Bozok University School of Medicine, Yozgat, Turkey

ORCID ID of the authors
GG: 0000-0001-5716-8750
MK: 0000-0002-9291-4197
EÇ: 0000-0001-9651-6068

Corresponding author / Sorumlu yazar:
Gülhan Gürel
Address / Adres: Bozok Üniversitesi, Tıp Fakültesi, Dermatoloji Bölümü, Yozgat, Türkiye
E-mail: gulhanozturkgurel@hotmail.com

Ethics Committee Approval: Bozok University Faculty of Medicine Ethics Committee Decision No: 18/03 Date: 01.11.2016.
Etik Kurul Onayı: Bozok Üniversitesi Tıp Fakültesi Etik Kurulu Karar No: 18/03 Tarih: 01.11.2016.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 30.05.2018
Accepted / Kabul Tarihi: 27.06.2018
Published / Yayın Tarihi: 03.07.2018

Abstract

Aim: Rosacea is a chronic inflammatory dermatosis characterized by several features such as temporary erythema (flushing), permanent erythema, papules, pustules and telangiectasia in the face. In this study, our aim is to investigate the role of serum vitamin D levels in the pathogenesis of rosacea.

Methods: 50 patients with rosacea and 50 age and gender matched healthy controls were included in this study. In patients with rosacea and control group, serum parathyroid hormone (PTH), vitamin D levels and serum calcium levels were measured and the results were compared statistically.

Results: Serum vitamin D levels in patients with rosacea were significantly higher than the control group (respectively 10,55 ng/ml and 8,50 ng/ml). The median of serum calcium level was found to be 8,20 mg/dl in the group of patients with rosacea and 8,55 mg/dl in the control group. Serum calcium levels of the control group were significantly higher than the group of patients with rosacea. There was no statistically significant difference in terms of serum parathormone levels between the group of patients with rosacea and control group. The increase in serum vitamin D levels may lead development of rosacea.

Conclusion: As a result, the increase in serum vitamin D levels is associated with rosacea.

Keywords: Rosacea, Vitamin D, Cathelicidin, Parathormone

Öz

Amaç: Rozasea yüz bölgesinde geçici eritem (flushing), kalıcı eritem, papül, püstül ve telenjiektazi gibi çeşitli özelliklerle karakterize olan kronik inflamatuvar bir dermatozdur Bu çalışmada amacımız rozasea patogenezine etki edebilecek serum vitamin D düzeylerinin rolünü araştırmaktır.

Yöntemler: Dermatoloji polikliniğine başvuran 50 rozasea hastası ile yaş ve cinsiyet açısından eşleştirilmiş 50 sağlıklı kontrol grubu alındı. Rozasealı hastalarda ve kontrol grubunda serum paratiroid hormonu (PTH), D vitamin seviyeleri, serum kalsiyum düzeyleri ölçüldü ve istatistiksel olarak karşılaştırıldı.

Bulgular: Rozasealı hasta grubunun serum 25-hidroksivitamin D düzeyi medianı 10,55 (6,30-38,60) ng/ml, kontrol grubunun ise 8,50 (4,50-25,60) ng/ml olarak saptandı. Rozasea'lı hasta grubunun serum vitamin D düzeyi kontrol grubundan anlamlı olarak yüksek bulundu (p=0,013). Rozasealı hasta grubunun serum kalsiyum düzeyi medianı 8,20 (7,20-9,20) mg/dl, kontrol grubunun ise 8,55(7,60-11,40) mg/dl olarak saptandı. Kontrol grubunun serum kalsiyum düzeyi rozasealı hasta grubundan anlamlı olarak yüksek bulundu (p=0,000). Rozasealı hasta grubu ve kontrol grubu arasında serum parathormon düzeyleri açısından istatistiksel olarak anlamlı farklılık saptanmadı (p=0,194).

Sonuç: Serum vitamin D düzeylerinin yükselmesi rozasea gelişimi ile ilişkili olabilir.

Anahtar kelimeler: Rozasea, Vitamin D, Katelisidin, Parathormon

How to cite / Atıf için: Gürel G, Karadöl M, Çölgeçen E. A case-control study on rosacea and vitamin D levels. J Surg Med. 2018;2(3):269-272.

Introduction

Rosacea is a chronic inflammatory dermatosis characterized by several features such as temporary erythema (flushing), permanent erythema, papules, pustules and telangiectasia in the face area [1]. Secondary features such as skin burning, tingle, dry appearance, edema, ocular involvement and phymatous changes may also be seen in patients [2]. There are four subtypes of Rosacea; erythematous-telangiectatic, papulopustular, ocular and phymatous type. The most common type is the erythematous-telangiectatic type [3]. The prevalence has a wide range, from 0.1% to 22% [2]. Although a relation has been determined between rosacea and various chronic systemic diseases (gastroesophageal reflux, hyperlipidemia, hypertension, cardiovascular diseases), the pathophysiology is not clear [4]. The pathogenesis of rosacea has not been clearly understood yet. The expression of various genes that play a role in the innate and acquired immune systems has been shown to increase in patients with rosacea. Microorganisms such as *Demodex folliculorum*, *Staphylococcus epidermidis*, ultraviolet (UV) rays, and transient receptor potential family are among the blamed factors for the etiology [1,2,5].

Vitamin D is a steroid hormone synthesized in epidermal keratinocytes by UV-B light (290-315 nm) or taken with diet. In order to be active hormone, vitamin D should be converted to 1,25-dihydroxy vitamin D by 25- and 1-alpha hydroxylation [6]. There is now evidence that vitamin D plays an important role in cutaneous immunity in addition to its effects on calcium homeostasis and bone metabolism [7]. Vitamin D affects the acquired immune system by the activation of T cell and maturation of dendritic cells. It is also argued that it increases innate immunity in the skin and increases the antimicrobial defense which is effective in epithelial surfaces [8]. In recent years, vitamin D has become increasingly important in the management of diseases such as skin cancers, psoriasis, acne, rosacea, hair loss and atopic dermatitis [6].

The aim of this study is to investigate the role of serum vitamin D levels in patients with rosacea.

Materials and methods

Fifty patients with rosacea who admitted to dermatology outpatient clinic and 50 age and gender matched healthy controls were included in the study between November 2016 and February 2017. The study was approved by the ethics committee and all the patients participating in the study were signed a consent form. This is a case-control type study. Gender, age, body mass index, Fitzpatrick's skin type, smoking, sunscreen usage habit and daily sun exposure time (in minutes) of patients with rosacea and control group were recorded. According to dermatological examination findings, patients were grouped as erythematous-telangiectatic, papulopustular and phymatous type in addition to ocular involvement. All patients diagnosed with rosacea were referred to eye examination. The disease duration of patients with rosacea was recorded as 1-3 years, 3-5 years and >5 years.

The individuals under the age of 18, using any medication that could affect vitamin D levels, receiving calcium supplements and with chronic systemic disease were excluded from the study. The control group was matched with the patient group in terms of age, sex, and body mass index. People in the control group had no systemic disease, healthy subjects without vitamin D and calcium supplementation. The control group was preferred to those living in the same society and similar in lifestyle.

Serum parathyroid hormone (PTH) and vitamin D levels were measured by Abbott Architect ci8200 device using chemiluminescence method, serum calcium levels were measured by Abbott Architect ci8200 autoanalyzer.

Statistical analysis

The findings of this study were analyzed by SPSS-18.0 statistical program. Normal distribution fitting of continuous variables was tested by Kolmogorov-Smirnov test. The descriptive statistics of continuous variables with non-normal distribution were expressed as median (minimum-maximum). The presence of statistically significant difference for continuous variables between groups were examined by Student t test and Mann Whitney U test for nonparametric variables. Chi-square test was used for proportional correlations. $P<0.05$ was accepted as the threshold of statistical significance for all tests.

Results

Twenty-five (50%) female and 25 (50%) male patients with rosacea were included in the study. Twenty-five (50%) female and 25 (50%) male healthy volunteers were included in the study as a control group. The mean age of the group of patients with rosacea was 50 (±11.44) and the mean age of the control group was 51,04 (±11,82). There was no statistically significant difference between the group of patients with rosacea and control group in terms of age and gender ($p>0.05$). The mean of body mass index (BMI) was 29.58 (±3.80) in the group of patients with rosacea and 29.33 (±3.53) in the control group. 17 individuals in the rosacea group and 24 individuals in the control group were smoking. There was no statistically significant difference between the group of patients with rosacea and control group in terms of BMI and smoking ($p>0.05$). 14 individuals in the group of patients with rosacea and 11 patients in the control group were using sunscreen. There was no statistically significant difference between the group of patients with rosacea and control group in terms of sunscreen use, daily sun exposure and Fitzpatrick's skin type ($p>0.05$). The comparative demographic characteristics of the group of patients with rosacea and the control group are shown in Table 1.

In the group of patients with rosacea, there were 26 (52%) patients with a disease duration of 1-3 years, 14 (28%) patients between 3-5 years and 10 (20%) patients with a disease duration of >5 years. Twenty-one (42%) of patients had erythematous-telangiectatic type, 11 (22%) of them had papulopustular type, 6 (12%) of them had erythematous-telangiectatic type with ocular involvement, 10 (20%) of them had papulopustular type with ocular involvement and 2 (4%) of them had phymatous type with ocular involvement.

The median of serum 25-hydroxyvitamin D level was found to be 10.55 (6.30-38.60) ng/ml in the group of patients with rosacea and 8.50 (4.50-25.60) ng/ml in the control group. Serum vitamin D levels of the group of patients with rosacea were significantly higher than the control group ($p=0.013$). The

median of serum calcium level was found to be 8.20 (7.20-9.20) mg/dl in the group of patients with rosacea and 8.55 (7.60-11.40) mg/dl in the control group. Serum calcium levels of the control group were significantly higher than the group of patients with rosacea (p=0.000). There was no statistically significant difference in terms of serum parathormone levels between the group of patients with rosacea and control group (p=0.194). The laboratory values of the patient group with rosacea and control group are comparatively shown in table 2.

Table 1: Demographic characteristics of patients with rosacea and control group

	Patients with Rosacea N=50	Control N=50	p*
Age	50±11.44	51.04±11.82	0.65
Gender (F/M)	25/25	25/25	1
BMI (kg/m^2)	29.58±3.80	29.33±3.53	0.74
Smoking (Yes)	17	24	1
Sun Exposure			
<10 min	3 (%75)	1 (%25)	
10-20 min	9 (%47.4)	10 (%52.6)	0.124
20-30 min	7 (%30.4)	16 (69.6)	
>30 min	31 (%57.4)	23 (%42.6)	
Use of sunscreen (Yes)	14 (%28)	11 (%22)	0.48
Fitzpatrick's skin type			
Type 1	4 (%8)	3 (%6)	
Type 2	22 (%22)	24 (%48)	0.905
Type 3	22 (%22)	22 (%44)	
Type 4	2 (%4)	1 (%2)	

* Chi-Square Test

Table 2: Laboratory parameters of patients with rosacea and control group

	Patients with Rosacea N=50	Control N=50	P
25-Hydroxy vitamin D (ng/ml)	10.55(6.30-38.60)	8.50(4.50-25.60)	0.013 *
Calcium (mg/dl)	8.20(7.20-9.20)	8.55(7.60-11.40)	0.000 *
Parathormone (pg/ml)	47.30(13.60-120.60)	47.60(17.70-187.10)	0.194

***** p<0.05

Discussion

Rosacea is a chronic inflammatory skin disease that mostly affects middle-aged blonde women with light skin and blue eye, although it can be seen in any person [5,9]. Rosacea has multi-factorial pathology including vasoactive and neurocutaneous components as well as innate and acquired immunity. Each of these factors contributes to the disease in different proportions [2]. Under normal physiological conditions, triggering of the innate immunity leads to a controlled increase in cytokines and antimicrobial peptides (AMP) in the skin. These normal signal pathways are disrupted in patients with rosacea. It has been shown that basal levels of cathelicidin, an AMP, and kallikrein 5 (KLK 5), a serine protease that breaks down cathelicidin into its active peptide form, LL-37 are increased in patients with rosacea [10,11]. KLK 5 and LL-37 are higher in the skin with rosacea as well as their structures are different. In the skin with rosacea, LL-37 is converted into shorter fragments that regulate processes such as leukocyte chemotaxis, angiogenesis and expression of extracellular matrix components [11-13].

The expression of cathelicidin in keratinocytes is strongly induced by vitamin D, which is activated in keratinocytes by UV light, which is a well-known trigger of rosacea [14]. In addition, toll-like receptor 2 (TLR 2) and matrix metalloproteinase levels, which activate KLK 5 have also increased in patients with rosacea [15,16].

Nowadays, the impairments in the expression, function, or processing of cathelicidin LL-37 are blamed in the etiology of diseases such as atopic dermatitis, psoriasis and rosacea [17]. Atopic dermatitis is a type of chronic inflammatory eczema. Some studies suggest that the underlying mechanism is initially epidermal dysfunction and subsequently immunological activation, but many animal studies, case reports, and randomized clinical trials have suggested that vitamin D may alleviate the symptoms of atopic dermatitis via various mechanisms including immunomodulation [6]. Mutgi et al. and Heimbeck et al. have shown in their studies that in patients with atopic dermatitis and vitamin D deficiency, the disease improved and the severity of the disease reduced as a result vitamin D replacement [18,19]. In the treatment of psoriasis, vitamin D analogs have been used for many years, but the molecular mechanisms behind the clinical effects are not clearly understood [6,17]. Topical vitamin D analogues, such as calcipotriol, reduce proinflammatory cytokines in the skin and strongly increase the expression of cathelicidin. Some studies have begun to investigate whether or not serum vitamin D levels correlate with cutaneous AMP expression in psoriatic patients [17]. Kim et al. have found in their study that cathelicidin expression in the lesional skin of patients with psoriasis was higher in the group with sufficient serum vitamin D level than in the group with serum vitamin D deficiency [20].

When we look at the studies in which serum vitamin D levels were investigated in patients with rosacea, the only one study has been conducted by Ekiz et al., from our country. In this study, serum vitamin D levels in patients with rosacea were found to be higher when compared to the control group, and it was argued that high serum vitamin D levels may lead development of rosacea [21]. Similarly, in our study, serum vitamin D levels were statistically significantly higher in the rosacea group than in the control group, whereas serum vitamin D levels in both groups were lower than those of in the study of Ekiz et al. This difference could be attributed to the fact that our study was performed in the Central Anatolian region, the blood samples were taken from the patients in the winter period (November-February) and the mean age and BMI was higher.

Conclusion

As a result, the increase in serum vitamin D levels is associated with rosacea. In the future, new therapeutic approaches that block the expression of cathelicidin via the vitamin D pathway may come into question. Prospective clinical trial or metaanalysis with larger series in different centers which will support these results are needed.

References

1. Two AM, Wu W, Gallo RL, Hata TR. Rosacea: part I. Introduction, categorization, histology, pathogenesis, and risk factors. J Am Acad Dermatol. 2015;72:749-58.
2. Picardo M, Eichenfield LF, Tan J. Acne and Rosacea. Dermatol Ther (Heidelb). 2017;7(Suppl 1):43-52.
3. Wilkin J, Dahl M, Detmar M, et al. Standard classification of rosacea: Report of the National Rosacea Society Expert Committee on the Classification and Staging of Rosacea. J Am Acad Dermatol. 2002;46:584-7.
4. Rainer BM, Fischer AH, Luz Felipe da Silva D, et al. Rosacea is associated with chronic systemic diseases in a skin severity-dependent manner: results of a case-control study. J Am Acad Dermatol. 2015;73:604-8.
5. Mikkelsen CS, Holmgren HR, Kjellman P, et al. Rosacea: a Clinical Review. Dermatol Reports. 2016;8:6387.

6. Mostafa WZ, Hegazy RA. Vitamin D and the skin: Focus on a complex relationship: A review. J Adv Res. 2015;6:793-804.
7. Bikle DD. What is new in vitamin D: 2006-2007. Curr Opin Rheumatol. 2007;19:383-8.
8. Schauber J, Gallo RL. The vitamin D pathway: a new target for control of the skin's immune response? Exp Dermatol. 2008;17:633-9.
9. Lanoue J, Goldenberg G. Therapies to improve the cosmetic symptoms of rosacea. Cutis. 2015;96:19-26.
10. Yamasaki K, Di Nardo A, Bardan A, et al. Increased serine protease activity and cathelicidin promotes skin inflammation in rosacea. Nat Med. 2007;13:975-80.
11. Yamasaki K, Schauber J, Coda A, et al. Kallikrein-mediated proteolysis regulates the antimicrobial effects of cathelicidins in skin. FASEB J. 2006;20:2068-80.
12. Koczulla R, von Degenfeld G, Kupatt C, et al. An angiogenic role for the human peptide antibiotic LL-37/hCAP-18. J Clin Invest. 2003;111:1665-72.
13. Morizane S, Yamasaki K, Mühleisen B, et al. Cathelicidin antimicrobial peptide LL-37 in psoriasis enables keratinocyte reactivity against TLR9 ligands. J Invest Dermatol. 2012;132:135-43.
14. Schauber J, Dorschner RA, Coda AB, et al. Injury enhances TLR2 function and antimicrobial peptide expression through a vitamin D-dependent mechanism. J Clin Invest. 2007;117:803-11.
15. Di Nardo A, Vitiello A, Gallo RL. Cutting edge: mast cell antimicrobial activity is mediated by expression of cathelicidin antimicrobial peptide. J Immunol. 2003;170:2274-8.
16. Jang YH, Sim JH, Kang HY, et al. Immunohistochemical expression of matrix metalloproteinases in the granulomatous rosacea compared with the non-granulomatous rosacea. J Eur Acad Dermatol Venereol. 2011;25:544-8.
17. Reinholz M, Ruzicka T, Schauber J. Cathelicidin LL-37: an antimicrobial peptide with a role in inflammatory skin disease. Ann Dermato.l 2012;24:126-35.
18. Mutgi K, Koo J. Update on the role of systemic vitamin D in atopic dermatitis. Pediatr Dermatol. 2013;30:303-7.
19. Heimbeck I, Wjst M, Apfelbacher CJ. Low vitamin D serum level is inversely associated with eczema in children and adolescents in Germany. Allergy. 2013;68:906-10.
20. Kim SK, Park S, Lee ES. Toll-like receptors and antimicrobial peptides expressions of psoriasis: correlation with serum vitamin D level. J Korean Med Sci. 2010;25:1506-12.
21. Ekiz O, Balta I, Sen BB, et al. Vitamin D status in patients with rosacea. Cutan Ocul Toxicol. 2014;33:60-2.

J Surg Med. 2018;2(3):273-277.
DOI: 10.28982/josam.429059

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

The effect of osteoporosis on cochlear function in postmenopausal women: An observational study

Postmenapozal kadınlarda koklear fonksiyona osteoporozun etkisi: Gözlemsel bir çalışma

Saime Sağıroğlu [1], Tuba Tülay Koca [2]

[1] Sütçü İmam Üniversitesi, Faculty of Medicine, Department of Otorhinolaringology, Kahramanmaraş, Turkey
[2] Sütçü İmam University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Kahramanmaraş, Turkey

ORCID ID of the authors
SS: 0000-0003-2608-7274
TTK: 0000-0002-4596-858X

Corresponding author / Sorumlu yazar:
Tuba Tülay Koca
Address / Adres: Sütçü İmam University, Fiziksel Tıp ve Rehabilitasyon Anabilim Dalı, Kahramanmaraş, Türkiye
E-mail: tuba_baglan@yahoo.com

Ethics Committee Approval: The study was approved by local Ethics Committee.
Etik Kurul Onayı: Çalışma için onay Etik Kurulundan alınmıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 31.05.2018
Accepted / Kabul Tarihi: 26.06.2018
Published / Yayın Tarihi: 03.07.2018

Abstract

Aim: Hearing loss and osteoporosis are common geriatric syndromes. Evidence suggests that osteoporosis may have an effect on cochlear function in a small number of clinical trials. Here, cochlear function in osteoporosis patients was assessed by otoacoustic emission test (OAET) measurements.

Methods: The study designed as cross-sectional and observational. Forty female patients were included in the postmenopausal period at the age of 40-75 years. Age, body mass index (BMI), vitamin D level were recorded in all patients. Audiometric threshold testing was used to measure air- and bone-conduction hearing sensitivity. Bone mineral density (BMD) of the hip and vertebra was measured using dual-energy X-ray absorptiometry (DEXA). According to vertebra L1-4 t score <-2.5 osteoporosis, -2.5 to -1 osteopenic, the group divided into two and all parameters were compared. Transiently evoked (TE), and distortion-product (DP) otoacoustic emissions were recorded.

Results: The mean age of the whole group was 58.6 ± 7.9 years. Accordingly, TE left was significantly different in the higher frequency in the osteopenic group at 0.75 Hz (p = 0.015). In audiometric tests, only the osteopenic group at 6,000 Hz was significantly different in the higher frequency of both ears (p = 0.049 / p = 0.016).

When the group divided into two according to femur t score <-1.0; TEright_3.5 (p = 0.04), TEright_overall (p = 0.030), TEleft_1.7.5 (p = 0.043) and TEleft_overall (p = 0.046), DPright_1 (p = 0.049) and DPleft_6 (p = 0.039) were observed to occur at higher frequencies in the osteoporotic group. Lomber t score was positively correlated with BMI (p = 0.042 / r = 0.288). BMI was lower in the osteoporotic group. The tympanogram results of all patients were Type A. The TE positivity rate (S / N> 3) was 60.8% and the DP positivity rate (S / N> 3) was 39.2%.

Conclusion: According to hip BMD scores, osteopenic-osteoporotic (T scor <-1) group showed higher frequencies in both cochlear and hearing tests than normal subjects. The high frequencies in both OAET results and odiologic data in osteoporotic group support the adverse effect of osteoporosis on cochlear and hearing function. Individuals with hearing loss should be screened for osteoporosis.

Keywords: Bone mineral density, Osteoporosis, Hearing loss, Cochlear function

Öz

Amaç: İşitme kaybı ve osteoporoz sık görülen geriatrik sendromlardandır. Az sayıda klinik çalışmada osteoporozun koklear fonksiyona etkisi olabileceği yönünde delil bulunmuştur. Burada osteoporoz hastalarında kohlear fonksiyon, otoaküstik emisyon test (OAET) ölçümleri ile değerlendirildi.

Yöntemler: Çalışma kesitsel gözlemsel olarak düzenlendi. Çalışmaya 40-75 yaş aralığında postmenapozal dönemde 50 kadın hasta dahil edildi. Tüm hastalarda yaş, vücut kitle indeksi (BMI), vitamin D düzeyi kayıt edildi. Hava ve kemik iletimli işitme hassasiyetini ölçmek için odiyometrik eşik testi kullanıldı. Kalça ve omurganın kemik mineral yoğunluğu (BMD) dual enerji X-ışını absorpsiyometri (DEXA) kullanılarak ölçüldü. Vertebra L1-4 t skor<-2,5 osteoporoz, -2,5 ila -1 arası osteopenik olarak grup ikiye ayrıldı ve tüm parametreler karşılaştırıldı. Geçici olarak uyarılmış (TE) ve distorsiyon ürünü (DP) otoakustik emisyonları kaydedildi.

Bulgular: Tüm grup yaş ortalaması 58,6±7,9 yıl idi. Buna göre TE left 0.75 Hz'de osteopenik grupta daha yüksek frekansda anlamlı farklı idi (p=0,015). İşitme testlerinde sadece her iki kulak 6.000 Hz'de osteopenik grup daha yüksek frekansda anlamlı farklı idi (p=0,049 / p=0,016).

Femur t skor<-1,0 göre grup ikiye ayrıldığında TEright_2.5 (p=0,015), TEright_3.5 (p=0,04), TEright_overall (p=0,030), TEleft_1.7.5 (p=0,043), TEleft_overall (p=0,046), DPright_1 (p=0.049), DPleft_6 (p=0,039) osteoporotik grupta daha yüksek frekanslarda sonuçlar olduğu gözlendi. Lomber t skor BMI ile pozitif korele (p=0,042/r=0,288) idi. Osteoporotik grubda BMI daha düşük idi. Hastaların tamamında timpanogram sonuçları Tip A idi. TE pozitiflik oranı (S/N>3) %60,8, DP pozitiflik oranı (S/N>3) %39,2 idi.

Sonuç: Kalça BMD skorlarına göre, osteopenik_osteoporotik grup (T skor<-1) hem koklear hem da işitme testlerinde normal kişilere göre yüksek frekanslar gösterdiler. Osteoporotik grupta hem OAET sonuçları hemde odiyolojik verilerin daha yüksek frekanslarda olması osteoporozun koklear ve işitme fonksiyonuna olumsuz etkisini desteklemektedir. İşitme kaybı olan bireyler osteoporoz yönünden taranmalıdır.

Anahtar kelimeler: Kemik mineral yoğunluğu, Osteoporoz, İşitme kaybı, Koklear fonksiyon

How to cite / Atıf için: Sağıroğlu S, Koca TT. The effect of osteoporosis on cochlear function in postmenopausal women: An observational study. J Surg Med. 2018;2(3):273-277.

Introduction

Osteoporosis is the most common metabolic bone disease worldwide and leads to physical, psychosocial and economic consequences. It can be seen in both genders and at any age, usually with older women. Low bone mass and bone tissue result in increased bone fragility with impaired microstructure. It is usually insidious and diagnosed after the fracture has occurred. Because of postural kyphosis, balance problems are frequently observed by gravity center change. The quality of life of the elderly population is negatively affected by pain and physical disability [1-3].

Autoacoustic emissions (OAE) are mildly acoustical energy emissions from cochlear sources that are detected from the external auditory canal of humans and animals. In 1948 Gold became the first to speak of the fact that cochlear is not only a voice-receiving organ, but also produces acoustic energy. However, this mechanism was revealed only 30 years later by the British physicist Kemp (1978) [4-6]. In hearing screenings, hearing loss due to noise, presbyacusis, familial hearing loss, idiopathic sensorineural hearing loss, Meniere and acoustic neurinoma are used to determine the cochlea component [7,8]. OAE response with aging is statistically significant [5]. This reduction is not only related to age, but also to the level of hearing [6]. It may be possible to prevent the loss of hearing when the etiology causing the hearing loss is revealed and treated.

Physical and mental changes in the elderly population can affect the changing living conditions, increased age, and the experience of living alone with hearing loss. The complex nature of aging-related hearing problems involves changes in the auditory environment and in the central mechanisms that process the sound input [9]. The association of osteoporosis and pediatric disorders has been the subject of various investigations [10]. Hearing loss is thought to be one of the clinical manifestations of metabolic bone diseases. Demineralization can cause ossicular mass to decrease. Paget's disease may cause a decrease in mineral density in cochlear bones. According to some researchers, osteopenia and osteoporosis may be associated with idiopathic benign positional vertigo (BPV). It is thought that osteoporosis can affect the audiological functions due to changes in structural and cochlear metabolism (calcium homeostasis) in the ear bones. The high incidence of hearing loss in metabolic bone diseases can lead to bone densitometry screening in people with hearing loss [9,10].

Odiologic complaints are common risk factors with common geriatric syndromes. For this reason, osteoporosis patients require a well-defined and multi-faceted approach to the otologic examination. It is supported by current publications that osteoporosis is a risk factor for age-related hearing loss. Here, the effects of osteoporosis to cochlear function were analyzed in elderly women.

Materials and methods

The study designed as cross-sectional and observational. Forty female patients were included in the study between the ages of 40-75 years in the postmenopausal period. The inclusion criteria for the study are being between 40 and 75 years age, being female, being in the postmenopausal period and not having any odiological problems before. Age, body mass index (BMI), vitamin D levels were recorded in all patients. Measurements of vertebra and femur bone mineral density (BMD) were performed with dual energy x - ray absorptiometry (DEXA). L1-L4 total T score from vertebral measurements; femur measurements were based on total T score. According to vertebra L1-4 t score <-2.5 osteoporosis, -2.5 to -1 osteopenic, the group divided into two and all parameters were compared.

Known neuropsychiatric disease, radiotherapy, malignancy, acute infection or inflammatory rheumatic disease and hearing loss due to acute and chronic otitis media, ear surgery, acoustic schwannoma, meningioma, sudden hearing loss, acoustic trauma, Meniere's disease and other causes were excluded.

Dual-energy x-ray absorptiometry (DEXA)

DEXA measurement is the gold standard for the assessment of bone mass index. DEXA provides the patient's T-score, which is the BMD value compared with the control of the BMD. According to the World Health Organization (WHO), the normal T score is defined as 1 standard deviation (SD) of the mean BMD of a healthy young adult. T-score of -1 to -2.5 SD indicates osteopenia, and T-score indicates less than -2.5 SD indicates osteoporosis. The T score is used to predict the risk of developing a fracture. The Z-score shows the standard deviation of your bone mineral density when compared to individuals of the same sex, same age, same weight, as you. A Z score of less than -2 decades suggests an abnormal bone loss other than aging, and your doctor may be able to detect the underlying problem [11-16].

Audiological Evaluation

Subjects with normal external ear canal and normal tympanic membrane on the otoscopic examination were included in the study. Tympanograms, stapes acoustic reflexes, pure audio audiometry, speech audiometry, otoacustic emission test (OAE) tests (transiently evoked OAE (TEOAE) and distortion product OAE (DPOAE) were applied in the clinic of the audiology.

Impedance audiometry tests were performed with the "AZ-26 Impedance Audiometer" (Interacoustics, Denmark) and tonal audiometry examinations with the "AC-40 Clinieal Audiometer" (Interacoustics, Denmark). Pure voice hearing tests were performed at 125 hz and 8000 hz intervals. For each set of tests, the mean values of air and bone conduction at each frequency value were calculated for both groups. OAE Test with TE and DP with Madsen Capella OAE device. The sound / noise (S / N) ratio arithmetic mean values were taken. The S / N data obtained above indicates the 3-point DPOAE and TEOAE positivity.

Otoacustic emission tests (OAETs)

Otoacoustic emission test (OAET) instruments are now entering routine audiological practice. Otoacoustic emissions measured in the external ear canal describe responses that the cochlea generates in the form of acoustic energy. For the convenience of discussing their principal features, emitted responses can be classified into several categories according to the type of stimulation used to evoke them. On this basis, four distinct but interrelated classes can be distinguished including spontaneous, transiently evoked (TE), stimulus-frequency, and

distortion-product (DP) otoacoustic emissions. The transient OAE type of method has proved very effective in screening applications, particularly in neonates. It is possible to perform noninvasive screening acoustic cochleography in about a minute. The technique is also useful for characterizing cochlear mechanical status prior to long term monitoring [17,18].

Statistics analysis:

Analyses were performed using Statistical Package for the Social Sciences 22 (IBM SPSS for Windows version 22, IBM Corporation, Armonk, New York, USA). Continuous data were presented as mean±SD and categorical variables were summarized as percentages. Kolmogorov Smirnov test was used for the evaluation of normal distribution. Comparisons between groups were made using chi-square tests for categorical variables, independent samples Student's t tests for normally distributed continuous variables and Mann-Whitney U tests when the distribution was skewed. Spearman test is used for correlation analysis. A p value <0.05 was considered statistically significant.

Results

The mean age of the whole group was 58.6 ± 7.9 years. According to vertebra L1-4 t score <-2.5 osteoporosis, -2.5 to -1 osteopenic, the group divided into two and all parameters were compared. According to this, the age, BMI, vitamin D level of both groups were similar (p = 0.9 / 0.3 / 0.6) (Table 1). Only TE left 0.75 Hz was significantly different with higher frequency in the osteopenic group (p = 0.015). No significant difference was observed in other parameters (Table 2, 3). In audiometric tests, only the osteopenic group at 6,000 Hz was significantly different with higher frequency of both ears (p = 0.049 / p = 0.016) (Table 4).

Table 1: Distribution of demographic data of both groups

	Osteoporosis (N=21)	Osteopenia (n=29)	P
Age (year)	58.6±8.1	58.6±7.8	0.9
BMI (kg/m2)	29.3±4.7	30.5±3.9	0.3
Lomber L1-L4 t score:*	-3.2±0.5	-1.3±1.2	0.00
Femur total t score:	-1.5±1.1	-1.2±0.79	0.22
Vitamin D (ng/mL)	24.7±23.9	21.4±23.5	0.6

BMI: body mass index, * statistically significant difference.

Table 2: Distortion products (DP) results of the groups

Hearing Frequency	Osteoporosis t score<(-2.5)	Osteopenia t score=(-2.5)-(-1.0)	P
DPright0.75	0.6±6.6	2.2±7.1	0.43
DPright1	1.9±9.9	3.3±5.7	0.52
DPright1.5	4.7±5.3	2.1±7.8	0.21
DPright2	4.2±5.9	3.6±6.6	0.73
DPright3	4.2±7.2	4.7±6.5	0.81
DPright4	3.7±7.7	4.3±6.9	0.76
DPright6	0.7±6.9	1.6±8	0.67
DPright8	0.4±4.5	0.85±6.6	0.83
DPleft0.75	0.6±6.5	2.2±5.2	0.38
DPleft1	2.7±5.7	3.6±5.1	0.59
DPleft1.5	4±6.03	4.5±5.4	0.79
DPleft2	4.9±3.7	1.5±7.6	0.078
DPleft3	5.2±5.2	4±7.1	0.52
DPleft4	4.5±5.2	4±9.5	0.82
DPleft6	0.7±5.9	2.2±7.6	0.48
DPleft8	1.5±5.3	2.3±6.4	0.7

DP: Distortion products, * statistically significant difference.

Table 3: Transiently evoked (TE) results of the groups

Hearing frequency	Osteoporosis t score<(-2.5)	Osteopenia t score=(-2.5)-(-1.0)	P
TE right 0.75 Hz	5.1±5.5	4.1±5.6	0.53
TE right 1.25	8.1±6.3	6.3±5.5	0.3
TE right 1.75	3.8±7.9	5±6.3	0.54
TE right 2.5	3.2±7.9	2.8±7.1	0.84
TE right 3.5	2.4±7.9	1.3±7	0.59
TE right overall	5.5±4.7	4.4±4	0.46
TE left 0.75 Hz*	2.9±5.2	6.6±.8	0.015
TE left 1.25	8±5.4	8±6.4	0.99
TE left 1.75	4.6±4.9	4.5±5.5	0.98
TE left 2.5	1.3±6	3.1±5.7	0.30
TE left 3.5	1.2±7	0.8±5.4	0.82
TE left overall	2.6±4.3	4.8±4	0.14

TE: transiently evoked, * statistically significant difference.

Table 4: Audiologic evaluation of the groups

Hearing frequency (db)	Osteoporosis t score<(-2.5)	Osteopenia t score=(-2.5)-(-1.0)	P
R_250	13.8±7.2	14.6±7.6	0.69
L_250	13±4.8	15.6±7.8	0.18
R_500	13.5±5.9	13.6±7.1	0.98
L_500	13±5.5	15±8.4	0.37
R_1000	16.4±8.5	17±10.6	0.82
L_1000	14±5.8	18.6±11	0.09
R_2000	16.4±10.3	22.2±15.5	0.143
L_2000	16.4±10.3	23.9±14.6	0.049
R_4000	23.3±11.7	28.6±20.7	0.3
L_4000	22.8±11.6	30.6±20.3	0.12
R_6000*	26.9±15.2	38.1±21.8	0.049
L_6000*	27.8±14.6	40.1±18.7	0.016
R_8000	29.7±16.9	41.3±25.8	0.79
L_8000	32.3±19.5	41.8±20.7	0.10

R: right; L: left, * statistically difference.

TEright_3.5 (p = 0.04), TEright_overall (p = 0.030), TEleft_1.7.5 (p = 0.043) and TEleft_overall (p = 0.046), DPright_1 (p = 0.049) and DPleft_6 (p = 0.039) were significantly higher in the osteoporotic group at higher frequencies.

The lumber T score was positively correlated with BMI (p = 0.042 / r = 0.288) (Figure 1). BMI was lower in the osteoporotic group. The tympanogram results of all patients were Type A. The TE positivity rate (S / N> 3) was 60.8% and the DP positivity rate (S / N> 3) was 39.2%.

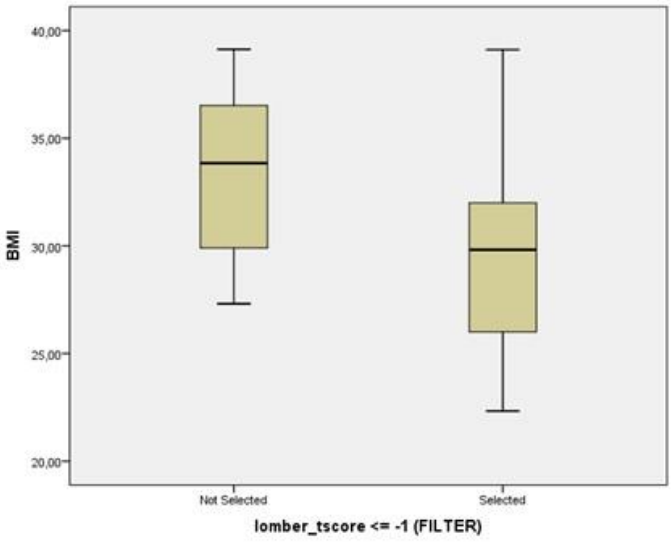


Figure 1: The graphical distribution of BMI according to lomber L1-L4 total T score≤-1,0

Discussion

Osteoporosis is a common metabolic disorder that causes progressive changes in bone structure. The association between menopause and osteoporosis was first described in 1960s [19]. A diagnosis of osteoporosis can be made on the basis of fractures without significant trauma or on the basis of low BMD measured by DEXA. To reduce the risk of osteoporosis, all postmenopausal women should be encouraged to maintain a healthy lifestyle, which includes physical activity and a balanced diet. Smoking and alcohol use should also be addressed. Calcium intake should be encouraged, preferably through diet [20,21].

Clinicians and community health associations should be sensitive to the elderly population. Sensory and cognitive changes, falls and weakness are common in these people. Some hearing loss is a part of the normal aging process and indicates a decrease in immunocompetence [22,23]. With the aging of the populations, hearing loss and osteoporosis are increasing. However, the pathophysiological aspect of this relationship has not yet been identified.

Laudisio et al [24] found that osteoporosis in elderly individuals was associated with hearing loss as correlated with high inflammation parameters. Kshithi et al [25] found that sensorineural hearing loss and pure tone thresholds were higher in osteoporotic women and the DPOAE results were significantly different. Upala S et al [26] suggest that there is a possible relationship between hearing loss and BMD in the meta-analysis. Jung DJ et al [27] did not find such a relationship in the study. In our study, there was no significant difference in osteoporotic patients based on the results of the vertebrae. But according to hip scores, osteopenic-osteoporotic (T score <-1) group showed higher frequencies in both cochlear and hearing tests than normal subjects. A significant difference in the results of the hip total T score without any difference in the results of the lumber vertebra total T score can be explained by the presence of degenerative processes such as osteoarthritis affecting the results of the vertebra. In addition, several recent studies have suggested that the widespread belief that obesity is protective against fracture and that obesity is a risk factor for certain fractures [28]. In our study BMI was significantly lower in osteoporotic individuals.

Changes in the bone remodeling process are associated with falls and fractures. Auditory system occurs from skeletal structures and is affected by changes in bone remodeling. In addition, the vestibule is composed of autoconia crystals, a form of calcium, and therefore calcium levels can affect vestibular functions. In many studies, audio-vestibular functions are significantly related to BMD. This association is related to bone mineral density and metabolic changes in the cochlea. [29,30] Demineralization of the cochlear capsule has been associated with healing loss in Paget's disease of the bone and otosclerosis. Osteoporosis may also result in cochlear capsule demineralization. In the study, Helzner et al [31] suggested that the axial and appendicular bone parameters may be modestly associated with hearing loss in older men, but not in women. According to the study by Kahveci et al [32] osteoporosis may be associated with hearing loss in elderly. Metabolic changes and possible degeneration of middle ear ossicles or cochlear capsule may cause hearing loss in patients with osteoporosis. Chen J et al [33] suggests that Ca (v) 1.3.3 calcium channel expression in the cochlea is reduced in the animal model. El-Zarea GA et al [34] found a relation between osteoporosis and hearing loss especially in higher frequencies. Benign paroxysmal positional vertigo (BPPV) is the most common cause of vertigo, which increases the risk of falls by affecting walking, balance in the older age group. Observations suggest an association between idiopathic BPPV and vitamin D deficiency and osteoporosis. Osteoporosis is thought to be a risk factor for the development of BPPV due to estrogen deficiency in postmenopausal period [35].

Limitation of the study

Small sample size (the number of patients is determined by power analysis) and inadequacy of osteoporosis data are the study limitations. Also they should be questioned whether they have taken osteoporosis supplements in the postmenopausal period. Medication may affect the study results, the mean vit D level was found high in our osteoporotic group without any significant difference.

Conclusion

Osteoporosis and hearing loss are common in geriatric syndromes. Osteoporosis can affect both hearing and cochlear function negatively. Screening of individuals with hearing loss for BMD may provide early detection of this insidious onset of illness.

References

1. Patricia B. Kricos AE. Holmest Efficacy of Audiologic Rehabilitation for Older Adults. J Am Acad Audiol.1996;7:219-29.
2. Saunders GH, Chisolm TH. Connected Audiological Rehabilitation: 21st Century Innovations. J Am Acad Audiol. 2015;26(9):768-76. doi:10.3766/jaaa.14062.
3. Grenness C, Hickson L, Laplante-Lévesque A, Davidson B. Patient-centred audiological rehabilitation: perspectives of older adults who own hearing aids. Int J Audiol. 2014;53(1):68-75. doi:10.3109/14992027.2013.866280.
4. Martin GK, Probst R, Lonsbury-Martin BL. Otoacoustic emissions in human ears: normative fmdings. Ear Hear. 1990;11:106-20.
5. Trine MT, Hirsch JE, Margolis RH. The effect of middle ear pressure on transient evoked otoacoustic emissions. Ear Hear. 1993;14:401-7.
6. Satoh Y, Kanzaki J, O-Uchi T, Yoshihara S. Age-related changes in transiently evoked otoacoustic emissions and distortion product otoacoustic emissions in normal-hearing ears. Auris Nasus Larynx. 1998;25:121-30.
7. Gates GA, Mills D, Nam B, D'Agostino R, Rubel EW. Effects of age on the distortion product otoacoustic emission growth functions. Hear Res. 2002;163:53-60.
8. Lonsbury-Martin BL, Martin GK, Luebke AE: İşitme ve vestibüler sistemlerin fizyolojisi. Otolaringoloji Baş ve Boyun Cerrahisi. Ballenger JJ (ed), Doğan Şenocak (ç.ed). Nobel Tıp Kitabevi, İstanbul. 2000;879-929.
9. Zatoński T, Temporale H, Krecicki T. [Hearing and balance in metabolic bone diseases].Pol Merkur Lekarski. 2012;32(189):198-201.
10. Parham K, Kuchel GA. A Geriatric Perspective on Benign Paroxysmal Positional Vertigo. J Am Geriatr Soc. 2016;64(2):378-85. doi: 10.1111/jgs.13926. Epub 2016 Jan 25.
11. Schousboe JT, Shepherd JA, Bilezikian JP, Baim S. Executive summary of the 2013 International Society for Clinical Densitometry Position Development Conference on bone densitometry. J Clin Densitom. 2013;16(4):455-66.
12. Gosfield E 3rd, Bonner FJ Jr. Evaluating bone mineral density in osteoporosis. Am J Phys Med Rehabil. 2000;79(3):283-91.

13. Kanis JA, McCloskey EV, Johansson H, Oden A, Melton LJ 3rd, Khaltaev N. A reference standard for the description of osteoporosis. Bone. 2008;42(3):467-75.
14. Silverman SL. Selecting patients for osteoporosis therapy. Ann N Y Acad Sci. 2007;1117:264-72.
15. Czerwinski E, Badurski JE, Marcinowska-Suchowierska E, Osieleniec J. Current understanding of osteoporosis according to the position of the World Health Organization (WHO) and International Osteoporosis Foundation. Ortop Traumatol Rehabil. 2007;9(4):337-56.
16. Kanis JA. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. WHO Study Group. Osteoporos Int. 1994;4(6):368-81.
17. Kemp DT , Ryan S , Bray P A guide to the effective use of otoacoustic emissions. Ear and Hearing 1990;11(2):93-105.
18. BLL Martin, GK Martin. A review of otoacoustic emissions. The Jour of Acoustic Society of Amer. 1991;89:2027. https://doi.org/10.1121/1.400897
19. Tella SH, Gallagher JC. Prevention and treatment of postmenopausal osteoporosis.J Steroid Biochem Mol Biol. 2014;142:155-70. doi:10.1016/j.jsbmb.2013.09.008.
20. Baccaro LF, Conde DM, Costa-Paiva L, Pinto-Neto AM. The epidemiology and management of postmenopausal osteoporosis: a viewpoint from Brazil.Clin Interv Aging. 2015;10:583-91. doi: 10.2147/CIA.S54614.
21. Diab DL, Watts NB. Postmenopausal osteoporosis. Curr Opin Endocrinol Diabetes Obes. 2013;20(6):501-9. doi: 10.1097/01.med.0000436194.10599.94.
22. Jaul E, Barron J. Age-Related Diseases and Clinical and Public Health Implications for the 85 Years Old and Over Population.Front Public Health. 2017;5:335. doi:10.3389/fpubh.2017.00335.
23. Y İnanç, Y Beckman, Y Seçil, M Başoğlu. The frequency of dementia and mild cognitive disorder in the nursing home population. Int J Surg Med. 2018;4(2):85-7.
24. Laudisio A, Navarini L, Margiotta DPE, Gemma A, Giovannini S, Saviano A, et al. Inflammation as a mediator of the association between osteoporosis and hearing loss in older subjects: a population-based study.Eur Rev Med Pharmacol Sci. 2018;22(5):1451-6. doi:10.26355/eurrev_201803_14492.
25. Kshithi K, Vijendra Shenoy S, Panduranga Kamath M, Sreedharan S, Manisha N, Khadilkar MN, et al. Audiological profiling in postmenopausal women with osteoporosis. Am J Otolaryngol. 2018;39(3):271-6. doi: 10.1016/j.amjoto.2018.03.004.
26. Upala S, Rattanawong P, Vutthikraivit W, Sanguankeo A. Significant association between osteoporosis and hearing loss: a systematic review and meta-analysis.Braz J Otorhinolaryngol. 2017;83(6):646-52. doi: 10.1016/j.bjorl.2016.08.012.
27. Jung DJ, Cho HH, Lee KY. Association of Bone Mineral Density With Hearing Impairment in Postmenopausal Women in Korea. Clin Exp Otorhinolaryngol. 2016;9(4):319-25.
28. Caffarelli C, Alessi C, Nuti R, Gonnelli S. Divergent effects of obesity on fragility fractures. Clin Interv Aging. 2014;9:1629-36. doi:10.2147/CIA.S64625.
29. Singh NK, Jha RH, Gargeshwari A, Kumar P. Altered auditory and vestibular functioning in individuals with low bone mineral density: a systematic review.Eur Arch Otorhinolaryngol. 2018;275(1):1-10. doi: 10.1007/s00405-017-4768-4.
30. Clark K, Sowers MR, Wallace RB, Jannausch ML, Lemke J, Anderson CV. Age-related hearing loss and bone mass in a population of rural women aged 60 to 85 years. Ann Epidemiol. 1995;5(1):8-14.
31. Helzner EP, Cauley JA, Pratt SR, Wisniewski SR, Talbott EO, Zmuda JM, et al. Hearing sensitivity and bone mineral density in older adults: the Health, Aging and Body Composition Study.Osteoporos Int. 2005;16(12):1675-82.
32. Kahveci OK, Demirdal US, Yücedag F, Cerci U. Patients with osteoporosis have higher incidence of sensorineural hearing loss. Clin Otolaryngol. 2014;39(3):145-9. doi: 10.1111/coa.12242.
33. Chen J, Chu H, Xiong H, Yu Y, Huang X, Zhou L et al. Downregulation of Cav1.3 calcium channel expression in the cochlea is associated with age-related hearing loss in C57BL/6J mice. Neuroreport. 2013;24(6):313-7. doi: 10.1097/WNR.0b013e32835fa79c.
34. El-Zarea GA, Abdel-Mottaleb AH, Mustafa Aİ, Hesse ALA. Hearing Function in Osteoporotic Patients. J Am Sci 2017;13(12):76-83.
35. Yamanaka T, Shirota S, Sawai Y, Murai T, Fujita N, Hosoi H. Osteoporosis as a risk factor for the recurrence of benign paroxysmal positional vertigo. Laryngoscope. 2013;123:2813–6. https://doi.org/10.1002/lary.24099

J Surg Med. 2018;2(3):278-282.
DOI: 10.28982/josam.422416

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Management of Bonsai intoxication at emergency service: A review of 61 cases

Acil serviste Bonsai intoksikasyonu yönetimi: 61 olgunun incelenmesi

Nadiye Karabulut [1], Seda Demirel Dengi [1], Sündüs Görükmez [1], Seçil Arıca [1], Selman Yeniocak [2]

[1] **Haseki Training and Research Hospital, Clinic of Family Practice, Istanbul, Turkey**
[2] **Haseki Training and Research Hospital, Emergency Clinic, Istanbul, Turkey**

ORCID ID of the authors
NK: 0000-0002-5539-7709
SDD: 0000-0002-5676-2034
SG: 0000-0001- 7926-580X
SA: 0000-0003-0135-6909
SY: 0000-0002-1124-396X

Corresponding author / Sorumlu yazar:
Nadiye Karabulut
Address / Adres: Haseki Eğitim ve Araştırma Hastanesi, Aile Hekimliği Kliniği, İstanbul, Türkiye
E-mail: nadiye_karabulut@hotmail.com

Ethics Committee Approval: This study was approved by ''Haseki Training and Research Hospital Ethical Committee of Non-Pharmacological Studies'' with approval number of 183 on 28.01.2015.
Etik Kurul Onayı: Bu çalışma, 28.01.2015 tarihinde 183 onay numarası ile "Haseki Eğitim ve Araştırma Hastanesi Farmakolojik Olmayan Araştırmalar Etik Komitesi" tarafından onaylanmıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 09.05.2018
Accepted / Kabul Tarihi: 05.07.2018
Published / Yayın Tarihi: 10.07.2018

Abstract

Aim: The aim of this study was to determine the effects of bonsai by assessing the correlation between the clinical and laboratory findings of cases diagnosed with bonsai intoxication who had been monitored in the emergency service.

Methods: This study was approved by ''Haseki Training and Research Hospital Ethical Committee of Non-Pharmacological Studies'' with approval number of:183 on 28.01.2015. A retrospective evaluation was performed on 61 bonsai intoxication cases who had been monitored and treated in the emergency service. The clinical findings of the pre- and post-treatment and laboratory findings of each case were evaluated.

Results: According to the initial clinical assessment of bonsai intoxication cases who were admitted to the emergency service, the Glasgow coma score (GCS) was found as 8 (E2, V2, M4), 9 (E2, V2, M5) and 4 (E1, V1, M2) in 87% (n=53), 10% (n=6) and 3.2% (n=2), respectively. The pupil reflex was fixed and dilated in 90% (n=52); whereas, it was normal in 10% (n=9). Although, the biochemical parameters (78.9%, n=49) and blood gas levels (98.6%, n=60) were within the normal physiological range in accordance with their age and gender, the elevated serum levels of creatine kinase (CK) and creatine kinase myocardial band (CK-MB) was determined in 21% of the cases (n=12). The pH value of venous blood gas of a case, in whom the elevated levels of CK-MB and CK were found to be directly proportional, was determined as 7.16. The level of troponin-I, electrocardiogram (ECG) findings, hemogram and coagulation parameters were also within the normal physiological range in accordance with their age and gender. The mean venous blood glucose levels were found as 120 ± 29 mg/dL (min: 78 mg/dL, max: 214 mg/dL), and a reverse correlation was detected between the hyperglycemic conditions of the cases and GCS scores on arrival. Of the bonsai intoxication cases, 60 had been treated with hydration therapy (0.9% NaCl solution, 15cc/min, 2000 cc), one was intubated by using midazolam, and monitored and treated in the emergency service.

Conclusion: Patients with different states of consciousness have been frequently encountered in the emergency service. This condition may depend on various factors such as alcohol, certain endocrine diseases (hypo-hyperglycemia, thyrotoxicosis, etc.), trauma, infections (central nervous system infections, sepsis, etc.), cerebrovascular disorders and intoxication. By considering the elevated synthetic cannabinoid (SC) abuse among the adolescents recently, the use of CB should be kept in mind for the pre-diagnosis of the juvenile patients who were brought to the emergency service with loss of consciousness.

Keywords: Bonsai intoxication, Cannabimimetic analogues, Emergency service

Öz

Amaç: Acil servisimizde takip edilen bonzai intoksikasyon vakalarının klinik ve laboratuar bulguları değerlendirilerek bonzainin etkilerinin belirlenmesi amaçlanmıştır.

Yöntemler: Bu çalışmada; 28.01.2015 tarihinde 183 onay numarası ile "Haseki Eğitim ve Araştırma Hastanesi İlaç Dışı Klınik Araştırmaları Etik Komitesi" tarafından onay alınarak acil serviste takip ve tedavi edilen 61 bonzai intoksikasyon vakası retrospektif olarak incelenmiştir. Her bir vakanın geliş klinik ve labovatuar bulguları ile takip ve tedavi sonrası klinik bulguları değerlendirilmiştir.

Bulgular: Acil servise getirilen bonzai intoxikasyon vakalarının ilk klinik değerlendirmesinde; glaskow koma skorları; % 87'sinde (n=53) 8 puan (E (eyes): 2, V(verbal): 2, M(motor): 4), %10 unda (n=6) 9 puan (E:2, V:2, M: 5), %3,2 (n=2) inde 4 puan (E:1, V:1, M:2) olduğu tespit edildi. Pupil reflexleri %90'ında (n=52) fixdilate iken, %10'unda (n=9) normal olarak değerlendirildi. Biyokimyasal değerlerinin %78,9 (n=49) kan gazı değerlerinin %98,6'sı (n=60) yaş ve cinsiyetlerine göre normal fizyolojik sınırlar içindeyken, vakaların %21,5'inde (n=12) CK ve CK-MB değerlerinin yüksek olduğu ve saptanan yüksek CK-MB değerleri ile CK değerlerinin doğru orantılı olduğu bir vakanın venöz kan gazı Ph değeri 7,16 olduğu görüldü. Troponin–I değerleri, EKG (elektrokardiyogram) bulguları, hemogram ve koagülasyon değerlerinin de vakaların yaş ve cinsiyetine göre normal fizyolojik sınırlarda olduğu tespit edildi. venöz kan glukoz değerleri ortalama 120 ± 29mg/dL olduğu (min:78mg/dL, max:214mg/dL) ve vakaların hiperglisemik durumları ile geliş glaskow koma skorları arasında da ters yönlü korelasyon ilişkisi olduğu saptandı. Gelen 60 bonzai intoksikasyonu vakasına hidrasyon tedavisi (%.0.9 NaCl solüsyonu, 15cc/dk, 2000 cc) verildiği, sadece bir vakanın da midazolam verilerek entübe edildiği ve acil servis yoğun bakımında takip ve tedavisinin yapıldığı görüldü.

Sonuç: Acil servislerde bilinç durum değişikliği olan hastalarla sıkça karşılaşılmaktadır. Bu durum; alkol, bazı endokrin hastalıklar (hipo-hiper glisemi, tirotoksikoz vb), travma, enfeksiyon (santral sinir sistemi enfeksiyonları, sepsis vb), serebrovasküler problemler ve zehirlenmeler gibi bir çok nedene bağlı olabilir. Son zamanlarda SK kullanımının toplumda gençler arasında yaygınlaştığı da bilinmektedir. Bu nedenle bilinç durum değişikliği ile Acil servise getirilen genç hastalarda SK kullanımının da ön tanıda akılda tutulması önemlidir.

Anahtar kelimeler: Bonzai intoksikasyonu, Sentetik kannabimimetik analoglar, Acil servis

How to cite / Atıf için: Karabulut N, Dengi SD, Görükmez S, Arıca S, Yeniocak S. Management of Bonsai intoxication at emergency service: A review of 61 cases. J Surg Med. 2018;2(3):278-282.

Introduction

Synthetic cannabinoids (SC) were first used in 2004 and became rapidly popular, especially among adolescents [1-5]. SCs have various names worldwide, with the most common one being "spice". However, in Turkey they are commonly known as "bonsai" [3]. Cannabinoids are classified into three groups as natural, endogenous and synthetic. The most well-known natural cannabinoid is delta 9-tetrahydrocannabinol (THC) which is the main ingredient of marijuana [6]. Endogenous cannabinoids consist of 2-arachidonoylglycerol and anandamide. However, SCs are made up of synthetic molecules in the laboratories to mimic the effects of THC [7,8]. SC are generally consumed in the form of cigarettes (with pipe, cigarette or hookah), however, vaporization, oral or rectal use were also reported [9]. The reported toxic symptoms of SC include agitation, seizures, hypertension, nausea, vomiting, hyperkalemia, anxiety, paranoia, tachycardia, nervousness, hallucination, paresthesia, somnolence and speech disorders [10-11].

Besides, there is certain evidence for an association between SC and psychiatric symptoms including psychosis [12]. In the present study, the state of consciousness of cases was evaluated by Glasgow coma score (GCS). GCS is an indicator which assesses the condition of central nervous system independently from the primary etiology. Drug intoxications and the use of narcotics may cause brain damage with loss of consciousness due to their effects on brain biochemistry [2,3]. The brain functions and the course of patient are evaluated according to the eye movements, verbal and motor responses in GCS. The GCS is scored between 3 and 15; 3 being the worst, and 15 the best. A score of 13 or higher is categorized as a recoverable brain injury, 9-12 as moderate, and 8 or below as severe brain injury [10].

A case was reported in whom the use of SC JWH-018 was considered to be associated with acute ischemic stroke [13]. Following the long-term use of SC, the syndromes of tolerance and abstinence are observed in patient. Tolerance has been developed rapidly which is thought to be relatively associated with high-addiction potential. Abstinence syndrome was defined as anxiety, increased sweating, excessive desire for drug abuse, tremor, headache, nightmares, insomnia, and irritability, difficulty in concentration, nausea and depression [9,10]. There were also various convulsion cases related to SC, and these are classified as tonic clonic seizure and they don't cause sequelae [5]. It is recommended to use benzodiazepine as an adjuvant therapy for the symptoms related to SC for the control of anxiety and agitation [14]. In the present study, the clinical and laboratory findings of bonsai intoxication cases who had been monitored in the emergency service were retrospectively evaluated.

Materials and methods

A retrospective evaluation was performed on 61 bonsai intoxication cases who were admitted to the emergency service of hospital by ambulance, between August and November of 2014. The cases were evaluated in terms of age, gender, arrival time to emergency service, GCS on arrival, physical examination findings, cardiac enzyme levels, ECG findings, biochemical parameters, hemogram and blood values levels, and pre-and-post therapy GCS and examination findings

Statistical analysis

SPSS 16.0 (Statistical Package for the Social Sciences) package program was used for the statistical analysis of the study data. Statistical descriptive methods were used for the assessment of the data (mean, standard deviation, median, frequency, ratio, minimum, maximum). The level of significance for the study was $p<0.05$.

Results

The mean age of the cases was 25.4 ±76 years (min: 15, max: 53), and it was determined that it was more frequently seen in age group of 20-30 years (44%, n=27) (Figure 1). The most common arrival time of the emergency service was between 8.00 pm and 2.00 am (86.6%, n=53), and they were all male except one case (98.6%, n=60).

According to the initial clinical assessment of bonsai intoxication cases, the pupil reflex was fixed and dilated in 90% (n=52); whereas, it was normal in 10% (n=9). The GCS scores on arrival were found as 8 (E2, V2, M4), 9 (E2, V2, M5) and 4 (E1, V1, M2) in 87% (n=53), 10% (n=6) and 3.2% (n=2), respectively (Table 1). The mean venous blood glucose level was 120±29 mg/dL (min: 78 mg/dL, max: 214 mg/dL) on arrival. A reverse correlation was detected between the hyperglysemic conditions of the cases and GCS scores on arrival (r=-0.25, p= 0.021). The most common symptoms and findings were determined as agitation (83%, n=51), vomiting (37%, n=23), dizziness/lethargy (98.6%, n=60), confusion (97%, n=59), changes in consciousness (98.1%, n=60), hypoglycemia (3.7%, n=2) and hyperglycemia (86.3%, n=53) (Table 2).

The ECG of the cases revealed no pathological findings on the emergency arrival. When the laboratory findings on arrival were evaluated, the level of troponin-I, hemogram and coagulation parameters were within the normal physiological range in accordance with their age and gender.

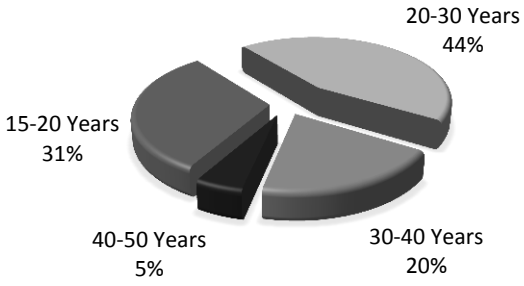


Figure 1: The age distribution of bonsai intoxication cases who were monitored and treated in the emergency service

Table1: The GCS scores of bonsai intoxication cases before the treatment

Number of cases	GCS scores
53 Cases (86.8%, n=53)	8 Point (E2, V2,M4)
6 Cases (1%, n=6)	9 Point (E2, V2, M5)
2 Cases (3.2%, n=2)	4 Point (E1, V1, M2)

Abbreviations: GCS: Glasgow Coma Scale, E:Eye Opening Response, V:Verbal Response, M:Motor Response

Table 2: The most common symptoms and findings of bonsai intoxication cases who were monitored and treated in the emergency service

Symptoms and findings of the cases at the initial assessment		
Agitation	51 Cases	87% (n=51)
Vomiting	23 Cases	37% (n=23)
Dizziness/lethargy	60 Cases	98, 6% (n=60)
Confusion	59 Cases	97% (n=59)
Changes in consciousness	60 Cases	98.1% (n=60)
Hypoglycemia	2 Cases	3.7% (n=2)
Hyperglycemia	53 Cases	86.3% (n=53)

Of the cases, 21.5% had elevated serum levels of creatine kinase (CK) and creatine kinase myocardial band (CK-MB), and the pH value of venous blood gas of one case, in whom the elevated levels of CK-MB and CK were found to be directly proportional, was determined as 7.16. The laboratory findings of the cases were summarized in Table 3. According to the anamnesis that was obtained from the patients and their relatives, none of the cases had a history of diabetes mellitus and elevated blood lactate levels in their blood gas values. All bonsai intoxication cases were monitored closely for 24 hours following their emergency department triage. The cases were treated by hydration therapy (0.9% NaCl solution, 15cc/min, 2000 cc), except one case, who was intubated by using midazolam as a result of respiratory depression and metabolic acidosis (pH of venous blood gas: 7.16), and monitored and treated in the emergency service.

The pupil reflexes of the cases were able to be measured after 3.7 ± 2.1 hours in average during their follow-up and treatment. The mean GCS scores was 14.38 at the 12th hour; it was scored as 15, 14 and 13 in 39% (n=24; E4, V5, M6), 59% (n=36; E4, V4, M6) and 2% (n=1; E4, V4, M5) of the cases, respectively (Table 4).

Table 3: Laboratory findings on arrival of bonsai intoxication cases who were monitored and treated in the emergency service

Test	Parameter	Min	Max	Mean	Normal range
Venous Blood Gas	Ph	7.1	7.5	7.35±0.07	7.31 - 7.41
	pO_2 mmHg	15.9	92.8	54.1±32.6	35 - 45
	pCO_2 mmHg	29	80	54.1±32.6	41 - 51
	HCO_2 mmol/L	19.7	42	27.9±4.3	24 - 28
	SO_2 %	19	99.50	73.3±20.5	55 - 70
Biochemisty	Glucose mg/dL	78	214	120±29	74 - 106
	CK U/L	57	3700	149	<145
	CK-MB ng/mL	0.6	121	2	0.6-6.3
	Troponin-l ng/mL	0.01	0.03	0.01±0.004	0 - 2.00
	Urea mg/dL	14	54	30.0±8.4	17 - 43
	Creatine mg/dL	0.5	1.3	0.8±0.1	0.51-0.95
	AST U/L	14	171	25	<35
	ALT U/L	6	262	17.5	<35
	LDH U/L	72	645	236	<247
	Ca mg/dL	7.8	10.5	9.2±0.6	8.4 - 10.5
	Na mg/dL	132	145	136±3.0	136 - 145
	K mg/dL	3.3	5.8	3.9±0.4	3.3 - 5.1
	Cl mg/dL	92.6	100.8	100±12	98 - 107
Complete Blood Count	Wbc 10e9/ul	4.5	18.3	9.9±4.4	4.00 - 10.00
	Hgb g/dL	12.4	17.6	14.7±1.3	11.0 - 16.0
	Hct %	37	53	44.1±3.4	37.0 - 54.0
	Platelet 10e9/ul	148	431	258±65	100 - 300 l
Bleeding Time	INR	0.8	1.5	1.0±0.1	0.8 - 1.2
	APTT sn	19.8	27.7	23.0±7.0	23 - 35
	Prothrombin time sn	10.3	14.6	11.8±1.2	10 - 14

Abbreviations: CK: creatine kinase, CK - MB: creatine kinase myocardial band

Table 4: The GCS scores of bonsai intoxication cases who were monitored and treated in the emergency service at the 12th hour

Number of cases	GCS scores
24 Cases (39.3%, n=24)	15 Point (E4, V5,M6)
36 Cases (59%, n=36)	14 Point (E4, V4, M6)
1 Case (1.7%, n=1)	13 Point (E4, V4, M5)

Abbreviations: GCS: Glasgow Coma Scale, E:Eye Opening Response, V:Verbal Response, M:Motor Response

During the follow up of the cases in the emergency service for 24 hours, the clinical and laboratory findings were completely improved and none of them developed any complications. Therefore, they were discharged from the hospital by informing them and their relatives about the drug addiction and by referring them to the addiction control centers.

Discussion

SCs were initially noticed in European Union, however the recent reports on the abuse of these compounds spread all around the world [15-20]. The most common form of natural cannabinoid is 9-THC [3,6]. Cannabinoids affect the CB1 and CB2 receptors in the body and they show these effects generally based on a CB1 like mechanism of action, impaired consciousness, sleep changes and cardiovascular effects. Whereas the role of CB2 is poorly understood, it is known that THC acts only through CB1. This is different than SC's, which act both through the CB1 and CB2 receptors and are more effective than THC [15,17]. The binding affinity, and thereby the effects of the SCs to the CB1 receptors show variations; it has higher affinity and stronger effect than 9-THC [16]. The clinical findings of the SCs may be different due to the variations in their composition. These drugs can cause anxiety or panic as well as opposing effects like repressed anxiety. The most frequent cardiovascular effects are hypertension and tachycardia, but effects such as bradycardia and hypotension have also been reported [4,6]. In a study performed by Hoyte et al., the most common symptoms were detected as tachycardia (40%), agitation (23.4%), vomiting (15.3%), dizziness/lethargy (13.5%), confusion (12%), nausea (10%), hallucination (9.4), hypertension (8.1%), drowsiness (7.3%), chest pain (4.7%), syncope (2.1%), hypotension (1.3%) and bradycardia (1.3%) in 1,353 patients who were exposed of a single component of SC [1]. The reason of variations in the clinical findings is still unknown; however, the type of SCs, the amount of toxic substances, the frequency of use, personal liability and the chronic toxicity effect of SC might cause these variations [5,18].

In the present study, symptoms and findings were similar to those reported in the literature and the results were presented in Table 2 and 3.

According to the laboratory findings, the serum levels of CK-MB was determined as normal in 92% (n=5); whereas it was elevated in 8% (n=6) of the cases. The serum levels of CK-MB and CK were found to be directly proportional. These elevated serum values might be related to the initial medical approaches that were performed in the emergency service. Although, the action time is shorter than 8 hours in most the SC intoxication cases, it has reported that it might take more than 24 hours in certain individuals [2]. It is recommended to use benzodiazepine as an adjuvant therapy for the symptoms related to SC for the control of anxiety and agitation [9]. In the present study, only hydration therapy was performed on cases and they were closely monitored for 24 hours. Only one patient was intubated for 3 hours and monitored under the conditions of intensive care. It was determined that the duration of confusion did not proceed more than 24 hours in none of the cases during their 24-h follow-up in the emergency service, and the consciousness was completely recovered after 5.7 ± 2.2 hours in average.

The number of abusers of synthetic cannabinoids and cathinones has increased remarkably worldwide. The chemical structures of the distributed drugs are skillfully changed so that the drugs may pass through screenings for detection. Simple screening methods are required for detection of these drugs in seized and biological materials. There are currently no commercial kits or devices for the routine screening of these drugs. Colorimetric, immunochemical, and chromatographic methods have been introduced in reviews; a suitable method

must be chosen for each laboratory. Although various human sample matrices are available for testing, urine and blood are of the first choices. However, many of these drugs, especially unchanged synthetic cannabinoids, exist in urine and blood for only a short period. Therefore, other matrices that can prove the consumption of these drugs, such as hair and saliva, are likely to receive more attention in the future [21].

The diagnoses of bonsai intoxication is done according to the information obtained from patient's relatives and ambulance personnel who make the first intervention and transfer, physical examination and clinical findings of the cases. The routine screening tests for SCs have not yet been performed in hospitals connected to Ministry of Health, and it was determined that SC screening test was not applied to 61 cases included in our study. It is required to include SC screening test to the routine procedures, and to perform more detailed studies regarding the detection of connection between the symptoms and findings in these cases by means of determining the metabolites of SC. Recently, SC has become the widely consumed substance worldwide. The age range of the users is pretty wide and bonsai has become popular especially among adolescents. It is predicted that the number of users will continue to increase gradually due to its cheaper price and ease of accessibility. The legal arrangement directed to these substances should be reviewed, and it is necessary to apply criminal sanction especially to the dealers, to determine the profile of the users, to educate the individuals who are fitting to this profile about drug abuse and to take precautions as soon as possible. In collaboration with the Ministry of Education and the Ministry of Health, educational seminars should be organized about the use of bonsai and other addictive substances for children in the primary and secondary education period and their families. Moreover, the conditions of rehabilitation centers should be improved by the Ministry of Health and the awareness of the society should be raised by means of organizations including the Ministry of Health, media and nongovernmental organizations.

These substances are affecting all body systems and cause psychiatric disorders in addition to the loss of physical health in juvenile population. Besides, it raises the crime rate, it also hinders education and causes loss of job and educational power, and the chronic use of these substances may result with death in the end.

Patients with different states of consciousness have been frequently encountered in the emergency service. This condition may depend on various factors such as alcohol, certain endocrine diseases (hypo-hyper glycaemia, thyrotoxicosis, etc.), trauma, infection (central nervous system infections, sepsis, etc.), cerebrovascular disorders and intoxication. By considering the elevated synthetic cannabinoid (SC) abuse among adolescents recently, the use of CB should be kept in mind for the pre-diagnosis of the juvenile patients who were admitted to the emergency service with loss of consciousness. As an early diagnosis, the possibility of using SC should be considered in all juvenile cases who are admitted to the emergency service and are suffering from changes in consciousness due to the proliferation of SCs among the adolescence.

The limitation of our study is the lack of bonsai screening tests in the monitored individuals due to the currently available facilities of the hospitals. The screening tests may identify the metabolites of the SC along with their associated signs and symptoms. Therefore, further studies, which will be conducted with larger study populations and which will provide results evidenced by laboratory tests are warranted in order to elaborate a clearer insight on the effects of bonsai use.

In conclusion, it is certain that Bonsai use is gradually increasing and it will continue to be a health problem. Therefore, the need for the identification of the chemicals contained in these substances and the necessary examination, equipment and experience for reporting will also increase day by day.

References

1. Hoyte CO, Jacob J, Monte AA, Al-Jumaan M, Bronstein AC, Heard KJ. Characterization of synthetic cannabinoid exposures reported to the National Poison DataSystem in 2010. Ann Emerg Med. 2012;60:435-8.
2. Rosenbaum CD, Carreiro SP, Babu KM. Here today, gone tomorrow and back again? A review of herbal marijuana alternatives (K2, Spice), synthetic cathinones bath salts), Kratom, Salvia divinorum,methoxetamine, and piperazines. J Med Toxicol. 2012;8:15-32.
3. Gurdal F, Asirdizer M, Aker RG, Korkut S, Gocer Y, Kucukibrahimoglu EE, et al. Review of detection frequency and type of synthetic cannabinoids in herbal compounds analyzed by Istanbul Narcotic Department of the Council of Forensic Medicine, Turkey. J Forensic Leg Med. 2013;20:667–72.
4. Hohmann N, Mikus G, Czock D. Effects and risks associated with novel psychoactive substances: mislabeling and sale as bath salts, spice, and research chemicals. Dtsch Arztebl Int. 2014;111:139–47.
5. Harris CR, Brown A. Synthetic cannabinoid intoxication: a case series and review. J Emerg Med. 2013;44: 360-6.
6. Ashton CH. Pharmacology and effects of cannabis: abrief review. Br J Psychiatry. 2001;178(2):101-6.
7. Pacher P, Bátkai S, Kunos G. The endocannabinoidsystem as an emerging target of pharmacotherapy. Pharmacol Rev. 2006;58(3):389-462.
8. Ottani A, Giuliani D. HU 210: a potent tool forinvestigations of the cannabinoid system. CNS Drug Rev. 2001;7(2):131-45.
9. Vandrey R, Dunn KE, Fry JA, Girling ER. A survey study to characterize use of Spice products (synthetic cannabinoids). Drug Alcohol Depend. 2012;120:238-41.
10. Moosmann B, Kneisel S, Girreser U, Brecht V, Westphal F, Auwärter V. Withdrawal phenomena and dependence syndrome after the consumption of "spice gold". Dtsch Arztebl Int. 2009;106:464-7.
11. Seely KA, Brents LK, Radominska-Pandya A, EndresGW, Keyes GS, Moran JH, Prather PL. A major glucuronidatedmetabolite of JWH-018 is a neutral antagonist at CB1 receptors. Chem Res Toxicol. 2012;25:825-7.
12. Hurst D, Loeffler G, McLay R. Psychosis associatedwith synthetic cannabinoid agonists: a case series. Am J Psychiatry. 2011;168(10):1119.
13. Freeman MJ, Rose DZ, Myers MA, Gooch CL,Bozeman AC, Burgin WS. Ischemic stroke after use ofthe synthetic marijuana "spice". Neurology. 2013;81(24):2090-3.
14. Rosenbaum CD, Carreiro SP, Babu KM. Here today,gone tomorrow and back again? A review of herbal marijuana alternatives (K2, Spice), synthetic cathinones bath salts), Kratom, Salvia divinorum, methoxetamine, and piperazines. J Med Toxicol. 2012;8:15-32.
15. Pertwee RG, Howlett AC, Abood ME, Alexander SP, Di Marzo V, Elphick MR, et al. International Union of Basic and Clinical Pharmacology. LXXIX. Cannabinoid receptors and their ligands: beyond CB_1 and CB. Pharmacol Rev. 2010;62:588–631.
16. Huffman JW, Padgett LW. Recent developments in the medicinal chemistry of cannabinomimetic indoles, pyrroles and indenes. Curr Med Chem. 2005;12:1395-411.

17. Jerry J, Collins G, Streem D. Synthetic legal intoxicating drugs: the emerging 'incense' and 'bath salt' phenomenon. Cleve Clin J Med 2012;79:258–64.
18. Wood DM, Dargan PI. Novel psychoactive substances: How to understand the acute toxicity associated with the use of these substances. Ther Drug Monit. 2012;34:363-7.
19. Andrej Grigoryev, Sergey Savchuk, Aleksandra Melnik, Natal'ja Moskaleva, Jurij Dzhurko,Mihail Ershov et al. Chromatography–mass spectrometry studies on the metabolism of synthetic cannabinoids JWH-018 and JWH-073, psychoactive components of smoking mixtures. J Chromatogr B Analyt Technol Biomed Life Sci. 2011;879:1126-36.
20. Uchiyama N, Kikura-Hanajiri R, Ogata J, Goda Y. Chemical analysis of synthetic cannabinoids as designer drugs in herbal products. Forensic Sci Int. 2010;198:31-8.
21. Akira Namera, Maho Kawamura, Akihiro Nakamoto, Takeshi Saito, and Comprehensive review of the detection methods for synthetic cannabinoids and cathinones. Forensic Toxicol. 2015;33(2):175–94.

J Surg Med. 2018;2(3):283-287.
DOI: 10.28982/josam.424328

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

The incidence of isthmocele may be higher than reported

İsthmocele'in insidansı bildirilenden daha fazla olabilir

Pervin Karlı [1], Banuhan Şahin [1], Fadıl Kara [1]

[1] Department of Obstetrics and Gynecology, Amasya University, Research Hospital, Amasya, Turkey

ORCID ID of the authors:
PK: 0000-0003-4907-5890
BŞ: 0000-0002-8711-1584
FK: 0000-0001-9029-8733

Corresponding author / Sorumlu yazar:
Pervin Karlı
Address / Adres: Amasya Üniversitesi, Araştırma Hastanesi, Obstetrik ve Jinekoloji Bölümü, Amasya, Türkiye
E-mail: parpi2300@hotmail.com

Ethics Committee Approval: The study was approved by local Ethics Committee.
Etik Kurul Onayı: Çalışma için onay Etik Kurulundan alınmıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 17.05.2018
Accepted / Kabul Tarihi: 06.07.2018
Published / Yayın Tarihi: 09.07.2018

Abstract

Aim: Isthmocele, a long-term complication of Cesarean section (CS) surgery, has drawn increasing worldwide interest. However, not all women with this Cesarean scar defect (CSD) present with clinical symptoms. We studied a group of non-pregnant women with a CS history to determine the prevalence of isthmocele, the potential risk factors for its development, and the most common clinical complaints.

Methods: This study included women who had a cesarean operation more than 6 months ago, who were not pregnant between April 2017 and April 2017 and applied to the gynecology clinic for any reason. The exclusion criteria were the patients in the menopause period. Data was collected on 115 participants, including age, body mass index, duration after CS, and the number of CS surgeries that had been performed. Standardized scar parameters (residual myometrial thickness (RMT) and the depth and width of the triangular hypoechoic niche) were measured using transvaginal-ultrasonography (TVS). Isthmocele symptoms were categorized as asymptomatic, postmenstrual spotting, menometrorrhagia, chronic pelvic pain, dysmenorrhea, and infertility. Associations between isthmocele and menstrual complications were investigated. The relationship between isthmocele development and the reasons for the CS surgery were evaluated.

Results: TVS examination diagnosed 17 women (14.78%) with isthmocele. Women who had undergone recurrent CS surgeries tended to have more visible isthmocele than those with a single CS surgery. The average isthmocele depth was 6.006 ± 0.7970 mm. Among the women with isthmoceles, elective CS surgery had been performed in six (35.3%), while 11 (64.7%) had the surgery at parturition. The presence of an isthmocele was frequently symptomatic, predominantly as postmenstrual spotting. Women with an isthmocele had significantly lower RMT values (5.57 ± 0.60 mm versus 8.78 ± 0.22 mm) than those without an isthmocele. There was no correlation between age, body mass index, and the presence of an isthmocele ($p > 0.05$).

Conclusions: The incidence and prevalence of CSD is greater than most gynecologists realize. Isthmoceles can develop after just one CS surgery, leading to long-term complications that morbidly effect women for the rest of their lives. A reduction in the number of CS surgeries is the most effective way to decrease the prevalence of isthmoceles.

Keywords: Isthmocele, Uterine niche, Postcoital bleeding, Pelvic pain

Öz

Amaç: İsthmosel, dünyada gittikçe yaygınlaşan sezaryen operasyonunun uzun dönem bir komplikasyonudur. Ancak sezaryen skar defektli kadınların (SSD=İsthmosel) tamamında semptom görülmez. Biz çalışmamızda isthmosel prevalansı, gelişimi için risk faktörleri ve en yaygın semptomlarını araştırmak istedik.

Yöntemler: Bu çalışmaya 6 aydan daha uzun bir süre önce sezaryen operasyonu olan, 2017 Ocak 2017 Nisan tarihleri arasında gebe olmayan, jinekoloji polikliniğine herhangi bir nedenle başvuran kadınlar dahil edildi. Menapoz döneminde ki hastalar çalışma dışı bırakılma kriteri olarak alındı. Sezaryen olan 115 kadının verileri yaşı, vücut kitle indexi, sezaryen sonrası geçen süre ve geçirilmiş sezaryen sayısını içerecek şekilde kayıt altına alındı. Standardize edilen skar parametreleri (residual myometrial kalınlık (RMK), triangular hipoekoik nishe'in genişlik ve derinliği ölçümü) transvajinal ultrasonografi (TVUSG) ile yapıldı. İsthmosel semptomları asemptomatik, postmenstrual spotting tarzı kanama, menoraji, kronik pelvik ağrı, dismenore ve infertilite olarak kategorize edildi. İsthmosel ve menstruel komplikasyonlar arasındaki ilişki araştırıldı. İsthmosel gelişimi ve sezaryen sebebleri arasındaki ilişkiler değerlendirildi.

Bulgular: Hastaların TVUSG ile değerlendirmesinde 17 tanesinde (%14,78) isthmosel tespit edildi. Birden fazla sezaryen olan hastalar tek sezaryen olan hastalara göre daha fazla isthmosel geliştirme eğilimindeydiler. Ortalama isthmosel çapı 6,006 ± 0,7970 mm'di. İsthmoselli kadınların 6 tanesi (%35,3) elektif alınan sezaryen vakalarında gelişmiş iken, 11 tanesi (%64,7) doğum eylemi başladıktan sonar yapılmıştı. İsthmosel olan hastaların çoğunluğu semptomatikti ve daha çok spotting tarzda kanama görülüyordu. İsthmosel görülen kadınların RMK değerleri isthmosel görülemyenlerden belirgin olarak düşüktü (5,57 ± 0,60 mm vs 8,78 ± 0,22 mm).

Sonuç: SSD prevalans ve insidansı kadın doğum hekimlerinin tahmin ettiğinden çok daha fazladır. İsthmosel bir sezaryen sonrası bile gelişebilir ve o kadınlarda uzun vadeli yaşamları boyunca morbidite sebebi olarak görülür. Sezaryen oranlarının azaltılması isthmosel prevalansını azaltmada çok etkili olacaktır.

Anahtar kelimeler: İsthmosel, Uterin niş, Postkoital kanama, Pelvik ağrı

How to cite / Atıf için: Karlı P, Şahin B, Kara F. The incidence of isthmocele may be higher than reported. J Surg Med. 2018;2(3):283-287.

Introduction

Cesarean section (CS) surgery is often preferred by obstetricians to terminate high risk labor, and the number of recurrent CS surgeries is increasing in clinical practice around the world [1]. CS delivery provides a healthy birth for the baby. For the mother, however, this procedure can cause long-term complications related to defects in the surgical incision scar [2].

Cesarean scar defects (CSD) are clinically encountered as uteroperitoneal fistula, niche, or isthmocele and can be detected by ultrasonographic and hysterosonographic imaging as a hypoechoic area in the CS scar [3]. The term isthmocele was first described in 1995 by Dr. Hugh Morris [4]. This anatomic defect is a diverticulum that comprises a thin insufficient myometrium on the anterior wall of the uterine isthmus at the presumed incision site. In women who underwent emergency CS surgery, the defect can be located distally near the internal cervical os, while in women who had elective surgery, the defect is located proximally on the lower uterine segment. There is currently no standardization for isthmocele assessment [5]. Several factors may affect isthmocele development, including a retroflexed uterus. Smoking or uncontrolled diabetes may cause the wound to heal poorly. Surgical techniques such as low (cervical) hysterotomy, single or double layer closure, or the use of locking sutures as well as recurrent operations could contribute to defect formation [6].

Most isthmoceles are asymptomatic, and there is no consensus on the determining characteristics of size and location [7,8]. Isthmocele prevalence has been reported in a wide range (24–70%) when the condition is assessed by transvaginal-ultrasonography (TVS) [9]. The exact incidence is unknown, but it could be as high as 61% after a primary CS and 100% after three CS surgeries [10,11].

Isthmocele may cause dysmenorrhea, dyspareunia, menometrorrhagia, and secondary infertility as well as obstetrical complications, such as uterine rupture, Cesarean scar pregnancies, and abnormal placental implantation in future pregnancies [12,13]. The intensity of symptoms is directly related to the defect size. Small uterine scar defects can be asymptomatic, while the larger scar defects seen after multiple CS surgeries generally cause more symptoms [14].

This cross-sectional study sought to identify the prevalence of isthmocele in non-pregnant women with a history of CS surgery as well as the primary symptoms of the condition and the potential risk factors for its development.

Materials and methods

In this cross-sectional study, women who were in their reproductive period and who had delivered by CS at hospital from 2012 to 2017 were invited to undergo ultrasonographic evaluation of their CS scar at least six months after the operation. All the CS surgeries were performed using Kerr techniques for the uterine incision and a single layer continuous locking suture for closure. The study protocol was accepted by ethics committee on 17 October 2017 (approval no 2017-78), and all participants signed an informed consent form before they were included the study. The study was conducted in accordance with the 1964 Helsinki declaration and its later amendments.

The examinations were made by two gynecologists using a Mindray DP-5 (B&W Ultrasound System) ultrasound machine with a 6.5 MHz endocavity probe. All subjects were assessed three to six days after menstruation, when the endometrial stripe was thin. A standardized definition for imaging and measuring a CS scar with TVS was applied [15-17]. Isthmocele was diagnosed by the presence of a hypoechogenic zone under the myometrial layer of the lower uterine segment, at the site of the hysterotomy incision. The measurements were obtained in the sagittal plane of the uterus. The residual myometrial thickness (RMT) was defined as the distance between the apex of the hypoechoic triangle and the serosa at the site of the hysterotomy incision. The depth of the isthmocele was defined as the distance between the apex of the hypoechoic triangle and the posterior base of the endometrial cavity. The width of the isthmocele was defined as the distance from the widest point of this triangle to the surface of the endometrium in the posterior uterine wall (Figure 1).

The pregnancy and operation histories of the participants were reviewed, and the applicability of clinical symptoms such as postmenstrual spotting, dysmenorrhea, chronic pelvic pain, and dyspareunia was determined by a questionnaire after the women had been screened.

Women with a history of uterine surgery (other than low transverse incision) were excluded as well as those having other uterine pathologies (such as polyps, hyperplasia, myomas, malignancy, or congenital uterine malformations), chronic corticosteroid administration, or a recent pregnancy.

Statistical analysis

The statistical analysis was performed using the GraphPad Prism version 6.00 (GraphPad Software, La Jolla California USA). The data was expressed as a mean ± standard deviation (SD). One Way ANOVA was used for the descriptive statistics. To determine the statistical significance of the differences between the groups, the student t test was used for continuous variables, and the chi-squared test was used for categorical data. Results were evaluated within a 95% confidence interval, and the criteria for statistical significance were set at $p < 0.05$.

Results

The study included 115 non-pregnant women with a previous CS surgery. After the women were assessed by TVS, 17 (14.78%) were diagnosed as having an isthmocele. An intact CS scar without an isthmocele was detected in 98 women (85.22%). The average depth of the isthmoceles was 6.006 ± 0.7970 mm. Women with an isthmocele had significantly lower RMT values (5.57 ± 0.60 mm versus 8.78 ± 0.22 mm) than those without an isthmocele ($p < 0.05$). There was no statistically significant difference between the two groups in terms of age, height, weight, time to CS surgery, and the duration of the CS surgery (Table 1).

CS surgery had been performed electively in 91 women (79.1%), and in 24 women (20.9%) it was performed at parturition with cervical dilatation. Women who had undergone recurrent CS surgeries tended to have a more visible isthmocele than those who had undergone a single operation.

The relationship between complaints and the presence of an isthmocele is presented in Table 2. The presence of an isthmocele was frequently symptomatic. Postmenstrual spotting (35.3%) was the most common symptom, followed by menometrorrhagia (23.5%). Six women with an isthmocele were asymptomatic.

Study participants without an isthmocele had more regular menses than those with an isthmocele. This difference was statistically significant ($p < 0.05$). However, eleven of the women with an isthmocele had regular menstruations (64.7%) (Table 3). The development of an isthmocele was frequently seen in women who had had a CS surgery while in parturition (64%), but this statistical value did not reach significance (Table 4). There was no statistical significance between the group of women with an isthmocele and the group of women without an isthmocele with indications of a CS delivery ($p > 0.05$) (Table 5). There was no correlation between the size of the isthmocele and the magnitude of the symptoms (Table 6).

Table 1: Comparison of the groups with and without an isthmocele in terms of demographic and ultrasonographic parameters

	Isthmocele (+) (n = 17)	Isthmocele (-) (n = 98)	p
Age (years)	36.29 ± 1.2	36.79 ± 0.65	0.926
Height (cm)	158.2 ± 1.13	161.3 ± 0.61	0.063
Weight (kg)	69.94 ± 3.32	69.93 ± 1.86	0.822
The duration after CS (years)	6.94 ± 1.14	7.46 ± 0.52	0.855
RMT (mm)	5.57 ± 0.60	8.78 ± 0.22	< 0.001*
CS times	1.88 ± 0.20	1.68 ± 0.067	0.435

Values were given as mean ± standar deviation, CS: Cesarean section, RMT: Residual myometrial thickness, * There was statistical significance between the groups ($p < 0.05$)

Table 2: The ratio of complaints in the groups with and without an isthmocele

	Isthmocele (+) (n = 17)		Isthmocele (-) (n = 98)		χ^2	p
	n	%	n	%		
Asymptomatic	6	35.3	62	63.4		
Spotting	6	35.3	4	4		
Menometrorrhagia	4	23.5	17	17.4	17.77	0.001*
Pelvic pain	1	5.9	9	9.2		
Dysmenorrhea	-	-	2	2		
Infertility	-	-	4	4		

* There was statistical significance between the groups ($p < 0.05$)

Table 3: The relationship between the presence of an isthmocele and menstrual period complications

	Isthmocele (+) (n = 17)		Isthmocele (-) (n = 94)		χ^2	p
	n	%	n	%		
Regular menstruation	11	64.7	80	85.1	4.056	0.04*
Irregular menstruation	6	35.3	14	14.9		

* There was statistical significance between the groups ($p < 0.05$)

Table 4: The ratio of the timing of the CS operation in the groups with and without an isthmocele

	Isthmocele (+) (n = 17)		Isthmocele (-) (n = 98)		χ^2	p
	n	%	n	%		
CS in parturition	11	64.7	41	41.8	3.058	0.08*
Elective CS	6	35.3	57	58.2		

* There was no statistical significance between the groups ($p > 0.05$)

Table 5: The distribution of the indications of CS delivery in subjects with and without an isthmocele

	Isthmocele (+) (n = 17)		Isthmocele (-) (n = 98)		χ^2	p
	n	%	n	%		
Unprogressive labor	4	23.6	13	13.3		
Maternal option	4	23.6	40	40.8		
Breech presentation	2	11.7	17	17.4	4.973	0.290*
Fetal distress	5	29.4	13	13.3		
Dystocia	2	11.7	15	15.2		

* There was no statistical significance between the groups ($p > 0.05$)

Table 6: The relationship between the isthmocele size and the diversity of complaints

	Complaints				
	None (n=6)	Spotting (n=6)	Irregular menses (n=4)	Pelvic pain (n=1)	p
Isthmocele extension (mm)	5.2 ± 0.8	7.1 ± 2.0	5.5 ± 1.0	6.0 ± 0	0.50

* There was no statistical significance between the groups ($p > 0.05$)

Discussion

The clinical significance of a CSD is mostly benign; however, an isthmocele is typically identified in women who have undergone at least one previous CS surgery and who are presenting with complaints such as postmenstrual spotting, dysmenorrhea, dyspareunia, chronic pelvic pain, and infertility [11]. Isthmocele prevalence has been reported to be as high as 52% after one CS surgery [18]. The likelihood of development increases with recurrent CS surgeries [19], and these women often experience one or more symptoms [14]. In our study population, we detected an isthmocele prevalence of 14.78%, less than the rates reported in the literature. Our low rate may be because all the surgeons in our hospital used the Kerr incision, a unique surgical technique, for the uterine gash and a single layer continuous locking suture for closure.

TVS is an easily accessible, noninvasive, low-cost imaging method that should be considered the first step in screening for an isthmocele [20]. As shown by TVS, the isthmocele image is defined as an anechoic zone shaped like an isosceles triangle that exists between the uterus isthmus and the cervical canal. The best interval during a woman's cycle to display the isthmocele with TVS is a few days after menses. We examined all subjects three to six days after their menses by TVS with a high-resolution transducer. Residual myometrium on the isthmocele was characterized by erythro-ectasic vessels covered by a flabby mucosa. In the early proliferative phase, the cavity was filled with menstrual blood that could be presented by TVS examination [21]. In our study, TVS examination identified isthmoceles in 14.78% of the women, a prevalence that is lower than in some other reports [22]. Notably, we only used TVS to determine whether an isthmocele was present. If our study had also applied hysteroscopy and sonohysterography, the numbers of detected isthmoceles could have been much higher.

When patients who have had a CS surgery complain of postmenstrual bleeding or intermittent spotting, isthmocele should be considered as a potential cause. Non-coordinated muscle contractions can allow the menstrual blood to accumulate in the reservoir-like pouch [11]. Chronic inflammatory fibrin debris induces distortions and widens the lower uterine segment; endometrial congestion, lymphocytic infiltrations, and capillary dilatation with inflamed blood cells in the endometrial stroma have been found at the site of scar formation [23]. The isthmocele size (width and depth) expands, and the thickness of the myometrium (in one that is insufficiently contractible) decreases without discharging the redundant product [14]. Menstrual blood flows heavily through a cervical canal with an isthmocele, allowing the coagulant blood to accumulate in the pouch and depress the contractility of the uterine muscles around the defect [24]. Continuous incoming blood and densely viscous mucus production that are not fully drained can accumulate in the reservoir-like pouch [25].

The combination of persistent menstruation accumulation and blood with an increased local mucous secretion due to abundant vascularization may lead to postmenstrual abnormal uterine bleeding (PAUB) [13]. PAUB is a clinical symptom in which dark hematic spotting or discharge occurs days after menstruation. The presence of an isthmocele

has been implicated in underdiagnosed PAUB in non-pregnant women who have had a CS surgery. Increased CSD awareness may help physicians identify the cause of PAUB in more patients. In our study, the most common symptoms in women with isthmocele were postmenstrual spotting and irregular menstruation.

Secondary infertility is also common with isthmocele, likely due to the accumulated blood degrading the sperm and the cervical mucus quality obstructing sperm transportation through the cervical canal and the endometrial cavity, interfering with embryo implantation [26]. In addition, the presence of local inflamed fibrotic tissue in the isthmocele causes pelvic pain such as dysmenorrhea and dyspareunia [27].

A high prevalence of isthmocele in women whose CS surgery was performed intrapartum implies that the hysterotomy incision was made through effaced and dilatated cervical tissue, which is difficult to distinguish from the uterine wall during uterine contractions [28]. This could explain why there appears to be a greater risk of isthmocele development in women with cervical dilatation of more than 5 cm and duration of labor longer than five hours [29]. We detected fewer isthmocele in women who had elective CS surgery; however, that difference was not statistically significant. While data was collected on CS indications such as unprogressive labor, maternal option, breech presentation, fetal distress, and dystocia, the study did not include information about cervical dilatation and effacement at the time of the CS surgery. Surgical materials used in surgery can be effect on isthmocele development [30].

Our study was limited in that the women were only examined by TVS to identify the presence of an isthmocele. This practice may have underdiagnosed the number of women with isthmoceles in our study group. A unique feature of our study was that the same CS surgical technique (a Kerr incision and a single layer continuous locking suture closure) had been performed on all women during their previous CS surgeries. This made the standardization of variables easy to assess.

Conclusion

Not all women with a CS history develop a visible isthmocele, so it is important to define the risk factors that may lead to the principal symptoms. If the percentage of CS deliveries continues to increase, the long-term complications will be seen more and more in daily practice. If the use of CS can be minimized, potential clinical ailments such as isthmoceles will be reduced.

References

1. World Health Organization Human Reproduction Programme. WHO statement on caesarean section rates. Reprod Health Matters. 2015;23:149-50.
2. Sipahi S, Sasaki K, Miller CE. The minimally invasive approach to the symptomatic isthmocele - what does the literature say? A step-by-step primer on laparoscopic isthmocele - excision and repair. Curr Opin Obstet Gynecol. 2017;29(4):257-65.
3. Tower AM, Frishman GN. Cesarean scar defects: an underrecognized cause of abnormal uterine bleeding and other gynecologic complications. J Minim Invasive Gynecol. 2013;20(5):562-72.
4. Morris H. Surgical pathology of the lower uterine segment caesarean section scar: is the scar a source of clinical symptoms? Int J Gynecol Pathol. 1995;14:16-20.
5. Vervoort AJ, Uittenbogaard LB, HehenkampWJ, et al. Why do niches develop in Caesarean uterine scars? Hypotheses on the aetiology of niche development. Hum Reprod. 2015;30:2695-702.
6. Nezhat C, Grace L, Soliemannjad R, et al. Cesarean scar defect: what is it and how should it be treated? OBG Management. 2016;28:32-53.
7. Roberge S, Boutin A, Chaillet N, Moore L, Jastrow N, Demers S, et al. Systematic review of Cesarean scar assessment in the nonpregnant state: imaging techniques and uterine scar defect. Am J Perinatol. 2012;29:465-471.
8. Schepker N, Garcia-Rocha GJ, von Versen-Hoynck F, et al. Clinical diagnosis and therapy of uterine scar defects after cesarean section in non-pregnant women. Arch Gynecol Obstet. 2015;291:1417-23.
9. Bij de Vaate AJ, van der Voet LF, Naji O, Witmer M, Veersema S, Brölmann HA, et al. Prevalence, potential risk factors for development and symptoms related to the presence of uterine niches following Cesarean section: systematic review. Ultrasound Obstet Gynecol. 2014;43:372-82.
10. Tulandi T, Cohen A. Emerging manifestations of Cesarean scar defect in reproductive-aged women. J Minim Invasive Gynecol. 2016;23:893-902.
11. Osser OV, Jokubkiene L, Valentin L. High prevalence of defects in Cesarean section scars at transvaginal ultrasound examination. Ultrasound Obstet Gynecol. 2009;34:90-7.
12. Florio P, Filippeschi M, Moncini I, Marra E, Franchini M, Gubbini G. Hysteroscopic treatment of the cesarean-induced isthmocele in restoring infertility. Curr Opin Obstet Gynecol. 2012;24:180-6.
13. Bij de Vaate AJ, Brölmann HA, van der Voet LF, van der Slikke JW, Veersema S, Huirne JA. Ultrasound evaluation of the Cesarean scar: relation between a niche and postmenstrual spotting. Ultrasound Obstet Gynecol. 2011;37:93-9.
14. Wang CB, Chiu WW, Lee CY, Sun YL, Lin YH, Tseng CJ. Cesarean scar defect: correlation between Cesarean section number, defect size, clinical symptoms and uterine position. Ultrasound Obstet Gynecol. 2009;34:85-9.
15. Pomorski M, Fuchs T, Zimmer M. Prediction of uterine dehiscence using ultrasonographic parameters of cesarean section scar in the nonpregnant uterus: a prospective observational study. BMC Pregnancy Childbirth. 2014;14:365.
16. Vikhareva Osser O, Valentin L. Clinical importance of appearance of Cesarean hysterotomy scar at transvaginal ultrasonography in nonpregnant women. Obstet Gynecol. 2011;117:525-32.
17. Naji O, Abdallah Y, Bij De Vaate AJ, et al. Standardized approach for imaging and measuring Cesarean section scars using ultrasonography. Ultrasound Obstet Gynecol. 2012;39:252-9.
18. Regnard C, Nosbusch M, Fellemans C, Benali N, van Rysselberghe M, Barlow P,et al. Cesarean section scar evaluation by saline contrast sonohysterography. Ultrasound Obstet Gynecol. 2004;23:289-92.
19. Pomorski M, Fuchs T, Rosner-Tenerowicz A, et al. Morphology of the cesarean section scar in the non-pregnant uterus after one elective cesarean section. Ginekol. Pol 2017;88:174-9.
20. Fabres C, Aviles G, De La Jara C, Escalona J, Muñoz JF, Mackenna A, et al The Cesarean delivery scar pouch: clinical implications and diagnostic correlation between transvaginal sonography and hysteroscopy. J Ultrasound Med. 2003;22:695-700.
21. Sasaki K. Diagnosis and treatment of uterine isthmocele. OB Gyn News. 2015;50:8-9.
22. Ofili-Yebovi D, Ben-Nagi J, Sawyer E, Yazbek J, Lee C, Gonzalez J, et al. Deficient lower-segment Cesarean section scars: prevalence and risk factors. Ultrasound Obstet Gynecol. 2008;31:72-7.
23. Lin YH, Hwang JL, Seow KM. Endometrial ablation as a treatment for postmenstrual bleeding due to cesarean scar defect. Int J Gynaecol Obstet. 2010;111:88-9.
24. Florio P, Gubbini G, Marra E, Dores D, Nascetti D, Bruni L, et al. A retrospective case-control study comparing hysteroscopic resection versus hormonal modulation in treating menstrual disorders due to isthmocele. Gynecol Endocrinol. 2011;27:434-8.
25. Gubbini G, Centini G, Nascetti D, Marra E, Moncini I, Bruni L, et al. Surgical hysteroscopic treatment of Cesarean-induced isthmocele in

restoring fertility: a prospective study. J Minim Invasive Gynecol. 2011;18:234-7.
26. Uppal T, Lanzarone V, Mongelli M. Sonographically detected caesarean section scar defects and menstrual irregularity. J Obstet Gynaecol. 2011;31:413-6.
27. Chen Y, Han P, Wang YJ, et al. Risk factors for incomplete healing of the uterine incision after cesarean section. Arch Gynecol Obstet. 2017;296:355-61.
28. van der Voet LF, Bij de Vaate AM, Veersema S, et al. Long-term complications of caesarean section. The niche in the scar: a prospective cohort study on niche prevalence and its relation to abnormal uterine bleeding. BJOG. 2014;121:236-244.
29. Vikhareva Osser O, Valentin L. Risk factors for incomplete healing of the uterine incision after caesarean section. BJOG. 2010;117:1119-26.
30. Başbuğ A, Doğan O, Ellibeş Kaya A, Pulatoğlu, Ç, Çağlar M. Does Suture Material Affect Uterine Scar Healing After Cesarean Section? Results from a Randomized Controlled Trial. J Invest Surg. 2018 Apr 18:1-7.

J Surg Med. 2018;2(3):288-292.
DOI: 10.28982/josam.430050

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Incidental findings at abdominal ultrasonography in health personnel working with radiation sources

Radyasyon kaynakları ile çalışan sağlık personelinde abdominal ultrasonografideki insidental bulgular

Elif Gündoğdu [1], Mahmut Kebapçı [1]

[1] **Department of Radiology, Eskişehir Osmangazi University Faculty of Medicine, Eskişehir, Turkey**

ORCID ID of the authors
EG: 0000-0002-1729-6958
MK: 0000-0002-2856-9923

Abstract

Aim: In this study; we aimed to evaluate the incidental lesions detected by ultrasonography in the abdomen and their clinical trials at health personnel working in departments using radiation sources.

Methods: Ultrasonography reports on 52 health personnel working in departments using radiation sources were evaluated retrospectively, from the hospital report registry system. The findings were classified as anatomical variant, benign lesions and situations requiring further investigation.

Results: In 19 (36.53%) of the workers, the ultrasonography was completely normal. In 33 (63.46%) of the workers, lesions or sonopathological conditions were detected. There were incidental findings in 13 (25%) patients in hepatobilier system, 8 (15.38%) patients in genitourinary system and 12 (23.07%) patients in both of them. 6 (11.53%) workers had a anatomic variant, 24 (46.15%) workers had a benign lesion or condition, and 26 (50%) workers required further examination.

Conclusion: Incidental findings are widespread at health personnel working in departments using radiation sources. Some of the findings were benign, while a significant number of cases required further investigation. Knowing commonly detected lesions prevents unnecessary anxiety, while it can ensure that cases requiring further investigation are considered sufficiently.

Keywords: Incidental findings, Ultrasonography, Health personnel

Öz

Amaç: Bu çalışmada radyasyon kaynakları ile çalışılan departmanlarda görevli sağlık personelinde ultrasonografi ile abdomen bölgesinde saptanan insidental lezyonların ve bu lezyonların klinik öneminin değerlendirilmesi amaçlanmıştır.

Yöntemler: Radyasyon kaynakları ile çalışılan departmanlarda görevli 52 sağlık çalışanının ultrasonografi raporları hastane rapor kayıt sistemi üzerinden retrospektif olarak değerlendirildi. Elde edilen bulgular anatomik varyant, benign lezyon ve ileri araştırma gerektiren durumlar olarak sınıflandırıldı.

Bulgular: 19 (%36,53) sağlık çalışanında ultrasonografi incelemeleri tamamen normaldi. 33 (%63,46) personelde lezyon ya da sonopatolojik durum tespit edildi. 13 (%25) çalışanda hepatobilier sistemde, 8 (%15,38) çalışanda genitoüriner sistemde ve 12 (%23,07) çalışanda ise hem genitoüriner hem hepatobilier sistemde bulgu saptandı. 6 (%11,53) çalışanda anatomik varyant, 24 (%46,15) çalışanda benign lezyon veya durum, 26 (%50) çalışanda ise ileri araştırma gerektiren durum tespit edildi.

Sonuç: Radyasyon kaynakları ile çalışılan departmanlarda görevli sağlık personelinde insidental bulgular yaygın olarak gözlenir. Bu bulguların bir kısmı benign iken önemli bir kısmı araştırılması gereken durumları içerir. Yaygın saptanan insidental bulguların bilinmesi gereksiz endişeyi önlerken, ileri araştırma gerektiren durumlara gerekli önemin verilmesini de sağlar.

Anahtar kelimeler: İnsidental bulgular, Ultrasonografi, Sağlık personeli

Corresponding author / Sorumlu yazar:
Elif Gündoğdu
Address / Adres: Eskişehir Osmangazi University, Faculty of Medicine, Department of Radiology, Meşelik Yerleşkesi, 26480, Eskişehir, Türkiye
E-mail: elif_basbay@hotmail.com

Ethics Committee Approval: The Medical Faculty of Eskişehir Osmangazi University ethics committe approved the study (no: 14, date: 15.05.2018).
Etik Kurul Onayı: Eskişehir Osmangazi Üniversitesi Tıp Fakültesi etik kurulu çalışmayı onayladı (no: 14, tarih: 15.05.2018).

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 03.06.2018
Accepted / Kabul Tarihi: 11.07.2018
Published / Yayın Tarihi: 13.07.2018

How to cite / Atıf için: Gündoğdu E, Kebapçı M. Incidental findings at abdominal ultrasonography in health personnel working with radiation sources. J Surg Med. 2018;2(3):288-292.

Introduction

Incidental radiological findings; are lesions or conditions that are diagnosed during examinations performed for other purposes and do not produce symptoms in the patient [1,2]. Increasing frequency of using imaging techniques has also increased the detection rate of these lesions [1-3]. Detected lesions are usually small-sized and benign, but also detection of cases requiring detailed evaluation is not so less [4]. The lesions and their ratios determined according to the examined body region vary. Abdomen is one of the most common anatomical localizations of incidental lesions [4].

Health personnel working with radiation sources are at a higher risk for precancerous lesions and various malignancies such as thyroid and hematopoietic system than other parts of the society. For this reason, some radiological examinations are carried out at certain periods for screening purposes. Incidental lesions can be detected during these examinations and how the management in this group can be confusing from time to time.

In this study; it was aimed to evaluate the incidental lesions and conditions detected by ultrasonography (USG) in the abdominal region and their clinical trials in health personnel working in departments using radiation sources who is fully asymptomatic and no history of known disease.

Materials and methods

Between October 2017 and January 2018, abdominal ultrasound reports of 52 health personnel (35 female, 17 male) aged 23-54 years working in departments with radiation sources were evaluated retrospectively. While, the mean age of females 36.68±6.56, the mean age of males 40.29±9.62. In the group included in the study, the health workers were completely asymptomatic and none had previously known illness. Sonographic examination was performed by a single radiologist- 10 years of experience- with 12 hours of fasting and full filled bladder with USG. All examinations were made the same USG device (Toshiba Aplio 500) and 3-6 MHz convex probe. All examinations were performed by transabdominal approach. Detected lesions or conditions were reported in detail for each organ. All patients' records were accessed via the hospital report registry system. In retrospectively examined reports, lesions and findings were determined for each organ. The findings were classified as anatomic variant, benign lesions and cases requiring further examination. For anatomical variants, no follow-up examination was required. Benign lesions had typical ultrasonographic features and were not needed further examination. In some of them, follow-up was unnecessary (e.g. simple renal cyst) and in some of them (e.g. hemangiomas) ultrasonographic follow-up was sufficient. For some of the lesions or conditions requiring further investigation (e.g. splenomegaly), laboratory findings and etiological research were required, while in some (e.g. hydronephrosis) advanced radiological evaluation was required.

Statistical analysis was performed using SPSS 20.0 (Chicago, IL) software.

Ethical committee approval from Eskişehir Osmangazi University Faculty of Medicine was taken for the study.

Results

While the examination was satisfactory at 48 (92.30%) of the study group; examination was suboptimal at 4 (7.70%) of the study group, because of intensive gas distension, obesity or no breathing cooperation. The pancreas could not be assessed for these reasons in the group where the examination was insufficient. In 19 (36.53%) of the study group, abdominal USG examination was completely normal and no sonopathologic condition was detected. In 33 (63.46%) of the study group had lesions or sonopathological conditions in the intraabdominal organs. There were incidental findings in the hepatobiliary system in 13 (25%), genitourinary system in 8 (15.38%), and both genitourinary and hepatobiliary systems in 12 (23.07%).

Twenty-five (48.07%) of the study group had incidental findings in the hepatobiliary system. The detected findings are shown in Table 1. The most frequent incidental finding was hepatosteatosis. Grade 1 steatosis in 14 health personnel and grade 2 steatosis in 7 health personnel were detected. None of health personnel had Grade 3 steatosis. In a case in whom a simple hepatic cyst was detected, the number of cysts was more than 10, the largest cyst was 14 mm in diameter, and all cysts showed anechoic simple cyst characteristics. 3 health personnel had hemangiomas with typical ultrasonographic features (Figure 1). There were a total of 4 gallbladder polyp (2 in 1 patient) in 3 personnel. All of the polyps were smaller than 5 mm and did not carry any suspicious findings in terms of malignancy. One personnel had a single gallstone with a diameter of 13 mm, and the other patient had multiple stone which were smaller than 1 cm. Four of the personnel had one accessory spleen; all of the accessory spleens were localized in splenic hilum. No incidental findings were found in the pancreas in any of the personnel.

Twenty (38.46%) of the study group had incidental findings in the genitourinary system. The detected findings are shown in Table 2. A total of 8 renal cysts (2 in 1 patient, 3 in 1 patient, and 1 in 3 patients) were observed in 5 personnel (Figure 2). Seven of these cysts were simple cysts, while 1 had fine septations. A total of 6 kidney stones were observed in 3 patients (3 in 1 patient, 2 in 1 patient, 1 in 1 patient) (Figure 3). All stones were smaller than 1 cm in size, and concomitant calyceal ectasia was not present. Hydronephrosis was detected in 1 personnel and it was grade 1. There were 7 myoma (2 subserous in 1 patient, 2 intramural in 1 patient, 1 in 3 patients) in 5 personnel. None of the male patients had any pathology in the seminal vesicles and also in adrenal gland and bladder in both genders.

Patients were categorized to anatomic variation (accessory spleen, hypoplasic kidney, septate uterus) , benign incidental findings (hepatic cyst, hemangiomas, bile stones, polyps, sludge, medullary nephrocalcinosis, renal cysts, stones, hemorrhagic / simple ovary cysts, paraovarian cysts, endometrioma, PCOS, myoma, prostate hyperplasia) and the findings to be investigated (hepatosteatosis, hepatomegaly, splenomegaly, hydronephrosis, focal calyceal ectasia, medullary nephrocalcinosis). Categories are shown in Table 3. The patient with hydronephrosis was suggested to evaluate with other radiological imaging modalities (computed tomography (CT)); and for other patients were suggested to evaluate with clinical and laboratory findings.

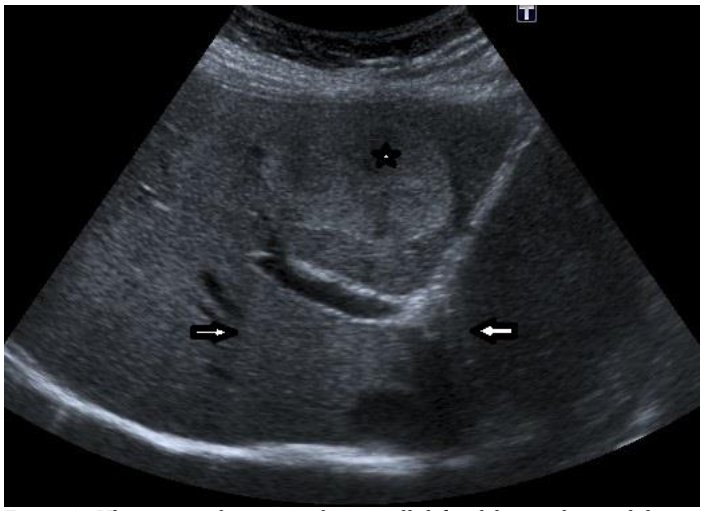


Figure 1: Ultrasonography image shows well-defined hyperechoic solid mass (asterisk) in liver parenchyma. Posterior acoustic enhancement (arrows) is typical for hepatic hemangiomas.

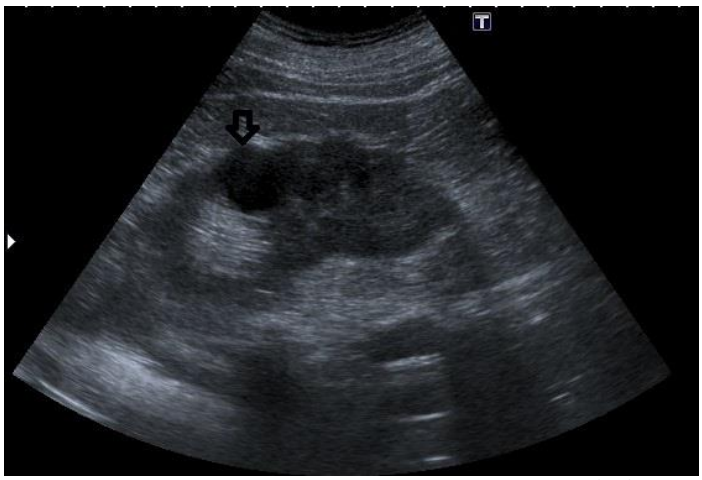


Figure 2: A hypoechoic cystic lesion (arrow) is seen upper pole of left kidney without any solid component or septa (simple cortical cyst).

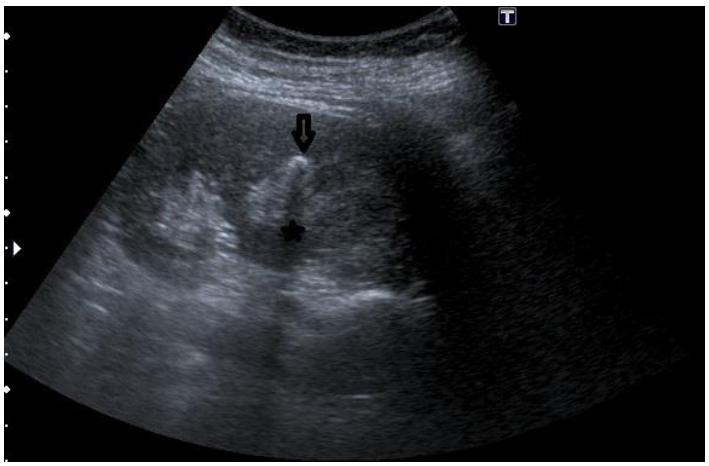


Figure 3: Ultrasonography image shows an echogenic foci (arrow) in calyceal system with posterior acoustic shadowing (asterisk) without any findings of obstruction.

Table 1: Incidental findings detected in hepatobilier system

Incidental Findings Hepatobilier System	Organ	Number (n)	Ratio (%)
	Liver		
Grade 1 / Grade 2 Hepatosteatosis		14/7	40.38
Hepatomegaly		5	9.61
Simple hepatic cyst		1	1.92
Hemangioma		3	5.76
Focal fatty- protection area		3	5.76
	Gall Bladder		
Stone		2	3.84
Sludge		1	1.92
Polyp		3	5.76
	Spleen		
Splenomegaly		2	3.84
Accessory Spleen		4	7.69

Table 2: Incidental findings in the genitourinary system

Incidental Findings Genitoüriner System	Organ	Number (n)	Ratio (%)
	Kidney		
Renal cyst		5	9.61
Renal stone		3	5.76
Focal caliectasy		2	3.84
Hydronephrosis		1	1.92
Medullary nephrocalcinosis		1	1.92
Hypoplasic kidney		1	1.92
	Female Genital System		
Subserous / Intramural Myom		2/3	14.28
Septate uterus		1	2.85
Nabothian cyst		1	2.85
Simple ovarian cyst		5	14.28
Hemorrhagic ovarian cyst		1	2.85
Endometrioma		2	5.71
Paraovarian cyst		1	2.85
Polycystic ovary syndrome (PCOS)		2	5.71
	Male Genital System		
Prostate Hypertrophy		2	11.76

Table 3: Categories according to findings

Categories	Number (n)	Ratio (%)
Category 1 (Anatomical Variants)	6	11.53
Accessory spleen		
Septate uterus		
Hypoplasic kidney		
Category 2 (Benign lesions or conditions)	24	46.15
Hepatic cyst, Hemangioma, Focal fatty- protection area		
Gall bladder stone/sludge/polyp		
Kidney cyst/stone		
Uterine myoma, nabothian cyst		
Simple/hemorrhagic ovarian cyst, paraovarian cyst, endometrioma, PCOS		
Prostate Hypertrophy		
Category 3 (situations need to be investigated)	26	50.00
Hepatosteatosis, Hepatomegaly		
Splenomegaly		
Hydronephrosis, Focal caliectasy, Medullary Nephrocalcinosis		

Discussion

Along with the increasing use of imaging techniques, there is also an increase in incidental findings [1-5]. There are many studies on this topic, especially in trauma patients, with incidental findings in CT [1,4,6]. Incidental findings were determined at varying rates in these studies. One of the most frequently detected anatomic localizations of incidental lesions is abdomen [4]. Since there is no literature study on incidental lesions detected by abdominal USG, was compare and evaluate the our study group with those performed with CT in the general population.

The most common organ which detected incidental finding in our study is the liver. Hepatosteatosis is the most common (40.68%) incidental finding. It has been reported that between %27 and 38 of general population in Western countries [7]. In autopsy series these rates were around 20% [8]. The incidence in our study group was found to be higher than the normal population and autopsy findings. There are many factors affecting hepatosteatosis such as sedentary lifestyle, obesity, metabolic syndrome, ethnicity and gender. This result which we have obtained to determine whether the increased rate of steatosis in health personnel working with radiation sources is due to radiation exposure alone needs to be compared to the normal population with similar risk factors (diabetes, family history, hyperlipidemia etc.) and characteristics (body mass index, sex, ethnicity etc.).

The hepatosplenomegaly has been detected at similar incidental rates both in health personnel working with radiation sources and in the normal population. This condition was in the

categories that need to be investigated in both groups. This issue is even more important because of the increased risk of hematopoietic malignancies in health personnel working with radiation sources, and further imaging may be needed with more detailed examination. Hydronephrosis is also a condition in the category that needs to be investigated. Hydronephrosis has been reported to be detected incidentally in the normal population in many studies [4,5]. Detection rates in our study group are not different from the normal population.

Hemangiomas are the most common benign lesions of the liver and are usually incidentally detected. It was reported in 0.4% to 7.3% of cases and in autopsy series these rates were between 3% and 20% [9]. In our study, the rate was 5.76%. The incidence of hemangiomas in our study group is similar to that of the normal population.

In the liver parenchyma, simple cysts are observed in 2.5 to 18% [10]. Incidence with age increases [10]. The rate of hepatic cyst in our study was found to be 1.92% and similar to the literature. The average age of our study was low and the incidence was likely to increase in older patient groups. There was no significant difference in the incidence of hepatic cysts between our study population and other parts of the community. Quattrocchi and friends found that the ratio incidentally detected of hepatic cyst was 0.3% with spinal magnetic resonance imaging (MRI) [5]. The modality difference and the fact that the liver is not fully involved in the study area may explain the lesser incidence compared to our study.

Bile stones incidence were found to be 3.84% in our study. It was seen in approximately 10% of the population and the incidence increases with age. The average age of our study group was the young adult age group and this may be the reason for the low incidence. The similar situation applies in the case of bile sludges. Gallbladder polyps were seen in 5-7% of the society and 90% were benign [11]. The rate of polyp detection in our study was 5.76%, similar to the general population. Accessory spleen were reported 6.7% in autopsy series [12]. In our study group, the ratio was 7.69 and similar. According to the study we think that working with radiation sources does not pose an increased risk for gallbladder stones, sludges, polyps and accessory spleen.

It is known that the incidence of renal cysts together with age increases and the rate of detection in CT examinations reaches 40% and incidental detection rate in pediatric age group reaches 0.2%. In our study group, the ratio was 9.6%, which was expected for the young population. It does not differ from the normal population.

Incidental kidney stones were detected in 5.76% of our study. This rate was found 13.9% in studies performed with CT colonoscopy and 0.1% in MR studies [5]. It is known that CT is more sensitive than USG in detection of stone less than 5 mm and MRI is less sensitive in stone detection. Because our study was performed with USG, the incidence is expected to be lower than CT.

Uterine myomas were seen in approximately 20-50% of the female in the reproductive age group. In our study, the rate was 15% and the incidence could be lower because some of the patients were in the postmenopausal period. Similarly, the incidence of endometrioma was less than that of the reproductive age group, and the same reason is valid for this situation.

There is no study of incidental findings in health personnel working with radiation sources, all of the studies we compared in the literature were conducted in the general population. When considered as a whole, there were not different for anatomical variants and benign incidental findings between the general population and our study group. Some benign incidental findings due to the limitations of age and imaging modality were detected less common than in the general population. No increase in the incidence of benign incidental findings in health personnel working with radiation sources was detected.

In studies involving incidental lesions; it was found that the presence and malignancy rates of incidental findings increases with age [1-5]. In our study, was also found that the incidence of incidental lesions increased with age. No malignant incidental findings were observed in our study. This may be because the average age of our patient population was low. There is no significant relationship between the detected anatomical variations and age, and for most of these congenital variations this is an expected outcome.

The most important limitation of our study was the small number of patient populations. The fact that the working group was made up of a relatively young adult population was another limitation. It was known that the incidence of incidental lesions increases with age. Studies involving a wider series of cases and diversification of age groups will yield more accurate results and thus more generalized results can be obtained.

Another potential limitation of our study was that the study were made with USG and because of the known limitations and technical factors of USG, it is difficult to evaluate the adrenal gland and pancreas. Adrenal lesions are one of the most common incidental lesions in the abdominal region. However, most of these studies were done with CT. In our study, we think that the reason for the absence of incidental lesion in the adrenal gland is due to the modality difference. This discrepancy may have occurred because the retroperitoneal area is difficult to assess by ultrasound and most incidental lesions are small in size.

Conclusion

Incidental findings are widespread in health personnel working with radiation sources. Some of the incidental findings are benign or anatomic variants and do not differ from the normal population. Knowing commonly observed benign incidental lesions allows us to avoid unnecessary anxiety and further examinations. On the other hand, situation are detected that need to be investigated at a considerably high rate. The detection of these conditions can ensure that they are taken seriously.

References

1. Lantinga MA, Gevers TJG, Drenth JPH. Evaluation of hepatic cystic lesions. World Journal of Gastroenterology. 2013;19(23);3543–54. https://doi.org/10.3748/wjg.v19.i23.3543
2. Patel S, Rajalakshmi BR, Manjunath GV. Histopathologic findings in autopsies with emphasis on interesting and incidental findings-A pathologist's perspective. Journal of Clinical and Diagnostic

Research. 2016;10(11);EC08-EC12. https://doi.org/10.7860/JCDR/2016/21106.8850
3. Wilkins T, Tadkod A, Hepburn I, Schade RR. Nonalcoholic fatty liver disease: diagnosis and management. Am Fam Physician. 2013;88(1);35–42.
4. Yao J, Burns JE. Extracolonic Findings on CT Colonography. Does the Benefit Outweigh the Cost? Academic Radiology. 2013;20(6);665–6. https://doi.org/10.1016/j.acra.2013.03.005
5. Quattrocchi CC, Giona A, Di Martino AC, Errante Y, Scarciolla L, Mallio CA, Zobel BB. Extra-spinal incidental findings at lumbar spine MRI in the general population: a large cohort study. Insights into Imagin. 2013;4(3);301–8. https://doi.org/10.1007/s13244-013-0234-z
6. Paluska TR, Sise MJ, Sack DI, Sise CB, Egan MC, Biondi M. Incidental CT findings in trauma patients: Incidence and implications for care of the injured. Journal of Trauma - Injury, Infection and Critical Care.2007;62(1);157–61. https://doi.org/10.1097/01.ta.0000249129.63550.cc
7. Hitzeman N, Cotton E. Incidentalomas: Initial management. American Family Physician. 2014;90(11);784–89.
8. Berland LL, Silverman SG, Gore RM, Mayo-Smith WW, Megibow AJ, Yee J, Taylor AJ. Managing incidental findings on abdominal CT: White paper of the ACR incidental findings committee. Journal of the American College of Radiology. 2010;7(10);754–73. https://doi.org/10.1016/j.jacr.2010.06.013
9. Taşeva A, Taşev V, Bulanov D, Dimitrov K, Popov V, Zivkov E, Dimitrova V. Diagnosis of liver hemangioma. Khirurgiia (Sofiia). 2013;(3);8-13.
10. Sperry JL, Massaro MS, Collage RD, Nicholas DH, Forsythe RM, Watson GA, Peitzman AB. Incidental radiographic findings after injury: Dedicated attention results in improved capture, documentation, and management. Surgery. 2010;148(4);618–24. https://doi.org/10.1016/j.surg.2010.07.017
11. Sarici IS, Duzgun O. Gallbladder polypoid lesions > 15 mm as indicators of T1b gallbladder cancer risk. Arab Journal of Gastroenterology. 2017;18(3);156-58. https://doi.org/10.1016/j.ajg.2017.09.003
12. Unver DN, Uysal L, Demirci S, Dogan KH, Kolcu G. Accessory spleens at autopsy. Clinical Anatomy.2011;24(6);757-62. https://doi.org/10.1002/ca.2011.04.006

J Surg Med. 2018;2(3):293-297.
DOI: 10.28982/josam.433344

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

The relationship between dialysis adequacy and the rate of change in uric acid level by hemodialysis

Hemodiyaliz ile ürik asit düzeyindeki değişim oranı ile diyaliz yeterliliği arasındaki ilişki

Oktay Bozkurt [1], Cevat Topal [2], Mevlüde İnanç [1]

[1] Department of Medical Oncology, Erciyes University Faculty of Medicine, Kayseri, Turkey
[2] Department of Nephrology, Medical Park Hospital, Trabzon, Turkey

ORCID ID of the authors
OB: 0000-0003-3551-5234
CT: 0000-0003-0624-9491
Mİ: 0000-0002-9612-9970

Corresponding author / Sorumlu yazar:
Oktay Bozkurt
Address / Adres: Erciyes Üniversitesi, Tıp Fakültesi, M.K. Dedeman Onkoloji Hastanesi, Tıbbi Onkoloji, 38035, Kayseri, Türkiye
E-mail: bozkurt.oktay8@gmail.com

Ethics Committee Approval: Approval was received from the local Ethics Committee.
Etik Kurul Onayı: Onay lokal Etik Kurul'dan alındı.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 12.06.2018
Accepted / Kabul Tarihi: 28.06.2018
Published / Yayın Tarihi: 14.07.2018

Abstract

Aim: Although one of the commonly used methods for determining dialysis adequacy is the urea kinetic model, it is not the gold standard. Different parameters are needed to determine dialysis adequacy. In our study, we investigated the relationship between urea reduction rate (URR) and Kt/V which are used to assess dialysis adequacy and the rate of change in uric acid, a purine metabolite, by hemodialysis.

Methods: A total of 133 patients who had undergone hemodialysis treatment due to renal failure between March 2010 and September 2010 were evaluated retrospectively. Urea kinetic modeling was used to measure dialysis adequacy. The following formula was used to do this; Kt/V=-ln(R-0.008xT)+(4-3.5xR)xUF/W[R; postdialysis blood ureanitrogen (BUN)/predialysis BUN, T; duration of dialysis (hr), UF; total ultrafiltration during dialysis (L), W; patient weight after dialysis (kg)]. The urea reduction rate was calculated using the formula; URR(%)=100x(1-postdialysis BUN/predialysis BUN). Uric acid reduction rate (UARR) was calculated using the formula; UARR(%)=100x(1-Uric acid after/Uric acid before). The relationship between URR and Kt/V ratios which are used to assess dialysis adequacy and UARR is evaluated.

Results: Median urea, uric acid and creatinine reduction rates were 72%, 74% and 63.9%, respectively. There was a statistically significant correlation between reduction rates of uric acid, creatinine and urea after dialysis ($p<0.001$). There was a statistically significant relationship between URR and Kt/V which are used to assess dialysis adequacy,and UARR ($p<0,001$). According to the ROC analysis in our study, we defined UARR value that will demonstrate dialysis adequacy as at least 65.8% (sensitivity 97.9% and specificity 82.6%, area under the ROC curve=0.880, $p<0.001$).

Conclusion: A significant relationship was found between the URR and Kt/V ratios which are used to assess dialysis adequacy and UARR. We also determined in our study that the UARR value that shows dialysis adequacy should be at least 65.8%. To our knowledge, this is the first study to evaluate the relationship between UARR and dialysis adequacy. However, thefindings need to be confirmed by large, prospective, clinical trials.

Keywords: Dialysis adequacy, Urea kinetic model, Kt/V, Uric acid

Öz

Amaç: Diyaliz yeterliliğini belirlemede sık kullanılan yöntemlerden biri üre kinetik modelleme olmasına rağmen altın standart değildir. Diyaliz yeterliliğinin belirlenmesinde farklı parametrelere ihtiyaç vardır. Biz çalışmamızda bir pürin metaboliti olan ürik asitin hemodiyaliz ile değişim oranına bakarak diyaliz yeterliliğini değerlendirmede kullanılan üre azalma oranı (URR) ve KT/V ile arasındaki ilişkiyi araştırdık.

Yöntemler: Çalışmamızda 2 merkezde Mart 2010 ile Eylül 2010 tarihleri arasında böbrek yetmezliği nedeniyle hemodiyaliz tedavisi gören toplam 133 hasta retrospektif olarak değerlendirildi. Diyaliz yeterliliğini ortaya koymak için üre kinetik modelleme kullanıldı. Bunun için Kt/V=–ln(R–0.008xt)+(4– 3.5xR)xUF/W([R=diyaliz sonrası kan üre azotu (BUN) / diyaliz öncesi BUN, t= diyaliz seansının süresi (saat), UF= diyalizde yapılan toplam ultrafiltrasyon (L), W= diyaliz sonrası hasta ağırlığı (kg)] formülü kullanıldı. ÜRR(%) = 100 x (1- BUNsonra / BUNönce) formülü kullanıldı. Ürik asit azalma oranı (UARR) (%) = 100 x (1- Ürik asit sonra / Ürik asit önce) formülü ile hesaplandı. UARR ile diyaliz yeterliliğini değerlendirmede kullanılan URR ve Kt/V oranları arasındaki ilişki değerlendirildi.

Bulgular: Ortanca üre, ürik asit ve kreatinin azalma oranı sırası ile %72, %74, %63,9 olarak bulundu. Ürik asit, kreatinin ve ürenin diyaliz ile azalma oranları arasında istatistiksel olarak anlamlı korelasyon saptandı ($p<0,001$). UARR ile diyaliz yeterliliğini değerlendirmede kullanılan Kt/V ve URR arasında istatistiksel olarak anlamlı ilişki bulunmuştur ($p<0,001$). Çalışmamızda, ROC analizine göre, diyaliz yeterliliğini gösterecek UARR değerinin en az %65,8 (duyarlılık %97,9, özgüllük %82,6, ROC eğrisinin altındaki alan =0,880, $p<0,001$) olarak belirledik.

Sonuç: UARR ile diyaliz yeterliliğini değerlendirmede kullanılan URR ve Kt/V oranları arasında istatistiksel açıdan anlamlı ilişki tespit edildi. Ayrıca çalışmamızda diyaliz yeterliliğini gösterecek UARR değerinin en az %65,8 olması gerektiğini belirledik. Bizim bilgimize göre bu çalışma UARR ile diyaliz yeterliliği arasındaki ilişkiyi değerlendiren ilk çalışmadır. Fakat bu bulgunun büyük, prospektif, klinik çalışmalar ile teyit edilmeye ihtiyacı vardır.

Anahtar kelimeler: Diyaliz yeterliliği, Üre kinetik model, Kt/V, Ürik asit

How to cite / Atıf için: Bozkurt O, Topal C, İnanç M. The relationship between dialysis adequacy and the rate of change in uric acid level by hemodialysis. J Surg Med. 2018;2(3):293-297.

Introduction

Chronic renal disease is a pathophysiologic process that results in reduction in nephron counts and nephronic functions and frequently progresses to end-stage renal failure resulted from many etiologic causes [1]. Patients with end-stage renal disease (ESRD) should be given one of the renal replacement therapies. Renal replacement treatments are hemodialysis, peritoneal dialysis, and kidney transplantation. As the kidney failure progresses, the serum concentration of many organic and inorganic substances, called uremic toxins, increases [2].

Despite the treatment of ESRD or uremic syndrome by dialysis, uremic toxins have not yet been fully understood. Uremic syndrome is the result of abnormal accumulation of various substances that inhibit physiological and biochemical functions in the body [2,3]. The size of these accumulating substances can vary from less than 300 daltons (such as urea) to 12000 daltons (such as medium-sized molecules, beta2 microglobin, myoglobin). The importance of each of the uremic toxin groups is still unclear.

Uric acid, xanthine, hypoxanthine, and guanosine are the most important purine metabolites that accumulate in the uremia. The purine metabolites that constitute the major class of uremic toxins cause impairment of calcitriol and vitamin D metabolism [3-6]. These metabolites play a role in the immunodeficiency seen in hemodialysis patients [7]. They were also found to be associated with loss of appetite and weight loss seen in patients with ESRD [8]. For this reason, it is important that uric acid and other purine metabolites are efficiently removed from blood by dialysis.

The purpose of this study is to investigate the relationship between the rate of reduction in uric acid levels and dialysis adequacy in patients undergoing hemodialysis due to renal insufficiency.

Materials and methods

In our study, a total of 133 patients who had undergone hemodialysis treatment due to renal insufficiency between March 2010 and September 2010 were evaluated retrospectively in two hemodialysis centers.

Inclusion criteria:

1. Patients undergoing hemodialysis treatment due to renal insufficiency

2. Patients informed about the study and accepted to participate

A total of 133 patients were enrolled. Patients' age, gender, medications, height and weight were recorded.

Blood samples were taken from patients after 12 hours of fasting from the needle attached to the artery before starting dialysis and receiving serum and heparin for biochemical parameters (glucose, creatinine, BUN, total cholesterol, LDL cholesterol, uric acid, sodium, potassium, calcium, phosphorus, albumin, hemogram). After hemodialysis, the blood pump rate of the instrument was reduced to 50ml/min for 15 seconds and blood sample was taken for uric acid, creatinine, and urea at the end of this period; then the dialysis procedure was terminated.

Uric acid was measured in Synchron LX20 autoanalyzer using the Syneron System Uric Acid Assay kit with enzymatic trinder method. Urea kinetic modeling was performed to demonstrate dialysis adequacy. The following formula was used to do this; Kt/V=-ln(R-0.008xT)+(4-3.5xR)xUF/W [R; postdialysis blood ureanitrogen (BUN)/predialysis BUN, T; duration of dialysis (hr), UF; total ultrafiltration during dialysis (L), W; patient weight after dialysis (kg)]. The urea reduction rate was calculated using the formula; URR(%)=100x(1-postdialysis BUN/predialysis BUN). Uric acid reduction rate (UARR) was calculated using the formula; UARR(%)=100x(1-Uric acid after/Uric acid before).

Statistical Analysis: Data analysis was done in SPSS 11.5 for Windows software package. The Shapiro-Wilk test was used to determine whether the distribution of continuous variables was close to normal. Descriptive statistics for continuous variables were expressed as mean, standard deviation, median, minimum, maximum while categorical variables were expressed as the number of cases and (%). Wilcoxon Signed test was used to assess whether statistically significant changes were observed in the input and output laboratory measurements. Spearman's correlation test was used to examine whether there was any significant correlation between continuous variables. P values of less than 0.05 ($p<0.05$) were regarded as statistically significant.

Results

Forty eight of 133 patients were female (36.1%) and 85 were male (63.9%). Median age of the patients included in the study was 60 years. The average time at which patients started dialysis is 43.5 months. All patients were dialyzed three times a week for 4 hours with bicarbonate dialysis solution using dialysers with a blood flow rate of 300 ml/min and dialysate flow rate of 500 ml/min and a surface area of 1.5 m2. 129 of the patients were dialyzed with AV fistula (97%) and 4 with subclavian catheter (3%). The etiologic causes of renal failure were determined as hypertension in 55 (41.4%), diabetic nephropathy in 32 (24.1%), glomerulonephritis in 10 (7.5%), stone disease in 5 (3.8%), VUR in 6 (4.5%), idiopathic in 4 (3%), PKD (polycystic kidney disease)in 20 (15%) and multiple myeloma in 1 (0.8%) of the patients. Hepatitis B infection was detected in 5 (3.8%) of the patients and hepatitis C infection was detected in 10 (7.5%) of the patients. 118 (88.7%) patients did not have any hepatitis infection (Table 1).

In our study, a statistically significant positive correlation was found between the uric acid reduction rate and Kt/V ($p <0.001$), URR ($p <0.001$). There was no statistically significant correlation between uric acid reduction rate and laboratory parameters such as albumin, hemoglobin, protein, calcium, phosphorus.

The mean urea, creatinine and uric acid levels of the patients before and after dialysis were 138.6/40.5 mg/dl, 8.2/3 mg/dl and 6.1/1.6 mg/dl, respectively and a statistically significant reduction was detected ($p<0.001$) (Table 2 and Figure 1-3). Median urea, uric acid and creatinine reduction rates were 72%, 74% and 63.9%, respectively (Table 3).

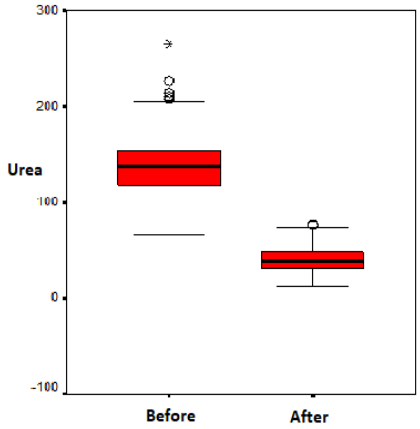


Figure 1: Urea levels of the patients before and after dialysis

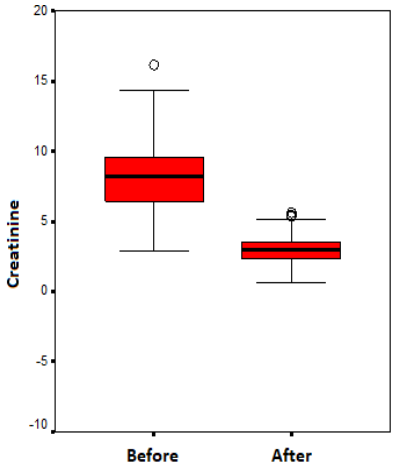


Figure 2: Creatinine levels of the patients before and after dialysis

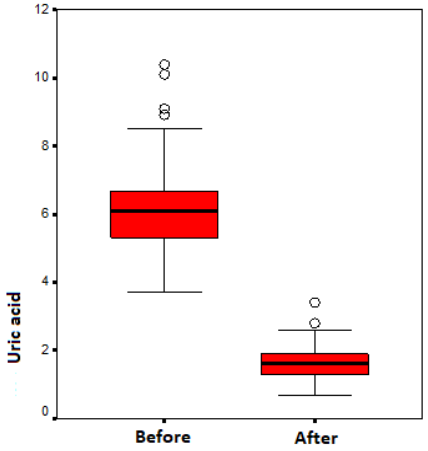


Figure 3: Uric acid levels of the patients before and after dialysis

Explanation for Figure 1-2-3: The horizontal line in the middle of each box shows the median value (50th percentile), while the lower and upper lines in the boxes show 25th and 75th percentiles, respectively. The lines in the lower and upper parts of the boxes show the minimum and maximum values, respectively. Circles indicate outliers, while stars indicate subjects with extreme values.

According to The European Best Practice Guidelines, single-pool Kt/Vurea is accepted as at least 1.4 (9). According to the urea kinetic model in our study, we considered Kt/V 1.4 and above as adequate dialysis. When ROC analysis was performed for dialysis adequacy, we determined the lower limit for UARR as 65.8% (sensitivity 97.9% and specificity 82.6%, area under the ROC curve = 0.880, p<0.001) (Figure 4).

Table 1: Demographic and Clinical Features Descriptive Statistics

Variables	n	%
Gender		
Female	48	36.1
Male	85	63.9
Vascular access		
AVfistula	129	97.0
Subclavian	4	3.0
Flow rate(ml/min)		
300	133	100.0
Hemodialysis duration (minutes)		
240	133	100.0
Hemodialysis Frequency (weeks)		
3	133	100.0
Etiology		
Hypertension	55	41.4
Diabetes Mellitus	32	24.1
Glomerulonephritis	10	7.5
Nephrolithiasis	5	3.8
Vesicoureteral reflux	6	4.5
İdiopathic	4	3.0
Polycystic kidney disease	20	15.0
Multiple myeloma	1	0.8
HEPATIT STATUS		
No hepatitis	118	88.7
HBV +	5	3.8
HCV +	10	7.5
Total	133	100.0

Tablo 2: Laboratory values before and after dialysis

Variables	Mean	SD	Median	Minimum	Maximum	p
Urea						<0.001
Before	138.6	32.82	138.0	65.0	265.0	
After	40.5	13.15	38.0	11.0	77.0	
Creatine						<0.001
Before	8.2	2.32	8.2	2.8	16.1	
After	3.0	0.98	2.9	0.6	5.6	
Uric acid						<0.001
Before	6.1	1.18	6.1	3.7	10.4	
After	1.6	0.46	1.6	0.7	3.4	

Table 3: Descriptive Statistics for Kt / V, URR, Uric Acid and Creatinine Reduction Rates

Variables	Mean	SD	Median	Minimum	Maximum
KTV	1.3	0.14	1.4	0.9	1.7
UARR(%)	73.3	6.18	74	53.5	88.3
Creatinine reduced rate (%)	63.7	6.15	63.9	42.6	84.3

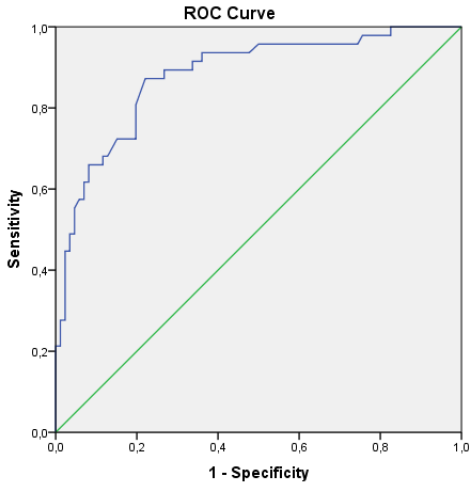


Figure 4: The predictive value of UARR for dialysis adequacy (sensitivity 97.9% and specificity 82.6%, area under the ROC curve = 0.880), p <0.001.

Discussion

Hemodialysis is the most commonly applied renal replacement method in Turkey and in the world. Despite the use of modern techniques, the average life span in hemodialysis patients is reported to be even shorter than those with malignant disease [10].

Urea is the most commonly used substance in clinically determining the clearance of small molecules. Nonetheless, the kinetic behavior of urea does not represent that of water-soluble small molecular weight uremic toxins [11]. Uric acid, xanthine, hypoxanthine and guanosine are the most important purine metabolites that accumulate in uremia. The major purine metabolites of uremic toxins were found to be associated with impaired calcitriol and vitamin D metabolism, immunodeficiency, loss of appetite and weight loss [3-8]. Hyperuricemia has also been associated with hypertension, heart failure, and atherosclerosis [12-14]. Therefore, effective removal of uric acid is important.

In a study by Vanholder and colleagues [15] on uremic toxins before and after hemodialysis, they found the highest rate of reduction after dialysis to be 66% for uric acid and hydroxyhippuric acid. In the same study, they found that the change rate of urea by dialysis as 60% and that of creatinine as 55%. In the same study, a high degree of correlation was found

between changes in uric acid, creatinine, and urea concentration. The reduction rates of urea (UR), creatinine (CR) and uric acid (UA) were found to be 73.8%, 69.5% and 75.1%, respectively, in a study conducted by De Smet et al [17] and the rate of reduction in UR, CR and UA were significantly correlated [16]. In a study by Ricardo and his colleagues, the rates of clearance of urea, creatinine, and uric acid were found to be correlated at every minute of dialysis.

In a study by Carlo and colleagues [18] in which they compared the removal of uremic toxins in a group dialyzed with standard 4-hour bicarbonate dialysate with a group dialyzed with 8-hour low-bicarbonate dialysate, the reduction rates of UR, CR, and UA were found to be 69.3%, 62.7%, 75.8% in 4-hour dialyzed group, respectively and 74.6%, 65.9%, 79.9% in 8-hour dialyzed group. There was also a statistically significant correlation between reduction rates of UR, CR, and UA in both groups. In our study, the rates of reduction in median UR, CR and UA were found to be 72%, 63.9% and 74%, respectively. There was a significant correlation between the reduction rates of uric acid, creatinine and urea in our study ($p < 0.001$). These findings were consistent with some previous studies [16-18]. In our study, a statistically significant relationship was found between UARR and Kt/V, URR. We also determined that UARR value that demonstrates dialysis adequacy should be less than 65.8% according to ROC analysis in our study. To our knowledge, this is the first study to evaluate the relationship between UARR and dialysis adequacy determined by urea-kinetic models. We suggest that UARR can be used to determine dialysis adequacy similar to URR.

Kt/V is influenced by many factors such as daily protein uptake, lack of consideration of postdialysis urea rebound, and residual renal function [19]. For this reason, despite giving valuable information about dialysis adequacy of patients, it is not acceptable as a gold standard. Therefore, methods and parameters other than Kt/V should be evaluated for determination of dialysis adequacy.

The limitation of this study is that postdialysis plasma levels of uric acid may be affected by various conditions. In some studies, plasma uric acid levels were higher than normal after hemodialysis. This is explained by ischemic events occurring during dialysis [20,21]. Ischemic events that occur during dialysis increase the hydrolysis of adenosine triphosphate, anaerobic glycolysis, proteolytic conversion ofxanthine dehydrogenase into xanthine oxidase, and degradation of adenine nucleotides [20,21]. All these mechanisms result in the breakdown of adenosine triphosphate and the increase in uric acid during ischemia. One of the most prominent ischemic events that occur during dialysis in patients with ESRD is intradialytic hypotension [22]. Studies by Shinzato and colleagues [22] assessing plasma levels of purine nucleotides in patients with intradialytic hypotension during hemodialysis have shown an increase in purine metabolite during hypotension. In this study, purine metabolites at the end of dialysis were found to be lower than before dialysis. However, in the same study, there was a marked decrease in purine metabolites after dialysis in the group where hypotension was prevented in comparison to the group where intradialytic hypotension was developed during dialysis. In our study, it was not taken into account whether hypotension developed during dialysis. In addition, other factors which may affect plasma uric acid levels after dialysis, such as use of diuretics, hypothyroidism, obesity, diabetes mellitus, are not excluded. Another limitation of our study is that it has been done retrospectively with a small number of patients. This may limit the generalization of the results.

As a result; a statistically significant relationship was found between the URR and Kt/V ratios which are used to assess dialysis adequacy and UARR. We also determined in our study that the UARR value that indicates the dialysis adequacy should be at least 65.8%. To our knowledge, this is the first study to evaluate the relationship between UARR and dialysis adequacy. We suggest that the rate of change in uric acid levels before and after dialysis may be used to evaluate dialysis adequacy. However, it needs to be confirmed by large, prospective, clinical trials.

References

1. Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rossert J, et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int. 2005;67(6):2089-100.
2. Meert N, Schepers E, De Smet R, Argiles A, Cohen G, Deppisch R, et al. Inconsistency of reported uremic toxin concentrations. Artif Organs. 2007;31(8):600–11.
3. Vanholder R, Meert N, Schepers E, Glorieux G, Argiles A, Brunet P, et al. European Uremic Toxin Work Group (EUTox) : Review on uraemic solutes II—variability in reported concentrations: causes and consequences. Nephrol Dial Transplant. 2007;22(11):3115–21.
4. Vanholder R, De Smet R, Glorieux G, et al. Review on uremic toxins: classification, concentration, and inter individual variability. Kidney Int. 2003;63(5):1934-43.
5. Heinig M, Johnson RJ. Role of uric acid in hypertension, renal disease, and metabolic syndrome. Cleve Clin J Med. 2006;73(12):1059-64.
6. Chen W, Roncal-Jimenez C, Lanaspa M, Gerard S, Chonchol M, Johnson RJ, et al. Uric acid suppresses 1 alpha hydroxylase in vitro and in vivo. Metabolism. 2014 Jan;63(1):150-60.
7. Sampol J, Dussol B, Fenouillet E, et al. High adenosine and deoxy adenosine concentrations in mononuclear cells of hemodialyzed patients. J Am Soc Nephrol. 2001;12(8):1721-8.
8. Simmonds HA, Cameron JS, Morris GS, et al. Purine metabolites in uraemia. Adv Exp Med Biol. 1987;223:73-80.
9. European Best Practice Guidelines Expert Groupon Hemodialysis, European Renal Association. Section II. Hemodialysis adequacy. Nephrol Dial Transplant. 2002;17(7):16–31.
10. Makita Z, et al. Efficiency of removal of circulating advanced glycosylation end-product sand mode of treatment in patients with ESRD. Am Soc Nephrol. 1992;3:335.
11. Eloot S, Torremans A, De Smet R et al. Kinetic behavior of urea is different from that of other water-soluble compounds: thecase of the guanidin ocompounds. Kidney Int 2005;67(4):1566–75.
12. Kalil RS, Carpenter MA, Ivanova A, et al. Impact of Hyperuricemia on Long-term Outcomes of Kidney Transplantation: Analysis of the FAVORIT Study. Am J Kidney Dis. 2017;70(6):762-9.
13. Zuo T, Liu X, Jiang L, Mao S, Yin X, Guo L et al. Hyperuricemia and coronary heart disease mortality: a meta-analysis of prospective cohort studies. BMC Cardiovasc Disord. 2016;16(1):207.
14. Braga F, Pasqualetti S, Ferraro S, Panteghini M. Hyperuricemia as risk factor for coronary heart disease incidence and mortality in the generalpopulation: a systematic review and meta-analysis. Clin Chem Lab Med. 2016;54(1):7-15.
15. Vanholder RC, De Smet RV, Ringoir SM: Assessment of urea and other uremic markers for quantification of dialysis adequacy. Clin Chem. 1992;38:1429–36,

16. De Smet R, Dhondt A, Eloot S, et al. Effect of the super-flux cellulose triacetate dialyser membrane on the removal of non-protein-bound and protein-bound uraemic solutes. Nephrol Dial Transplant. 2007;22(7):2006–12.
17. Fagugli RM, De Smet R, Buoncristiani U, et al. Behavior of non-protein-bound and protein bound uremic solutes during daily hemodialysis. Am J Kidney Dis. 2002;40(2):339–47.
18. Basile C, Libutti P, Lucia A, Casino G.F, Vernaglione L, Tundo S, et al. Removal of uraemic retention solutes in Standard bicarbonate haemodialysis and long-hours low flow bicarbonate haemodialysis. Nephrol Dial Transplant. 2011; 26(4):1296-303.
19. Vanholder R, DeSmet R, Lesaffer G. Dissociation between dialysis adequacy and Kt/V. Semin Dial. 2002;15(1):3-7.
20. Fotbolcu H, Duman D, Ecder SA, Oduncu V, Cevik C, Tigen K, et al. Attenuated cardiovascular response to sympathetic system activation during exercise in patients with dialysis-induced hypotension. Am J Nephrol. 2011;33(6):491-8.
21. Aon MA, Cortassa S, Maack C, et al. Sequential opening of mitochondrial ion channels as a function of glutathione redox thiol status. J Biol Chem. 2007;282(30):21889-900.
22. Shinzato T, Miwa M, Nakai S, et al. Role of adenosine in dialysis-induced hypotension. J Am Soc Nephrol. 1994;4:1987-94.

J Surg Med. 2018;2(3):298-302.
DOI: 10.28982/josam.433898

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

The effects of perceived social support on postpartum depression

Algılanmış sosyal desteğin doğum sonrası depresyona etkisi

Halime Pınar Demiröz [1], Kenan Taştan [1]

[1] **Atatürk University Medical Faculty, Department of Family Medicine, Erzurum, Turkey**

ORCID ID of the authors
HPD: 0000-0002-0864-392X
KT: 0000-0002-0205-3638

Abstract

Aim: Links between pregnancy and depression, especially during the first postpartum months are well recognized. Pregnancy-related depression may harm the mother as well as her baby. We aimed to investigate the effects of social support on depression in mothers during the postpartum period.

Methods: A cross-sectional study was conducted in Erzurum city center involving 110 mothers. Data was collected using The Edinburgh Postpartum Depression Scale (EPDS) and Multidimensional Scale of Perceived Social Support (MSPSS).

Results: Mean age of the participants was 28.8±5.9 years. Majority of the participants were housewives (75.5%; n=83). Of the participants, 26.4% (n=29) reported of having depression history. According to the EPDS, 47.3% of the mothers (n=52) had scores above the cutoff. The mean EPDS and MSPSS scores were 12.0±4.7 and 58.3±13.0, respectively. There was a significant negative correlation between the EPDS and the MSPSS scores (r=-0.42; p<0.001)

Conclusion: Social support and postpartum depression are firmly connected. Effective screening methods and early detection of postpartum depression should be utilized in connection with the primary healthcare providers, especially in areas with high risk, to prevent harmful effects of postpartum depression on maternal, infant and family health.

Keywords: Depression, Postpartum, Social support, Depressive disorder, Risk assessment, Maternal health

Öz

Amaç: Özellikle doğumdan sonraki ilk aylarda gebelik ve depresyon arasındaki ilişki iyi bilinmektedir. Gebelikle ilgili depresyon hem anne, hem de bebek sağlığını tehlikeye atabilir. Bu araştırmada sosyal desteğin doğum sonrası dönemdeki annelerde depresyona olan etkisini araştırmayı amaçladık.

Yöntemler: Erzurum şehir merkezinde 110 anneyi içeren kesitsel bir araştırma yürütüldü. Veriler Edinburg Postpartum Depresyon skalası (EPDS) ve Çok Boyutlu Algılanmış Depresyon Skalası (MSPSS) ile toplandı.

Bulgular: Katılımcıların ortalama yaşı 28,8±5,9 yıl idi. Katılımcıların çoğunluğu ev hanımı idi (%75,5; n=83). Katılımcıların %26,4'ünün (n=29) depresyon öyküsü vardı. EPDS'ye göre annelerin %47,3'ü (n=52) kesme düzeyinin üzerinde puana sahipti. Ortalama EPDS ve MSPSS puanları sırasıyla 12,0±4,7 ve 58,3±13,0 idi. EPDS ve MSPSS puanları arasında anlamlı bir korelasyon saptandı (r=-0.42; p<0.001).

Sonuç: Sosyal destek ve doğum sonrası depresyon sıkı bir şekilde ilişkilidir. Depresyonun anne, bebek ve aile üzerindeki olumsuz etkilerini önlemek için özellikle yüksek risk altındaki bölgelerde birinci basamak sağlık hizmeti sunucularıyla bağlantılı olarak doğum sonrası depresyonun erken tanınması için etkili tarama yöntemleri kullanılmalıdır.

Anahtar kelimeler: Depresyon, Postpartum, Sosyal destek, Depresif bozukluk, Risk değerlendirmesi, Anne sağlığı

Corresponding author / Sorumlu yazar:
Kenan Taştan
Address / Adres: Atatürk Üniversitesi, Tıp Fakültesi, Aile Hekimliği, 25240, Erzurum, Türkiye
E-mail: ktastan2002@yahoo.com

Ethics Committee Approval: This study has been approved by the Ataturk University Faculty of Medicine Clinical Research Ethics Committee (No: B.30.2.ATA.0.01.00/168-Date:10.24.2016).
Etik Kurul Onayı: Bu çalışma Atatürk Üniversitesi Tıp Fakültesi Klinik Araştırmalar Etik Kurulu tarafından onaylanmıştır. (B.30.2.ATA.0.01.00 / 168-Tarih: 10.24.2016).

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 14.06.2018
Accepted / Kabul Tarihi: 07.07.2018
Published / Yayın Tarihi: 14.07.2018

How to cite / Atıf için: Demiröz HP, Taştan K. The effects of perceived social support on postpartum depression. J Surg Med. 2018;2(3):298-302.

Introduction

Pregnancy-related depression may harm the mother as well as the baby [1]. Links between pregnancy and depression, especially during the first postpartum months are well recognized [2].

According to the Diagnostic and Statistical Manual of Mental Disorders [3], postpartum depression is defined as a major depressive episode with onset in pregnancy or within four weeks of delivery. A certain proportion of postpartum depressive episodes begin during pregnancy and continue and often worsen afterward [4].

The World Health Organization has moved up depression to the fourth rank in the worldwide health problems requiring urgent attention, with an expectation that unipolar depression will climb up to number four in the year 2020 [5,6]. The frequencies of depressive symptoms during pregnancy have been reported to be between 10-30% [7–9]. One cohort study in Turkey has presented postnatal and antenatal depression prevalence as 13.9% and 49.7%, respectively [10]. Other studies have shown depression prevalence of 27.9-33.1% among Turkish pregnant women [11,12].

The quite high occurrence of pregnancy-related depression in Turkey suggests the involvement of local factors such as frequent pregnancies, low educational level, domestic violence, and insufficient social support [10]. Thus, screening of postpartum depression using the Edinburgh Postnatal Depression Scale (EPDS) [13] has been introduced to Turkish family practice centers.

Social support is a complex concept, and there are multiple pathways by which social support may influence mental and physical health. There is robust evidence linking social support to both morbidity and mortality [14]. Although many studies are addressing the connection between social support and health, most measurement scales used are non-specific and lacking internationally validation [15]. Translated into many languages, the Multidimensional Scale of Perceived Social Support (MSPSS) measures the backing of family, friends, and significant other people [16]. Although it is well-documented that social support is related to mothers' psychological health [15], there are few studies addressing Multidimensional Scale of Perceived Social Support and postpartum depression.

In this study, we hypothesized that perceived social support is related to postpartum depression. Hence, we aimed to investigate the effects of social support on depression in mothers during the postpartum period.

Materials and methods

The study was conducted in a descriptive, cross-sectional design, between November 2016 and November 2017. Study reporting was done following the STROBE guidelines [17].

Setting and Participants

The study population consisted of women applying to the five family practice units of the Department of Family Practice at Atatürk University Faculty of Medicine. Three of these units are located within the campus of the University, near the lodging of the university staff; the other two are located in the Aziziye District, which is 12 km away from the city center. The five family practice units are serving a population of about 17500 people. A total of 122 pregnant women were under follow-up during the study period.

Variables, Data Sources, and Measurement

A demographic information questionnaire, Beck Depression Scale for Primary Care (BDSPC), the EPDS, and the MSPSS were used as data collection tools.

Demographic information questionnaire

The demographic data questionnaire was developed by the researchers to collect data on a total of 20 characteristics of the mothers: maternal age, maternal education level, marital status, maternal occupation, family monthly income, marriage duration, working status, disease status, depression history, alcohol use, smoking status, substance use, drug use, number of children, presence of domestic violence, near loss, baby's health status, type of delivery, breastfeeding, and nursing difficulties.

BDSPC

As to the exclusion criteria, the BDSPC, developed by Beck et al. [18] and adapted into Turkish by Aktürk et al. [19] was applied in the antenatal period to detect depression. Scores of four and above points were considered as having depression.

EPDS

Developed by Cox et al. [13] and validated for Turkish by Engindeniz et al. [20], this instrument evaluates the risk of postpartum depression. The face-to-face-administered scale is of the four-point Likert type and consists of 10 items. Items 3, 5, 6, 7, 8, 9, and 10 show gradually decreasing strength and are scored as 3, 2, 1, and 0. Items 1, 2, and 4 are calculated in the form 0, 1, 2, and 3. The total score of the scale is obtained by adding the item scores together, where the lowest possible score is 0 and the highest possible score is 30. The cut-off point of the scale was determined as 12/13 with a Cronbach alpha reliability coefficient of 0.79 [21].

MSPSS

Developed by Zimet [16] and adapted into Turkish by Eker and Arkar [22], this instrument evaluates the qualitative presence of social support from three perspectives. Three different support groups can be identified from the tool: family (items 3, 4, 8, and 11), friends (items 6, 7, 9, and 12), and special people (questions 1, 2, 5, and 10). In addition, subscale scores can be added together to determine the total score of the scale. Each item is graded using a 7-point scale with Likert-type ratings. Totals of the subscale of the instrument vary between 4 and 28, while the total scores can be between 12 and 84. Higher scores indicate higher perceived social support. Accordingly, participants were grouped as “low social support” (12-48 points), “intermediate social support” (49-68 points), and “high social support” (69-84 points).

Data Collection

Study data were collected by the family medicine trainees working in the family practice units. All data collectors were instructed about how to fill out the data collection instruments. Data collection forms were administered to 119 women, who participated in the study voluntarily. Six women were excluded from the study because they had history of major depression. Three other women were excluded because they were mourning and the study was completed with 110 women

(Figure 1). Data collection was done during the scheduled fourth-week postnatal visit. Participants with a score of 12 and above were considered depressed. All women were interviewed face to face. After giving information about the study, informed consent was taken from all mothers.

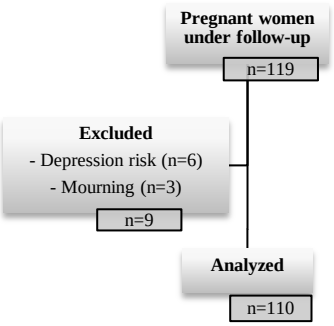


Figure 1: Study flow diagram.

Ethical aspects of the study

This study has been approved by the Ataturk University Faculty of Medicine Clinical Research Ethics Committee (No: B.30.2.ATA.0.01.00/168-Date:10.24.2016). Because the work was done in family health centers, additional permission was obtained from Erzurum Public Health Directorate.

Statistical Methods

The data were analyzed using SPSS for Windows (version 18.0) and Microsoft Excel 2010. The results were presented as n, %, mean, and standard deviation (SD). Normal distributions of numerical variables were evaluated using histogram graphs. The relationship between EPDS and MSPSS scores were analyzed using Pearson correlation analysis. To compare the EPDS scores between MSPSS social support groups, we used the One-Way ANOVA with post hoc LSD. Statistically, the significance limit was accepted as $p < 0.05$.

Results

Descriptive data

Data of 110 women were analyzed. Mean age of the participants was 28.8±5.9 years. Participant characteristics are presented in Table 1. 40.9% of the women were married for 1-5 years. The number of primary school and university graduates was equal and 29 (26.4%). Majority of the participants were housewives (75.5%; n=83). 55.5% of the participants (n=61) had a monthly income of 1000-5000 TL (ca. 260-1315 USD).

Table 1: Participant characteristics

		n	%
Duration married	< 1 year	29	26.4
	1-5 years	45	40.9
	5-10 years	21	19.1
	>10 years	15	13.6
Education	None	5	4.5
	Primary school	29	26.4
	Intermediate school	17	15.5
	High school	28	25.5
	University	29	26.4
	Masters	2	1.8
Occupation	Housewife	83	75.5
	Teacher	7	6.4
	Government employee	6	5.5
	Other	14	12.6
Monthly income	<500 TL	1	0.9
	500-999 TL	5	4.5
	1000-5000 TL	61	55.5
	>5000 TL	33	30.0
	Not disclosed	10	9.1
	Total	110	100

Of the participants, 26.4% (n=29) reported of having depression history. Tobacco/alcohol/drug usage was 12.7% (n=14). 47.3% (n=52) were primipar. 15.5% (n=17) had unintended pregnancies. All participants had employed husbands. 59.1% (n=65) were living in self-owned housings. Majority of the participants (79.1%; n=87) reported no unrest or violence at home. 63.6% of the women (n=70) delivered via normal vaginal route while 36.4% (n=40) had cesarean sections. Breastfeeding frequency was 95.5% (n=105).

Postnatal problems of the mothers in order of frequency were; none (49.1%; n=54), health problems of the baby (20.0%; n=22), health problems of the mother (13.6%; n=15), immunization concerns (10.9%; n=12), anxiety in noticing needs of the baby (2.7%; n=3), sleep problems (2.7%; n=3), and neonatal mortality (0.9%; n=1).

Outcome data

According to the EPDS, 47.3% of the mothers (n=52) were under risk for postnatal depression.

While the mean EPDS scores were 12.0±4.7, mean scores for MSPSS were 58.3±13.0 (Table 2). There was a significant negative correlation between the EPDS and the MSPSS ($r=-0.42$; $p<0.001$) (Figure 2).

Table 2: Distribution of the Edinburgh postpartum depression scale (EPDS) and multidimensional scale of perceived social support (MSPSS) scores

	Min	Max	Mean	SD
EPDS	0	30	12.00	4.72
MSPSS	13	79	58.39	13.04
MSPSS family subscale	6	28	21.36	4.96
MSPSS friends subscale	7	26	18.45	4.48
MSPSS special people subscale	7	28	18.52	4.29

SD: Standard deviation

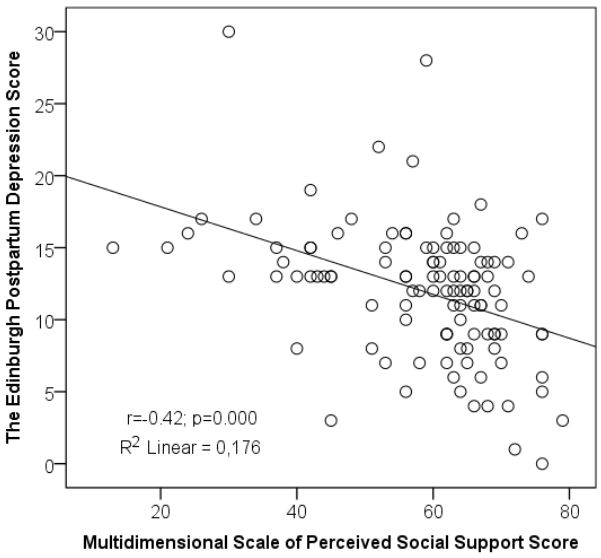


Figure 2: Correlation between the Edinburgh postpartum depression scale and multidimensional scale of perceived social support scores

Comparison of the mean EPDS scores according to the MSPSS groups with the One-Way ANOVA are given in Figure 3 ($p<0.001$). As to the Post Hoc LSD analysis, the EPDS scores were higher in the "low social support" (14.61±4.66) group compared with the "moderate" (12.06±4.20) and "high social support" (8.80±4.74) groups ($p<0.05$). The EPDS score in the "moderate" group was higher than the "high group" ($p=0.004$)

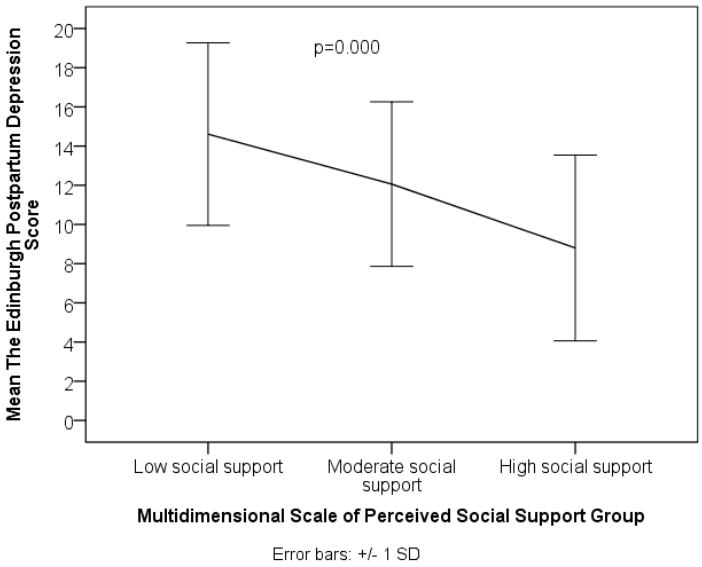


Figure 3: Mean values of the Edinburgh postpartum depression scale scores according to the multidimensional scale of perceived social support groups

Discussion

This study reveals the effects of social support on postpartum depression. Pregnancy, birth, and the postpartum period are complicated processes for the mother with numerous physical and psychological challenges. This is a time when the woman needs all the support that her family, close friends, and health professionals can provide.

The risk for postpartum depression (PPD) in Turkey was estimated as 14.0-34.6% by different studies [23–29]. Aydin et al. [28] studied 728 women in the same province and concluded that lack of husband's support, any stressful life event during the pregnancy, and infant with a health problem were associated with depression. Although our PPD rates seem high, compared with the general literature, Yildirim et al. [30] reported even higher proportions (51.3%). The inclusion of patients with past depression histories may have contributed to this difference. PPD prevalence in Asian countries range from 3.5% to 63.3% [31].

EPDS scores of women with past depression were comparatively higher. Strong associations have been reported between PPD and previous depression or anxiety disorders, increasing the frequency up to eight times [32]. As a requirement of the Turkish family structure, the relationships with the family of the mother's partner is also claimed as an essential factor affecting PPD [33]. Participants with extended families constituted more than 60% of our sample, which might be another contributing factor to the relative high EPDS scores.

There is a significant difference between the participants with and without family discomfort or violence concerning the EPDS scores. In the meta-analysis where Beck assessed factors increasing PPD risk, dissatisfaction with marriage is listed among the conditions that create prenatal anxiety [34].

Similar correlations between the EPDS and the MSPSS were shown in the study of Ege et al. [33] conducted in Malatya, another Eastern city, socio-demographically similar to Erzurum. The alleviating effect of social support on PPD might be related to the placental corticotropin-releasing hormone. Hahn-Holbrook et al. [35] have demonstrated that prenatal family support predicted significantly fewer depressive symptoms postpartum and more gradual increases in placental corticotropin-releasing hormone from 29 to 37 weeks' gestation.

Although there might be cultural differences in social support, it seems to be an inter-culturally prevailing entity. One study from Australia reported that women with low social support in pregnancy were more likely than well-supported women to report poorer health during pregnancy and postnatally, to seek medical help more frequently, and to be more depressed postnatally [36].

While studies in Western cultures have shown that mothers are more individualized in the postpartum period, mothers in Asian cultures rely more on the social support of their mothers, their spouses and their mothers in law. In the classical Turkish tradition, the mother and baby are not left alone, supported, and helped with housekeeping and baby care for 40 days after delivery, which is proposed as a factor decreasing PPD [31].

Women who have little social support, poor health and a history of stressful life events are at risk of poor mental health during the perinatal period. On the other hand, primary healthcare providers are suggested to apply peer education in groups on emotional, physical or social problems that women may encounter after childbirth [37]. Efficient screening methods and early detection of postpartum depression should be utilized in connection with the primary healthcare providers, especially in areas with high risk, to prevent adverse effects of postpartum depression on maternal, infant, and family health. Easy accessibility, the first point of health-contact, as well as individualized and patient-centered approach put family medicine in the focus point in preventing and managing postpartum depression.

Limitations

This study included pregnant women applying to the five family practice units of a university family medicine department. The cohort served by the department may differ to some extent from the general population. Hence, despite the representativeness of the sample for the given population, caution is suggested to generalize the findings for the whole community. Future studies should concentrate on applying the instrument to different representative samples of the population.

References

1. Gabbard G. Mood disorders: psychodynamic etiology. Baltimore: Williams And Wilkins; 1995.
2. Brown S, Lumley J. Physical health problems after childbirth and maternal depression at six to seven months postpartum. BJOG An Int J Obstet Gynaecol 2000;107:1194–201. doi:10.1111/j.1471-0528.2000.tb11607.x.
3. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 5th ed., (DSM-5). Washington, DC: American Psychiatric Publishing; 2013.
4. Uher R, Payne JL, Pavlova B, Perlis RH. Major depressive disorder in DSM-5: Implications for clinical practice and research of changes from DSM-IV. Depress Anxiety 2014;31:459–71.
5. Libiger J. Depression is frequent in primary care. WPA Bull Depress 2005;10:1–4.
6. World Health Organization. The World Health Report 2013: Research for Universal Health Coverage. Luxembourg: 2013.
7. Da Costa D, Larouche J, Dritsa M, Brender W. Psychosocial correlates of prepartum and postpartum depressed mood. Prim Care Companion J Clin Psychiatry 2000;2:148. doi:10.1016/S0165-0327(99)00128-7.

8. Bowen A, Muhajarine N. Prevalence of Antenatal Depression in Women Enrolled in an Outreach Program in Canada. J Obstet Gynecol Neonatal Nurs 2006;35:491–8. doi:10.1111/j.1552-6909.2006.00064.x.
9. Pereira PK, Lovisi GM, Pilowsky DL, Lima LA, Legay LF. Depression during pregnancy: prevalence and risk factors among women attending a public health clinic in Rio de Janeiro, Brazil. Cad Saude Publica 2009;25:2725–36. doi:10.1590/S0102-311X2009001200019.
10. Karaçam Z, Ançel G. Depression, anxiety and influencing factors in pregnancy: a study in a Turkish population. Midwifery 2009;25:344–56. doi:10.1016/j.midw.2007.03.006.
11. Caliskan D, Oncu B, Kose K, Ocaktan ME, Ozdemir O. Depression scores and associated factors in pregnant and non-pregnant women: a community-based study in Turkey. J Psychosom Obstet Gynaecol 2007;28:195–200. doi:10.1080/01674820701450649.
12. Golbasi Z, Kelleci M, Kisacik G, Cetin A. Prevalence and correlates of depression in pregnancy among Turkish women. Matern Child Health J 2010;14:485–91. doi:10.1007/s10995-009-0459-0.
13. Cox JL, Holden JM, Sagovsky R. Detection of Postnatal Depression: Development of the 10-item Edinburgh Postnatal Depression scale. Br J Psychiatry 1987;150:782–6. doi:10.1192/bjp.150.6.782.
14. Holt-Lunstad J, Uchino BN. Social Support and Health. San Francisco, CA: John Wiley & Sons; 2015.
15. Razurel C, Kaiser B, Sellenet C, Epiney M. Relation Between Perceived Stress, Social Support, and Coping Strategies and Maternal Well-Being: A Review of the Literature. Women Health 2013;53:74–99. doi:10.1080/03630242.2012.732681.
16. Zimet GD, Powell SS, Farley GK, Werkman S, Berkoff KA. Psychometric Characteristics of the Multidimensional Scale of Perceived Social Support. J Pers Assess 1990;55:610–7. doi:10.1080/00223891.1990.9674095.
17. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. PLoS Med 2007;4:1623–7. doi:10.1371/journal.pmed.0040296.
18. Beck AT, Guth D, Steer RA, Ball R. Screening for major depression disorders in medical inpatients with the Beck Depression Inventory for Primary Care. Behav Res Ther 1997;35:785–91. doi:10.1016/S0005-7967(97)00025-9.
19. Aktürk Z, Dağdeviren N, Türe M, Tuğlu C. [The reliability and validity analysis of the Turkish version of Beck Depressıon Inventory for primary care]. Türk Aile Hekimliği Dergisi 2005;9:117–22.
20. Engindeniz A, Küey L, Kültür S. Edinburgh doğum sonrası depresyon ölçeği Türkçe formu geçerlilik ve güvenilirlik çalışması., 1996, p. 51–2.
21. Lee DT, Yip SK, Chiu HF, et al. Detecting postnatal depression in Chinese women. Validation of the Chinese version of the Edinburgh Postnatal Depression Scale. Br J Psychiatry 1998;172:433–7.
22. Eker D, Arkar H. [Factorial Structure, Validity, and Reliability of Revised Form of the Multidimensional Scale of Perceived Social Support]. Türk Psikol Derg 1995;10:45–55.
23. Ayvaz S, Hocaoglu C, Tiryaki A, Ak I. [Incidence of postpartum depression in Trabzon province and risk factors at gestation]. Turk Psikiyatri Derg 2006;17:243–51.
24. Nur N, Çetinkaya S, Bakir DA, Demirel Y. [Prevalence of Postnatal Depression and Risk Factors in Women in Sivas City]. CÜ Tip Fakültesi Derg 2004;26:55–9.
25. Sunter AT, Guz H, Canbaz S, Dundar C. [Postpartum Depression in Turkey: Prevalence and Related Factors]. Turk Soc Obs Gynecol 2006;3:26–31.
26. Danaci AE, Dinc G, Deveci A, Sen FS, Icelli I. The prevalence of postpartum depression in Manisa province and Influencing factors. Türk Psikiyatr Derg 2000;11:204–11.
27. Atasoy N, Bayar Ü, Sade H, et al. Clinical and sociodemographic risk factors effecting level of postpartum depressive symptoms during postpartum period. Turkiye Klin J Gynecol Obstet 2004;14:252–7.
28. Aydin N, Inandi T, Karabulut N. Depression and associated factors among women within their first postnatal year in Erzurum province in eastern Turkey. Women Heal 2005;41:1–12. doi:10.1300/J013v41n02_01.
29. Inandi T, Elci OC, Ozturk A, Egri M, Polat A, Sahin TK. Risk factors for depression in postnatal first year, in eastern Turkey. Int J Epidemiol 2002;31:1201–7. doi:10.1093/ije/31.6.1201.
30. Yildirim A, Hacihasanoglu R, Karakurt P. [The relationship between postpartum depression and social support and affecting factors]. Uluslararasi Insa Bilim Derg 2011;8:31–46.
31. Klainin P, Arthur DG. Postpartum depression in Asian cultures: A literature review. Int J Nurs Stud 2009;46:1355–73. doi:10.1016/j.ijnurstu.2009.02.012.
32. Stepanikova I, Kukla L. Is Perceived Discrimination in Pregnancy Prospectively Linked to Postpartum Depression? Exploring the Role of Education. Matern Child Health J 2017;21:1669–77. doi:10.1007/s10995-016-2259-7.
33. Ege E, Timur S, Zincir H, Geçkil E, Sunar-Reeder B. Social support and symptoms of postpartum depression among new mothers in Eastern Turkey. J Obstet Gynaecol Res 2008;34:585–93. doi:10.1111/j.1447-0756.2008.00718.x.
34. Beck CT. Predictors of Postpartum Depression. Nurs Res 2001;50:275–85. doi:10.1097/00006199-200109000-00004.
35. Hahn-Holbrook J, Dunkel Schetter C, Arora C, Hobel CJ. Placental corticotropin-releasing hormone mediates the association between prenatal social support and postpartum depression. Clin Psychol Sci 2013;1:253–65. doi:10.1177/2167702612470646.
36. Webster J, Linnane JWJ, Dibley LM, Hinson JK, Starrenburg SE, Roberts JA. Measuring social support in pregnancy: Can it be simple and meaningful? Birth 2000;27:97–101. doi:10.1046/j.1523-536x.2000.00097.x.
37. Myors KA, Schmied V, Johnson M, Cleary M. "My special time": Australian women's experiences of accessing a specialist perinatal and infant mental health service. Heal Soc Care Community 2014;22:268–77. doi:10.1111/hsc.12079.

J Surg Med. 2018;2(3):303-309.
DOI: 10.28982/josam.435234

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

The effects of health warning labels on cigarette packages on patients who apply to cardiology clinic

Sigara kutusu üzerindeki sağlık uyarı etiketlerinin kardiyoloji polikliniğine başvuran hastalar üzerindeki etkisi

Ercan Akşit [1], Coşkun Bakar [2], Özgür Özerdoğan [2], Özge Turgay Yıldırım [3], Fatih Aydın [3], Ayşe Hüseyinoğlu Aydın [3], Bahadır Kırılmaz [1], Emine Gazi [1], Ali Duygu [1]

[1] Department of Cardiology, Faculty of Medicine, Canakkale Onsekiz Mart University, Çanakkale, Turkey
[2] Department of Public Health, Faculty of Medicine, Canakkale Onsekiz Mart University, Çanakkale, Turkey
[3] Department of Cardiology, Eskisehir State Hospital, Eskişehir, Turkey

ORCID ID of the authors
EA: 0000-0002-4478-4324
CB: 0000-0002-5497-2759
ÖÖ: 0000-0003-2176-9073
ÖTY: 0000-0002-6731-4958
FA: 0000-0002-1017-1917
AHA: 0000-0002-3056-9981
BK: 0000-0002-5929-1426
EG: 0000-0002-0513-0870
AD: 0000-0001-6849-8894

Corresponding author / Sorumlu yazar:
Ercan Akşit
Address / Adres: Çanakkale Onsekiz Mart Üniversitesi, Kardioloji Departmanı, Kepez, Çanakkale, Türkiye
E-mail: ercanaksit@hotmail.com

Ethics Committee Approval: Ethical approval was obtained from the Canakkale Onsekiz Mart University Ethics Committee of Clinical Investigations on 27.09.2017 with the decision number of 2011-KAEK-27 / 2017-97682.
Etik Kurul Onayı: Etik onay, Çanakkale Onsekiz Mart Üniversitesi Klinik Araştırmalar Etik Kurulu'ndan 27.09.2017 tarihinde 2011-KAEK-27 / 2017-97682 sayılı kararla alındı.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 21.06.2018
Accepted / Kabul Tarihi: 11.07.2018
Published / Yayın Tarihi: 19.07.2018

Abstract

Aim: Health warning labels (HWLs) on cigarette packages, which describe the health problems that may be caused by smoking, have been used struggle against smoking for many years. There are no studies in Turkey that investigate how HWLs used abroad have an impact on the population, and especially on patients who apply to cardiology clinic. In this study, we investigated the effect of HWLs on patients who apply to cardiology clinic and compared the HWLs used in our country with those used abroad which we considered to be harsh and striking.

Methods: In this descriptive study, a questionnaire consisting of 45 questions was administered to 239 patients who applied to cardiology clinic. 14 different visuals used in our country and 9 different visuals used in foreign countries were compared.

Results: In our study, 28.9% of the participants who applied to cardiology clinic have never smoked, 36.0% of them still smoked and 35.1% of them were ex-smokers. 57.7% of the survey participants stated that the HWLs on cigarette packages were effective and 90.8% of the participants stated that warnings in foreign countries were more effective than the ones in Turkey.

Conclusion: This study shows that even among patients who apply to cardiology clinic, smoking is still common. When compared to the HWLs used in our country, the ones used abroad were found to be more effective by the majority of the participants. The use of harsher and more striking HWLs seem to be more effective to struggle against smoking.

Keywords: Health warning labels, Cigarette smoking

Öz

Amaç: Sigara kullanıcılarına, sigara tüketimine bağlı oluşabilecek sağlık sorunlarını anlatmaları bakımından sigara kutusu üzerindeki sağlık uyarı etiketleri (SUE) sigara kullanımı ile mücadelede yıllardır kullanılan bir yöntemdir. Ülkemizde yurt dışında kullanılan SUE'lerin toplum ve özellikle kardiyoloji polikliniğine başvuran hastalar üzerinde nasıl bir etki yaptığını araştıran çalışma yoktur. Biz bu çalışmada SUE'lerinin kardiyoloji polikliniğine başvuran hastalar üzerindeki etkisini araştırdık ve ülkemizde kullanılan SUE'ler ile yurt dışında kullanılan daha sert ve çarpıcı olduğunu düşündüğümüz SUE'leri karşılaştırdık.

Yöntemler: Tanımlayıcı tipte olan bu araştırmamızda kardiyoloji polikliniğine başvuran 239 hastaya 45 soruyu içeren bir anket uyguladı. Ülkemizdeki kullanılan 14 farklı görsel, yabancı ülkelere kullanılan 9 faklı görsel ile karşılaştırıldı.

Bulgular: Yaptığımız çalışmada kardiyoloji polikliniğine başvuran hastaların %28.9'nun hiç sigara kullanmadığı görülürken, %36.0'sı halen sigara kullanmakta olup, %35.1'i daha önce kullanıp bırakmıştır. Araştırmaya katılanların %57,7'si sigaralar üzerindeki görselleri sigarayı önleyici olarak etkili bulduğunu ve %90,8'i yabancı ülkelerde kullanılan görselleri, Türkiye'deki görsellerden daha etkili bulduğunu belirtti.

Sonuç: Bu çalışma göstermektedir ki kardiyoloji polikliniğine başvuran hastalar arasında bile halen sigara kullanımı yaygındır. Ülkemizde kullanılan SUE'ler ile karşılaştırıldığında yurt dışında kullanılan görselleri, katılımcıların büyük çoğunluğu daha etkili bulmuştur. Daha sert ve çarpıcı SUE'lerin kullanılmasının sigaraya karşı mücadelede daha etkili olabileceği gözükmektedir.

Anahtar kelimeler: Sağlık uyarı etiketleri, Sigara içmek

How to cite / Atıf için: Akşit E, Bakar C, Özerdoğan Ö, Yıldırım ÖT, Aydın F, Aydın AH, Kırılmaz B, Gazi E, Duygu A. The effects of health warning labels on cigarette packages on patients who apply to cardiology clinic. J Surg Med. 2018;2(3):303-309.

Introduction

Cigarettes and tobacco products are the major preventable cause of death and diseases worldwide [1]. According to the World Health Organization Report, about six million people die due to smoking and cigarette-related illnesses, and it is estimated that this number will be 8 billion by 2030 [2]. In Turkey, approximately 16 million people are smokers, and cigarette use frequency of those over the age of 15 is 31.2% [3]. The National Burden of Disease and Cost-effectiveness Study, Burden of Disease Report published in 2004 in Turkey shows that 54,699 of the 430,459 deaths that took place in the year 2000 could have been prevented by the cessation of smoking [4].

In order to prevent smoking, various health policies are implemented in many countries. In 2003, the World Health Organization adopted the Framework Convention on Tobacco Control, which aims to fight against tobacco use and control the tobacco market. Turkey signed the convention in 2004 and this agreement has been valid in our country since then. With this agreement, implementations such as the increase of cigarette taxes, smoke free airspace, and support for the provision of smoking cessation have initiated. HWLs have started to be used on cigarette packages with the same agreement [5]. Making attractive cigarette packages is one of the methods used to increase tobacco sales [6]. This method can also be used to make cigarette smoking unattractive and teach every part of the society about its harms [7]. A pack-a-day smoker sees a cigarette package 7300 times a day so; the HWLs put on the packages are more effective and cheaper than the news, ads and anti-smoking campaigns [8]. In Turkey, 'Procedures and Principles Regarding Protection from Harms of Tobacco Products by Production Methods, Labeling and Evaluation' has been valid since 2005 [9]. According to this regulation, 14 different written health warnings were printed on cigarette packages. In 2010, both pictorial and written health warnings have started to be printed on the cover of cigarette packages [10].

Health warnings on cigarette packages can be classified as gain-framed and loss-framed warning labels. Gain-framed messages emphasize the positive consequences of quitting smoking, while loss-framed messages emphasize the negative consequences of smoking. Studies indicate that health messages with loss-framed warnings increase the effectiveness of the messages [11-13].

Observations we made in smoking patients suggest that the effects of the HWLs used in our country are less effective when compared to images and texts used in foreign countries. The short-term objective of this study is to compare the efficacy of pictorial and written warnings on cigarette packages currently used in Turkey to the warnings used in foreign countries. The long-term objective is to ensure the use of the most effective cigarette package warning styles which can help us in the active struggle against smoking in our country by triggering our people to quit smoking.

Materials and methods

Study population

This descriptive study was performed in the the Çanakkale Onsekiz Mart University cardiology outpatient clinic from October to November 2017. The target population was defined as patients aged between 18-80 years who applied to the cardiology outpatient clinic. Determination of the sample size had not been done and volunteers who applied to the cardiology clinic on the specified dates and agreed to participate in the study were included in the study. Even smoking one cigarette a day is known to increase cardiovascular risk [14]. For this reason a person who smokes one or more cigarettes per day evaluated as a smoker. Noncooperable patients, patients with speech impairment or unwilling to participate were excluded from study. During the study period, 656 people between 18-80 years of age were admitted to the cardiology outpatient clinic and 239 (36%) of them participated in the study.

Research approach and sources of data

This research was carried out in the cardiology clinic of Çanakkale Onsekiz Mart University Application and Research Hospital. The questionnaire was applied to those who agreed to participate in the survey using face-to-face interview techniques. The data collection phase was carried out by cardiology, public health doctors and intern doctors who were studying at the public health department at that time. Prior to the study, cardiology and public health doctors provided 4 hours of training to intern doctors. The purpose of the education was to teach how to carry out a questionnaire.

The data collection phase was carried out between 26.10.2017 and 11.11.2017 under the supervision of cardiology and public health doctors in a room prepared for interviews in the cardiology clinic. The purpose and method of the study were explained to the volunteer participants by intern doctors. Verbal and written consent was obtained from each participant. Participants in the study were questioned about the efficacy of HWLs used on cigarette packages. The visual expressions related to the cigarette were questioned by showing the participants the pictorial warnings. For this purpose, the images were printed on 70x100 cm colored posters.

A questionnaire form was used for data collection of the study. The questionnaire consists of three parts containing 45 questions, in which socio-demographic characteristics, cigarette use habits and perceptions on HWLs were questioned.

Table 1 presented the meanings of the HWLs used in Turkey and foreign countries. For HWLs in Turkey, 14 HWLs implemented by the Tobacco Labelling Resource Center in 2010 were used. Examples of graphic warning labels from foreign countries were taken from the Tobacco Labelling Resource Center in Hong Kong, Brazil, Venezuela, Uruguay, England, Singapore, Iran, Thailand and New Zealand [15].

Statistical analysis

The data of the study was analyzed with the statistical package program SPSS 20.0. Number, percentage, mean, standard deviation, median, minimum, maximum values were used in the presentation of the data. Analyzes are based on the number of answers given for each question. The chi-square test was used in the analysis of categorical data. The statistical significance level was taken as $p < 0.05$.

Ethical approval

Ethical approval was obtained from the Çanakkale Onsekiz Mart University Ethics Committee of Clinical

Investigations on 27/09/2017 with the decision number of 2011-KAEK-27 / 2017-97682.

Table 1: Health warning labels in Turkey and foreign countries and their meanings

	Health warning labels in Turkey
Figure 1	Smokers die at a young age
Figure 2	Smoking clogs the arteries and causes heart attacks and strokes
Figure 3	Smoking causes fatal lung cancer
Figure 4	Smoking is harmful to the baby while pregnancy
Figure 5	Protect children: Don't let them breathe your smoke
Figure 6	Health care facilities can help you quit smoking
Figure 7	Smoking is highly addictive. do not start
Figure 8	Quitting smoking reduces the risk of fatal heart and lung diseases
Figure 9	Smoking can cause a slow and painful death
Figure 10	Ask for help from your doctor and your nearest health center to quit smoking
Figure 11	Cigarette smoking slows blood flow and causes sexual impotence
Figure 12	Smoking causes premature aging of the skin
Figure 13	Smoking reduces fertility by damaging sperm
Figure 14	Cigarette smoke contains cancer-causing substances such as benzene, nitrosamine, formaldehyde and hydrogen cyanide
	Health warning labels in foreign countries
Figure 15	Smoking kills
Figure 16	Smoking leads to gangrene and limb amputation
Figure 17	Smoking causes mouth and throat cancer
Figure 18	Smoking causes bad oral hygiene and decrease in taste perception
Figure 19	Smoking can cause a slow and painful death
Figure 20	Smoking causes neck cancer
Figure 21	Smoking causes painful skin cancer
Figure 22	Smoking causes head and neck cancer
Figure 23	Smoking causes mouth cancer

Results

The explanations of HWLs in Turkey and foreign countries used in the study were summarized in table 1 and shown in image1 and 2. 60.3% of the participants were male and the mean age was 47.9 ± 17.1 (median: 51, min-max: 18-80 years). 54.4% of the respondents were high school graduates and above. 72.7% of the participants were married and 76% had children. While 28.9% of the participants have never smoked, 36.0% of them still smoked and 35.1% of them were ex-smokers. The mean age at initiation of cigarette smoking for those who were still smokers or ex-smokers was 17.8 ± 4.8 (median: 17, min-max: 5-35 years), and the mean of active smoking period was 23.6 ± 16.1 (median: 20, max: 5-62) years (Table 2).

Table 2: The sociodemographic characteristics of the study group and distribution of smoking status, Çanakkale 2017

Sociodemographic Feature		
Gender	n	%
Male	144	60.3
Female	95	39.7
Total	239	100.0
Education Status		
Primary education and lower	109	45.6
High school and over	130	54.4
Total	239	100.0
Marital Status		
Married	173	72.7
Single / Widowed / Divorced	65	27.3
Total	238	100.0
Income Status		
Low	23	9.7
Average	160	66.9
High	56	23.4
Total	239	100.0
Cigarette or any of tobacco product use		
Still smoking	86	36.0
Ex-smoker	84	35.1
Never smoked	69	28.9
Total	239	100.0

n=Number, %=Percentage

Among the smoking prevention measures, the restriction of smoking in enclosed public spaces, increased cigarette prices, and HWLs were found most important by the study participants. 57.7% of the survey participants stated that the pictorial warnings on cigarette packages were effective and 50.2% stated that written warnings on cigarette packages were effective in the prevention of smoking. 83.4% of the participants indicated that pictorial warnings should be on both sides of the packages and 75.7% of them wanted written warnings to be on both sides of the cigarette packages. 51.2% of the participants stated that pictorial warnings were more important than written warnings. When warnings in other countries were compared to the warnings in Turkey, 90.8% of the participants indicated that warnings in foreign countries were more effective (Table 3).

Table 3: Considerations about graphic warning labels, Çanakkale 2017

Variables	n	%
Do you think pictorial warnings on cigarette pacts are effective to prevent people from smoking? (n=239)		
Yes	138	57.7
No	101	42.3
How do you thing pictorial warnings should be? (n=157)		
On one side of the pack	26	16.6
On both sides of the pack	131	83.4
Do you think written warnings on cigarette pacts are effective to prevent people from smoking? (n=237)		
Yes	119	50.2
No	118	49.8
How do you thing written warnings should be? (n=148)		
On one side of the pack	36	24.3
On both sides of the pack	112	75.7
Which kind of warning is more important to prevent people from smoking: Pictorial or written warnings? (n=203)		
Pictorial warnings are more important	104	51.2
Written warnings are more important	17	8.4
Both are equally important	82	40.4
Evaluate the pictures used in foreign countries. According to those in Turkey, assess how they affect you. (n=239)		
They did not affect	21	8.8
Indifferent	1	0.4
They affected more	217	90.8

n=number, %=Percent

20.9% of the participants in the survey decided not to buy cigarettes when they first noticed the images on the cigarette box, 20% had a memory of deciding not to smoke at that moment due to the visual on the cigarette box, and 14.3% requested a package change due to the visual on the cigarette package. 28.2% of the participants said they pay attention to the visuals and written warnings each time they buy cigarettes, 9.6% said that they had written and visuals on the packages when they started smoking cigarettes, 33.9% of the participants considered quitting smoking, 40.8% reduced or thought about reducing smoking, and 14.0% put the cigarettes in a box without warnings on it since the start of the usage of pictorial warnings. 23.8% declared that there were images they were not familiar with among the warnings used in Turkey. 4.1% stated that visual warnings had affected them to come to the cardiology clinic. 82.3% of the participants thought that the presence of these warnings in cardiology clinics would be effective, and 92.4% thought that the use of multiple pictures with all the images of warnings in cardiology clinics would be more effective (Table 4).

According to the cigarette or any other tobacco product use status, the response of the participants to the warnings on packages in foreign countries was examined. Current smokers were most affected by Figure 20, Figure 22, Figure 19 and Figure 23; ex-smokers were most affected by Figure 19, Figure 22, Figure 20; and non-smokers were most affected by Figure 16, Figure 19, Figure 20, Figure 21 and Figure 22. Results of the other figures are shown in Table 5. When examining the graphics of this data, the efficacy of the HWLs on current smokers is seen in graphic 1 and on ex-smokers is seen in graphic 2. Graphic 3 show that non-smokers were affected by the HWLs more than the other two groups.

Table 4: Effect of the graphic warning labels on cigarette packages on participants, Çanakkale 2017

Variables	n	%
When you first noticed the visuals on the cigarette bow, did you decide not to buy at that moment? (n=129)		
Yes	27	20.9
No	102	79.1
Did you ever decide not to smoke when you see the visual on the cigarette pack at that moment? (n=125)		
Yes	25	20.0
No	100	80.0
Did you ever request a package change due to the visual on the cigarette pack when you bought it? (n=126)		
Yes	18	14.3
No	108	85.7
Do you pay attention to the visuals and written warning each time you buy cigarette? (n=124)		
Yes	35	28.2
No	89	71.8
When you started smoking were there any texts and pictures on the packages? (n=146)		
Yes	14	9.6
No	132	90.4
Since pictorial warnings have been started to be used, did you ever think about quitting smoking? (n=121)		
Yes	41	33.9
No	80	66.1
Since pictorial warnings have been started to be used, did you reduce smoking or think about reducing smoking? (n=120)		
Yes	49	40.8
No	71	59.2
Since pictorial warnings have been started to be used, did you ever put the cigarettes in a box without pictures? (n=121)		
Yes	17	14.0
No	104	86.0
Are there any pictorial warnings you don't know about among these pictures we show? (n=172)		
Yes	41	23.8
No	131	76.2
Do the pictorial warnings have effect on you about coming to the cardiology clinic? (n=219)		
Yes	9	4.1
No	210	95.9
Would these warnings be effective in the cardiology clinic (n=237)		
Yes	195	82.3
No	42	17.7
In the cardiology outpatient clinic. which one would influence you more: one table with only one of these warnings. or a multi-picture table with all the images? (n=211)		
One picture	16	7.6
Multiple pictures	195	92.4

n=Number, %=Percentage

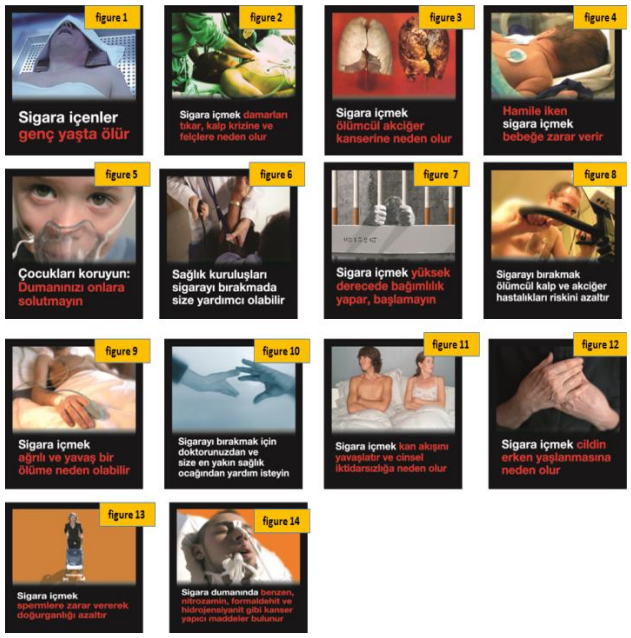


Image 1: Health warning labels in Turkey

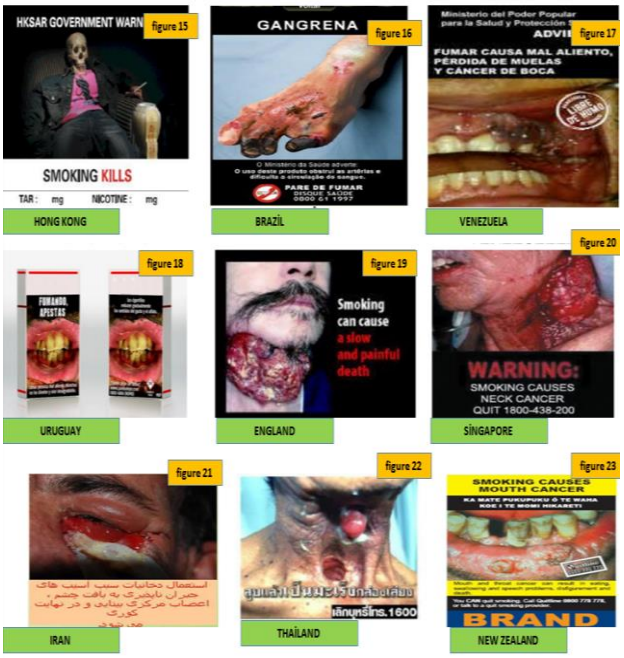
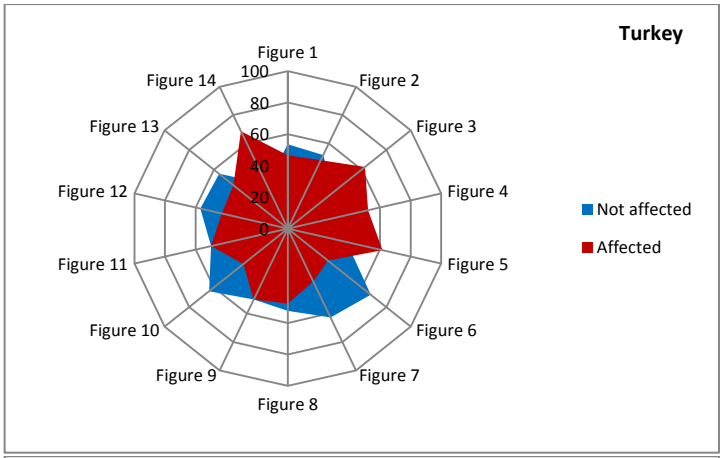


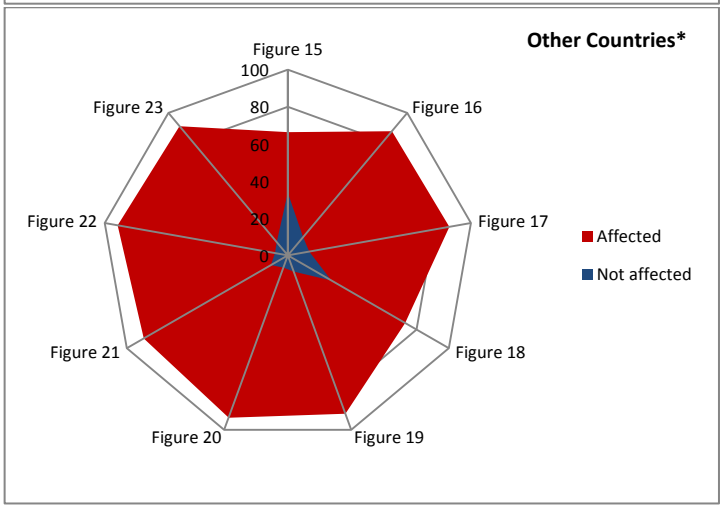
Image 2: Health warning labels in foreign countries

Table 5: According to the cigarette or any tobacco product use status, effects of pictorial warnings in cigarette pacts on participants in Turkey and other countries, Çanakkale 2017

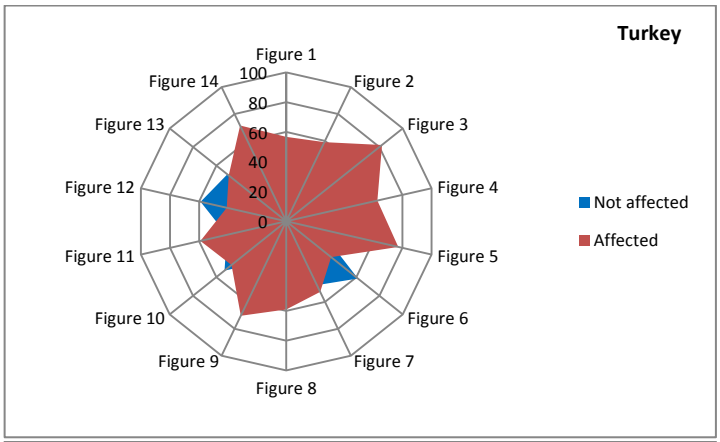
	Current smoker			Ex-smoker			Non-smoker			
Turkey	Not affected n (%)	Indifferent n (%)	Affected n (%)	Not affected n (%)	Indifferent n (%)	Affected n (%)	Not affected n (%)	Indifferent n (%)	Affected n (%)	p
Figure 1	37 (43.0)	9 (10.5)	40 (46.5)	29 (34.9)	7 (8.4)	47 (56.7)	19 (27.5)	12 (17.4)	38 (55.1)	0.178
Figure 2	35 (41.2)	9 (10.6)	41 (48.2)	18 (21.7)	16 (19.3)	49 (59.0)	21 (30.4)	10 (14.5)	38 (55.1)	0.084
Figure 3	20 (23.3)	12 (14.0)	54 (62.7)	6 (7.1)	9 (10.7)	69 (82.2)	6 (8.7)	11 (15.9)	52 (75.4)	0.012
Figure 4	24 (27.9)	17 (19.8)	45 (52.3)	21 (25.3)	10 (12.0)	52 (62.7)	12 (17.4)	9 (13.0)	48 (69.6)	0.220
Figure 5	18 (20.9)	15 (17.4)	53 (61.7)	16 (19.3)	3 (3.6)	64 (77.1)	9 (13.0)	14 (20.3)	46 (66.7)	0.015
Figure 6	43 (50.0)	15 (17.4)	28 (32.6)	36 (43.4)	15 (18.1)	32 (38.5)	28 (40.6)	12 (17.4)	29 (42.0)	0.772
Figure 7	39 (45.3)	15 (17.4)	32 (37.3)	32 (39.0)	7 (8.5)	43 (52.5)	30 (43.5)	11 (15.9)	28 (40.6)	0.239
Figure 8	37 (43.0)	8 (9.3)	41 (47.7)	24 (28.9)	10 (12.0)	49 (59.1)	18 (26.5)	12 (17.6)	38 (55.9)	0.132
Figure 9	34 (39.5)	9 (10.5)	43 (50.0)	17 (20.2)	8 (9.5)	59 (70.3)	25 (36.2)	10 (14.5)	34 (49.3)	0.032
Figure 10	48 (55.8)	7 (8.1)	31 (36.1)	35 (42.2)	9 (10.8)	39 (47.0)	36 (52.2)	8 (11.6)	25 (36.2)	0.435
Figure 11	33 (38.4)	10 (11.6)	43 (50.0)	27 (32.5)	7 (8.4)	49 (59.1)	24 (34.8)	11 (15.9)	34 (49.3)	0.538
Figure 12	38 (44.2)	11 (12.8)	37 (43.0)	36 (43.3)	13 (15.7)	34 (41.0)	28 (40.6)	9 (13.0)	32 (46.4)	0.954
Figure 13	38 (44.2)	10 (11.6)	38 (44.2)	30 (36.1)	12 (14.5)	41 (49.4)	26 (37.7)	11 (15.9)	32 (46.4)	0.815
Figure 14	19 (22.1)	8 (9.3)	59 (68.6)	13 (15.5)	11 (13.1)	60 (71.4)	9 (13.0)	12 (17.4)	48 (69.6)	0.403
Other Countries										
Figure 15	22 (25.6)	7 (8.1)	57 (66.3)	15 (18.3)	7 (8.5)	60 (73.2)	18 (26.1)	4 (5.8)	47 (68.1)	0.729
Figure 16	7 (8.1)	4 (4.7)	75 (87.2)	5 (6.0)	5 (6.0)	73 (88.0)	3 (4.3)	0 (0.0)	66 (95.7)	0.109
Figure 17	9 (10.5)	1 (1.2)	76 (88.3)	7 (8.5)	6 (7.4)	69 (84.1)	3 (4.3)	4 (5.8)	62 (89.9)	0.156
Figure 18	17 (20.0)	6 (7.1)	62 (72.9)	13 (15.9)	9 (11.0)	60 (73.1)	9 (13.0)	8 (11.6)	52 (75.4)	0.702
Figure 19	5 (5.8)	3 (3.5)	78 (90.7)	5 (6.0)	1 (1.1)	78 (92.9)	3 (4.3)	2 (2.9)	64 (92.8)	0.860
Figure 20	6 (7.0)	0 (0.0)	80 (93.0)	8 (9.6)	0 (0.0)	75 (90.4)	3 (4.3)	2 (2.9)	64 (92.8)	0.163
Figure 21	8 (9.3)	1 (1.2)	77 (89.5)	10 (12.2)	3 (3.7)	69 (84.1)	4 (5.8)	1 (1.4)	64 (92.8)	0.491
Figure 22	6 (7.0)	0 (0.0)	80 (93.0)	5 (6.0)	2 (2.4)	77 (91.6)	2 (2.9)	3 (4.3)	64 (92.8)	0.179
Figure 23	6 (7.0)	2 (2.3)	78 (90.7)	7 (8.4)	5 (6.0)	71 (85.6)	3 (4.3)	4 (5.8)	62 (89.9)	0.581

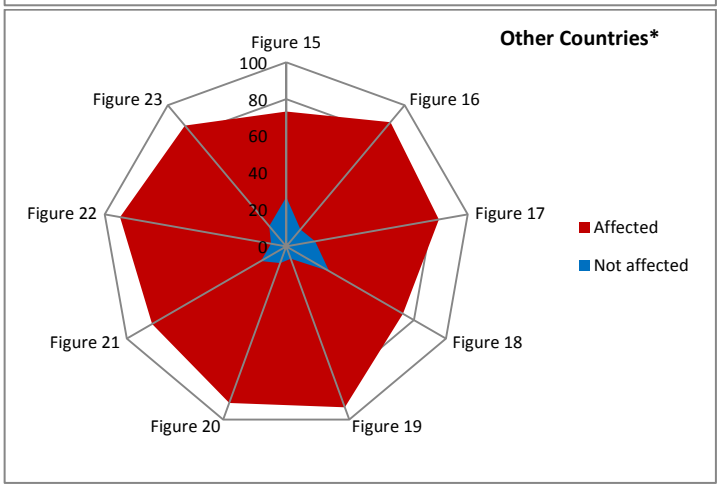
n=Number, %=Percentage, p: Chi-square test, *: Other Countries: Hong Kong, Brazil, Venezuela, Uruguay, United Kingdom, Singapore, Iran, Thailand and New Zealand



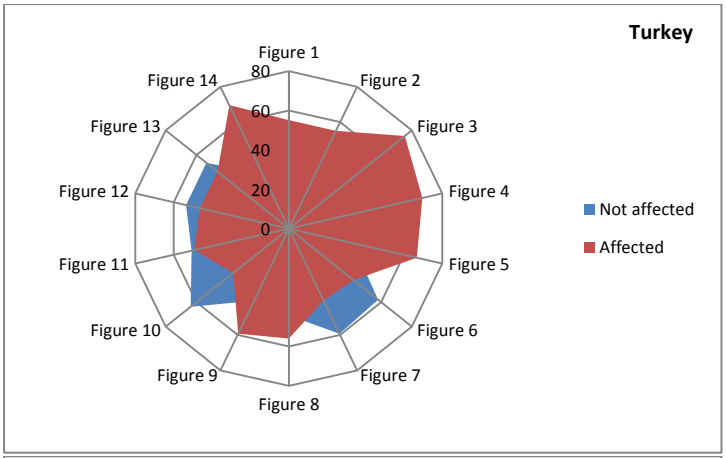


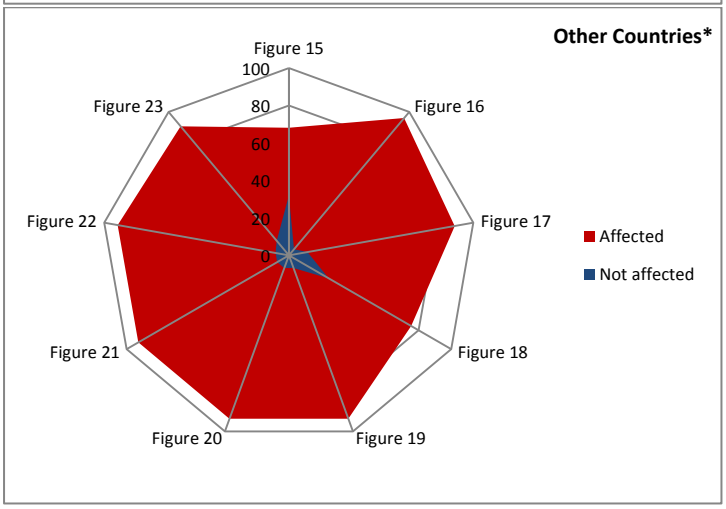
Graphic 1: Status of affection to the health warning labels of current smokers, Çanakkale 2017
*Other Countries: Hong Kong, Brazil, Venezuela, Uruguay, United Kingdom, Singapore, Iran, Thailand and New Zealand





Graphic 2: Status of affection to the health warning labels of ex-smokers, Çanakkale 2017
*Other Countries: Hong Kong, Brazil, Venezuela, Uruguay, United Kingdom, Singapore, Iran, Thailand and New Zealand





Graphic 3: Status of affection to the health warning labels of non-smokers, Çanakkale 2017
*Other Countries: Hong Kong, Brazil, Venezuela, Uruguay, United Kingdom, Singapore, Iran, Thailand and New Zealand

Discussion

The use of health-related texts and images on cigarette packages is one of the most important struggle tools against smoking in the world. In our country, 14 images determined by the Tobacco Products Market Regulation Board are still in use. However, for the same purpose around the world, many different images are used which we think are harsher and more striking. This is the first study to compare the HWLs used in our country to the HWLs with various, more striking images used abroad. This study is also the first study to evaluate the effects of HWLs on cardiology patients.

Smoking is a very important public health problem in all countries. In 2012, 56 million deaths occurred. Of these deaths, 38 million were caused by cardiovascular diseases, cancer, and chronic airway diseases. Smoking is considered to be one of the major and the most important preventable risk factor causing these diseases [16]. Considering that cardiovascular diseases are the most common cause of death in the world, struggle against smoking is an important area to be emphasized in preventive cardiology practice.

There is a downward trend in tobacco use in Turkey similar to that of the developed countries according to data presented by the Turkish Statistical Institute. However, 30% of the population over the age of 15 continue to use tobacco and tobacco products [2,3]. In our study, the smoking rate of patients who applied to the cardiology outpatient clinic was 36%. The patients continue to smoke even if they have suffered from cardiovascular events and survived. This is a relative indicator of

how strong the addiction is to the cigarettes. That is why HWLs seems to be a good tool for those who have never used cigarettes. In our study, we found that those who did not smoke cigarettes were more affected by the HWLs than those who were ex-smokers and those who continue to smoke.

At first glance, HWLs on cigarette packages seem to be insignificant; however, a study conducted in Korea in 2017 showed the situation is quite the opposite. This study showed that HWLs reduce smoking in men by 4.79% and women by 0.66%. As a result of this effect, it is estimated that within ten years a reduction in the incidence of 85238 diabetes mellitus, 67948 chronic obstructive pulmonary diseases, 31526 ischemic heart diseases, 21036 lung cancers, and 3972 oral cancer cases is expected [17]. In our study, 33.9% of the participants stated that they considered quitting smoking, and 40.8% of them reduced or considered reducing smoking since the start of the usage of HWLs.

It has been shown in previous studies that after a certain period of time, the HWLs on cigarette packages are ignored or not noticed by smokers [18,19]. In a study conducted by Ratneswaran et al. [20] in 2014 on smoking and non-smoking groups with chronic obstructive pulmonary disease, HWLs were found to be very effective on non-smokers, while smokers showed negligence and insensitivity to HWLs. Ratneswaran et al. [21] carried out a study in which they compared the effects of HWLs in London and Singapore and this study showed that HWLs were perceived differently among different cultures, and in both cities after a period of time, HWLs lost their influence on people. It is known that HWLs lose their initial effect on people after a while, however the duration is unclear. White et al. [22] found that this effect decreases after 5 years for adolescents. Similar studies have shown that this period changes in different cultures; however it is about 3 years [23,24]. It is known that exposure to new messages is more effective than previous known messages [25,26]. Strahan et al. [27] emphasized the importance of alternating the use of stimuli and changing the stimuli to avoid them from getting accustomed to. There are 14 HWLs on cigarette packages in our country since 2010 and they have never been updated to this date [10]. As a matter of fact, according to our study, 42.3% of participants did not find HWLs in our country effective in the prevention of smoking. This may be the result of the fact that the HWLs have not been changed in our country for seven years and the participants may have gotten used to the stimuli and become indifferent to them. In fact, the health effects of smoking are known by many segments of society; however this does not have much effect on smoking status. It is the development of the positive attitude that needs to be improved here. However, the development of attitude is the most difficult process. For this purpose, it is necessary to tackle every area. HWLs are one of these areas. However, it is evident that there is a need to constantly keep an eye on them. Otherwise, the HWLs are gotten used to and ignored by smokers, especially after a while.

Many diseases which are caused by smoking and which negatively affect many systems and organs are not known by smokers. A study involving 21 European countries showed a significant difference in the awareness of cardiac disease due to cigarette smoking [28]. Ratneswaran et al. [20] showed that Singaporeans have less awareness of oral laryngeal cancer, heart disease, and lung cancer than Londoners do. The ‘Smoking causes lung cancer’ warning was removed from the warnings used in Singapore in 2005; however it started to be used again in 2013. Also, one of the lesser known facts about smoking is that it causes blindness [29]. In 2012, the European Commission issued a new warning: ‘Smoking causes blindness'. In our study, 23.8% of the participants stated that there were HWLs they were not familiar with among the warnings used in Turkey.

4.1% of participants stated that HWLs had influenced them to come to the cardiology clinic. 82.3% of the participants thought that the presence of these warnings in the cardiology clinics would be effective and 92.4% thought that the use of multiple pictures with all the images of warnings in cardiology clinics would be more effective.

This is the first study that compares HWLs in our country and foreign countries, and the result of this study is that 90.8% of participants found the HWLs in other countries more effective. We can say this result may have emerged due to the fact that the HWLs we have shown as examples of those used in foreign countries are more striking and shocking, and that the HWLs used in our country are less harsh than those used abroad, and people have gotten used to the HWLs in our country because the same images have been being used for seven years. The study was conducted on a limited number of patients who applied only to the cardiology clinic without spreading to the community base. It is very important to reach young people for struggle against smoking. We performed this study on patients who applied to our cardiology clinic. Thus, the number of young patients in our study population was low. The number of patients who came to the cardiology clinic was low and the average age was too high. For this reason determination of the sample size could not be done.

For the struggle against smoking, the base of the society should be reached and the views of people from all ages and all walks of life should be examined regarding the harsher and more striking HWLs used in foreign countries. Given that cardiovascular diseases are the major cause of mortality in the world and smoking is one of the major risk factor for cardiovascular diseases, struggle against smoking is an important field for preventive cardiology. In the light of our study and other studies, it seems that replacing the HWLs used on cigarette packages in our country with the harsher visuals applied in other countries and renewing them periodically may be an effective method in the struggle against smoking.

Acknowledgements

We would like to thank Dr. Buse Yüksel, Int. Dr. Safa Kursun, Int. Dr. Özgür Çatalkılıç, Int. Dr.Esra Bedir, Int. Dr. Şahin Kaya, Int. Dr. Beyzanur Bulan, Int. Dr. Elif Eren Aksoy, Int. Dr. Pelin Cihan, Int. Dr. Tuğba Üst for contribution the data collection process.

References

1. Warren CW, Jones NR, Peruga A, Chauvin J, Baptiste JP, Costa de Silva V, et al. Global youth tobacco surveillance, 2000-2007. MMWR Surveill Summ. 2008;57:1-28.
2. World Health Organization Geneva: WHO report on the Global Tobacco Epidemic, the MPOWER package. (ISBN 978 92 4 159628 2) 2008 Jun (cited 2017 December 2): 1(1): (24 screens) Available from URL: http://apps.who.int/iris/bitstream/10665/43818/1/9789241596282_eng.pdf.

3. Public Health Institution of Turkey. Global Adult Tobacco Survey Turkey 2012. (ISBN 978-975-590-502-0) 2012 Dec (cited 2017 July 21): 1(1): (29 screens) Available from URL: http://www.halksagligiens.hacettepe.edu.tr/english/GATS_english.pdf.
4. TC. Ministry of Health, Refik Saydam Hıfzıssıhha Center Presidency Hıfzıssıhha School Directorate, Başkent University. National Burden of Disease and Cost Effectiveness Project. Disease Burden Final Report. Ankara, 2004 Dec (cited 2017 March 5): 1(1): (207 screens). Available from: URL: http://www.toraks.org.tr/userfiles/file/ulusal_hastalik_yuku_hastalikyukuTR.pdf.
5. Ergüder T. Framework Convention on Tobacco Control, Global Action for Global Health (The WHO Framework Convention on Tobacco Control). Ankara, (ISBN:978-975-590-247-0) 2008 Feb (cited 2017 July 5): 1(1): (9 screens). Available from: URL: https://sbu.saglik.gov.tr/Ekutuphane/kitaplar/t20.pdf.
6. Moodie C, Hastings G. Tobacco packaging as promotion. Tobacco Control. 2010;19:168–70.
7. Centers for Disease Control and Prevention. Cigarette package health warnings and interest in quitting smoking - 14 countries, 2008–2010.MMWR Morbidity & Mortality Weekly Report. 2011;60(20):645–51.
8. Durkin S, Brennan E, Wakefield MA. Mass media campaigns to promote smoking cessation among adults: An integrative review. Tobacco Control. 2012;21:127–38.
9. T. C. Official Newspaper. Regulation on Procedures and Principles for Production Shape, Labeling and Inspection for the Protection of Tobacco Products from Harms. Jan 6, 2005. Available from: URL: http://www.resmigazete.gov.tr/eskiler/2005/01/20050106-14.htm.
10. T. C. Official Newspaper. Regulation on Procedures and Principles for Production Shape, Labeling and Inspection for the Protection of Tobacco Products from Harms. Feb 27, 2010 Available from: URL: http://www.resmigazete.gov.tr/eskiler/2010/02/20100227-8.htm.
11. Bansal Travers M, Hammond D, Smith P, Cummings KM. The impact of cigarette pack design, descriptors, and warning labels on risk perception in the US. Am J Prev Med. 2011;40(6):674-82.
12. Zhao X, Nan X, Yang B, Iles IA. Cigarette warning labels: graphics, framing, and identity. Health Education. 2014;114(2):101-17.
13. Goodall C, Appiah O. Adolescents' perceptions of Canadian cigarette package warning labels: investigating the effects of message framing. Health Commun. 2008;23(2):117-27.
14. Inoue-Choi M, Hartge P, Liao LM, Hartge P, Caporaso N, Freedman ND. Association between long-term low-intensity cigarette smoking and incidence of smoking-related cancer in the national institutes of health-AARP cohort. Int J Cancer. 2018;142:271.
15. Tobacco Labelling Research Center. Available from: URL: http://www.tobaccolabels.ca/healthwarningimages/.
16. World Health Organization. Global Status Report on Noncommunicable Diseases. WHO (ISBN 978 92 4 156485 4 2014) 2014 Jun (cited 2017 June 1): 1(1): (232 screens). Available from: URL: http://apps.who.int/iris/bitstream/10665/148114/1/9789241564854_eng.pdf?ua=1.
17. Kang E. Assessing Health Impacts of Pictorial Health Warning Labels on Cigarette Packs in Korea Using DYNAMO-HIA. J Prev Med Public Health. 2017;50:251-61.
18. Strahan EJ, White K, Fong GT, Fabrigar LR, Zanna MP, Cameron R. Enhancing the effectiveness of tobacco package warning labels: a social psychological perspective. Tob Control. 2002;11:183-90.
19. Environics Research Group. Wave 9 Surveys. The Health Effects of Tobacco and Health Warning Messages on Cigarette Packages: Survey of Adults and Adults Smokers. Toronto, Environics Research Group Limited, 2005 (cited 2017 June 10): 1(1): (29 screens). Available from: URL: http://www.tobaccolabels.ca/wp/wp-content/uploads/2013/12/Canada-2005-The-Health-Effects-of-Tobacco-and-Health-Warning-Messages-on-Cigarette-Packages-A-Survey-of-Adults-and-Adult-Smokers-Government-report.pdf.
20. Ratneswaran C, Chisnall B, Drakatos P, Sivakumar S, Sivakunar B, Barrecheguren M, et al. A cross-sectional survey investigating the desensitization of graphic health warning labels and their impact on smokers, non-smokers and patients with COPD in a London cohort. BMJ Open. 2014;4:e004782.
21. Ratneswaran C, Chisnall B, Li M, Tan S, Douiri A, Anantham D, et al. Desensitization to cigarette package graphic health warnings: a cohort comparison between London and Singapore. BMJ Open. 2016;6:e012693.
22. White V, Bariola E, Faulkner A, Coomber K, Wakefield M. Graphic health warnings on cigarette packs: how long before the effects on adolescents wear out? Nicotine Tob Res. 2015;17:776–83.
23. Borland R, Wilson N, Fong GT, Hammond D, Cummings KM, Yong HH, et al. Impact of graphic and text warnings on cigarette packs: findings from four countries over five years. Tob Control. 2009;18:358–64.
24. Hammond D, Fong GT, Borland R, Cummings KM, McNeill A, Driezen P. Text and graphic warnings on cigarette packages: findings from the international tobacco control four country study. Am J Prev Med. 2007;32:202–9.
25. Tversky A, Kahneman D. Availability: a heuristic for judging frequency and probability. Cogn Psychol. 1973;5:207–32.
26. Wyer RS Jr, Hartwick J. The role of information retrieval and conditional inference processes in belief formation and change. Adv Exp Soc Psychol. 1980;13:241–84.
27. Strahan EJ, White K, Fong GT, Fabrigar LR, Zanna MP, Cameron R. Enhancing the effectiveness of tobacco package warning labels: a social psychological perspective. Tob Control. 2002;11:183-90.
28. Steptoe A, Wardle J, Smith H, Kopp M, Skrabski A, Vinck J, et al. Tobacco smoking in young adults from 21 European countries: Association with attitudes and risk awareness. Addiction. 1995;90:571–82.
29. Bidwell G, Sahu A, Edwards R, Harrison RA, Thornton J, Kelly SP. Perceptions of blindness related to smoking: a hospital-based cross-sectional study. Eye. 2005;19:945–8.

J Surg Med. 2018;2(3):310-314.
DOI: 10.28982/josam.436032

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

The effect of CPAP during preoxygenation and PEEP during induction upon the duration of non-hypoxic apnea and hemodynamic parameters

Genel anestezi sırasında preoksijenizasyonda CPAP uygulaması ile indüksiyonda PEEP uygulamasının non-hipoksik apne süresine ve hemodinamik parametrelere etkisi

Havva Esra Uyar Türkyılmaz [1], Asutay Göktuğ [2], Selçuk Tur [3], Hülya Başar [2]

[1] University of Health Sciences, Ankara Zekai Tahir Burak Women's Health, Health Application and Research Center, Department of Anesthesiology and Reanimation, Ankara, Turkey
[2] University of Health Sciences, Ankara Health Application and Research Center, Department of Anesthesiology and Reanimation, Ankara, Turkey
[3] Antalya Kepez State Hospital, Department of Anesthesiology and Reanimation, Antalya, Turkey

ORCID ID of the authors
HEUT: 0000-0002-5717-3610
AG: 0000-0003-0156-0678
ST: 0000-0001-8443-6124
HB: 0000-0003-2061-5056

Corresponding author / Sorumlu yazar:
Esra Uyar Türkyılmaz
Address / Adres: Sağlık Bilimleri Üniversitesi, Zekai Tahir Burak Kadın Sağlığı, Sağlık Uygulama ve Araştırma Merkezi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Ankara, Türkiye
E-mail: esrauyarturkyilmaz@yahoo.com

Ethics Committee Approval: Approval for the study was granted by the Local Ethics Committee (Ankara Training and Research Hospital, Ethics Committee, Decision No: 0208/1408).
Etik Kurul Onayı: Çalışmanın onayı Yerel Etik Kurul tarafından verildi (Ankara Eğitim ve Araştırma Hastanesi Etik Kurulu, Karar No: 0208/1408).

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 24.06.2018
Accepted / Kabul Tarihi: 06.07.2018
Published / Yayın Tarihi: 19.07.2018

Abstract

Aim: This study evaluated the effects of applying CPAP during preoxygenation and PEEP during mask ventilation upon the duration of non-hypoxic apnea and hemodynamic parameters.

Methods: This prospective randomized study included 100 patients allocated to 4 groups. In Groups I and III, preoxygenation was applied with CPAP mask without any pressure and during induction ventilation was performed with volume-controlled ventilation (CMV) in Group I and CMV + 6 cm H2O PEEP in Group III. In Groups II and IV, preoxygenation was applied with CPAP mask with 6 cmH2O pressure and during induction; ventilation was performed with CMV in Group II and CMV + 6 cm H2O PEEP in Group IV. After tracheal intubation, the tube was left open to air and the patient remained apneic until SpO2 reached 90%.

Results: The time for SpO2 to reach 90% is significantly longer in Group IV compared to the other groups. The durations were 412.50±97.37 sec in Group I, 443.52±88.84 sec in Group II, 415.20±117.45 sec in Group III and 522.92±83.44 sec in Group IV. Using only CPAP during preoxygenation and only PEEP during mask ventilation had no significant effect on duration of non-hypoxic apnea.

Conclusion: Especially for patients with difficult intubation, application of CPAP during preoxygenation followed with PEEP during mask ventilation safe, simple and it prolongs non-hypoxic apnea period.

Keywords: CPAP, Non-hypoxic apnea, PEEP, Preoxygenation

Öz

Amaç: Bu çalışmada preoksijenizasyonda CPAP ve maske ile ventilasyon sırasında PEEP uygulamanın non-hipoksik apne süresine ve hemodinamik parametrelere etkisi incelenmiştir. Yöntemler: Prospektif randomize çalışmada 100 hasta 4 gruba ayrılmıştır. Grup I ve III'te preoksijenizasyon CPAP maskesiyle uygulanmış ama hastalara basınç uygulanmamış ve indüksiyon sırasında Grup I'de hacim kontrollü ventilasyon (CMV), Grup III'te ise CMV+6 cmH2O PEEP uygulanmıştır. Grup II ve IV'te ise preoksijenizasyonda CPAP maskesi ile 6 cmH2O basınç uygulanmış; indüksiyon sırasında Grup II'de CMV ile ventilasyon sağlanmış, Grup IV'te ise CMV+6 cmH2O PEEP uyfulanmıştır. Trakeal entübasyondan sonra, tüp havaya açılmış ve hasta spO2 değeri %90'a düşene kadar apneik bırakılmıştır.

Bulgular: Saturasyonun %90'a düşme süresi Grup IV'te diğer gruplardan anlamlı olarak uzun bulundu. Süreler Grup I'de 412,50±97,37 sn, Grup II'de 443,52±88,84 sn, Grup III'de 415,20±117,45 sn ve Grup IV'de 522,92±83,44 sn şeklinde idi. Tek başına preoksijenizasyonda CPAP veya maske ile ventilasyon sırasında PEEP kullanmanın non-hipoksik apne süresine etkisi olmadığı görüldü.

Sonuç: Özellikle entübasyon güçlüğü düşünülen vakalarda preoksijenizasyon sırasında CPAP ve maske ile ventilasyon sırasında PEEP kullanmak güvenli, basit ve rahat tolere edilen bir yöntemdir ve non-hipoksik apne süresini uzatmaktadır.

Anahtar kelimeler: CPAP, Non-hipoksik apne, PEEP, Preoksijenizasyon

How to cite / Atıf için: Türkyılmaz HEU, Göktuğ A, Tur S, Başar H. The effect of CPAP during preoxygenation and PEEP during induction upon the duration of non-hypoxic apnea and hemodynamic parameters. J Surg Med. 2018;2(3):310-314.

Introduction

Using 100% oxygen during anesthesia induction is important in preventing hypoxia in the intubation period. The oxygen store in the body which is normally 1500 milliliters (mL) can rise to 3700 mL after preoxygenation with 100% oxygen [1]. When 100% oxygen is used in the induction period, the time for SpO2 to decrease to 90% is longer but using 100% oxygen is associated with atelectasis formation [2].

Atelectasis appears within minutes of induction of anesthesia in the lungs of 85–90% of healthy, non-obese patients [3,4]. Clinical studies have indicated that absorption atelectasis plays an important role in the genesis of anesthesia-related atelectasis and preoxygenation with 100% oxygen is the most important determinant in the formation of absorption atelectasis [5,6].

Formation of absorption atelectasis can be prevented by the application of positive end-expiratory pressure (PEEP) during the induction of anesthesia [7,8]. Herriger et al [9] reported that applying continuous positive airway pressure (CPAP) during preoxygenation and positive end-expiratory pressure (PEEP) during induction increases the duration of non-hypoxic apnea. Gender et al [10] had similar results in morbidly obese patients.

The aim of this study is to examine the effects of applying CPAP during preoxygenation and PEEP during mask ventilation upon the duration of non-hypoxic apnea and hemodynamic parameters and consequently to determine which technique is more effective.

Materials and methods

Approval for the study was granted by the Local Ethics Committee (Ankara Training and Research Hospital Ethics Committee, Decision No: 0208/1408). A total of 100 patients, ASA I or II, aged 19-60 years, admitted for elective surgery were enrolled into the prospective randomized study. Exclusion criteria included SpO_2 < 97% breathing room air, body mass index > 30 kg.m-2, smoking history, hospitalization for > 24 hours and all medical conditions that contraindicated even a short desaturation of oxygen or rise in $PaCO_2$ such as coronary artery disease, cerebrovascular disease, intracranial hypertension, epilepsy and severe pulmonary disease. It was also planned to exclude patients who were not intubated at the first attempt. Written informed consent was received from all patients.

The patients were randomly allocated to one of 4 groups using a computer-generated random number sequence. For all groups, without any premedication, anesthesia was induced using thiopenthal 5-7 mg.kg-1; fentanyl 1.5 µgr.kg-1; vecuronium 0.1 mg.kg-1 and maintained using sevoflurane 2% in N_2O_5 0% - O_2 50%.

In Group I, preoxygenation was applied with CPAP mask but without any pressure for 5 minutes and then during induction, ventilation was performed with volume-controlled ventilation (6-8 ml.kg-1). In Group II, preoxygenation was applied with CPAP mask with 6 cmH_2O pressure for 5 minutes and then during induction, ventilation was performed with volume-controlled ventilation (6-8 ml.kg-1). In Group III, preoxygenation was applied with CPAP mask but without any pressure for 5 minutes and then during induction, ventilation was performed with volume-controlled ventilation (6-8 ml.kg-1) + 6 cmH_2O PEEP. In Group IV, preoxygenation was applied with CPAP mask with 6 cmH_2O pressure for 5 minutes and then during induction, ventilation was performed with volume-controlled ventilation (6-8 ml.kg-1) + 6 cmH_2O PEEP.

All the patients were tracheally intubated. Preoxygenation, mask ventilation and tracheal intubation of all the patients were applied by the same investigator who had four years experience in anesthesia. A blinded observer assessed the non-hypoxic apnea period and adverse effects after intubation period. Correct placement of the tracheal tube was confirmed once by auscultation and capnogram after ventilation. The tracheal tube was left open to air at atmospheric pressure and the patient remained apneic until SpO_2 decreased to 90%. The time for SpO2 to decrease to 90% was recorded. Mean arterial pressure (MAP), heart rate (HR) and peripheral oxygen saturation (spO2) was recorded when the patient arrived at the operating table (T1), at the end of preoxygenation (T2), at the end of induction (T3), after intubation (T4) and when SpO_2 was 90% (T5). The hemodynamic side effects (hypotension, hypertension, bradycardia, tachycardia, and other arrhythmias) were recorded and the appropriate treatment was applied. Bradycardia was defined as heart rate <50 beats.min-1, tachycardia as heart rate > 100 beats.min-1, hypotension as a decrease in MAP <70 mmHg or a decrease >20% of baseline MAP, and hypertension as systolic arterial pressure>160 mmHg or diastolic arterial pressure>110 mmHg.

Statistical analysis

All statistical analyses were performed with SPSS 11.0 software (SPSS Inc. Chicago, IL. USA). The sample size of this study was calculated based on the sample size of previous studies, using a significance level of 5% (p=0.05) and power of 97.5%. Continuous values were stated as mean and standard deviation (SD), and categorical values as number and percentage. Normal distribution was determined using the Kolmogorov-Smirnov test for demographic data (age, weight, height and BMI) (mean ± SD). The difference between the groups was analyzed using One Way Variance Analysis (ANOVA). The Bonferroni post Hoc test was used to detect which group was different. As the distribution of the groups was normal, mean arterial pressure, peripheral oxygen saturation and heart rate values between the groups were analyzed with one way variance analysis and the Bonferroni test. Adverse effects were analyzed with the Chi square test. For all countable parameters, the Kolmogorov-Smirnov test was used. For the analysis inside the groups, the Friedman ANOVA test was used for dependent groups. A value of p<0.05 was accepted as statistically significant

Results

The demographic characteristics of the study participants are given in Table 1. There were no significant differences between the groups in respect of age, weight, or BMI (p>0.05). There was a difference between Group II and Group III in height (p=0.035). A patient from Group I was excluded from the study because of severe arrhythmia. All the patients were

intubated at the first attempt so none of the patients was excluded from the study because of intubation difficulties.

There was a statistically significant difference between Group II and IV in respect of mean arterial pressure (MAP) measured when the patient came to the operating room (T1) (p=0.026). There was no statistically significant difference within the groups or between the groups in respect of MAP at other measurement times (Table 2). A statistically significant difference was determined between Groups II and IV in respect of heart rate (HR) at the end of the preoxygenation period (T2) (p=0.012). There was no statistically significant difference within the groups or between the groups in HR at other measurement times (Table 3). At the end of the mask ventilation (T3), the peripheral saturation of oxygen (SpO_2) values of patients in Group I were significantly lower than those of Group III (p=0.038) and Group IV (p=0.038). There was no statically significant difference within the groups or between the groups in SpO_2 at other measurement times (Table 4, p>0.05). The time for SpO_2 to decrease to 90% (non-hypoxic apnea period) was statistically significantly longer in Group IV compared to the other groups. (p=0.001 Groups I-IV; p=0.030 Groups II-IV; p=0.001 Groups III-IV) (Table 5, Figure 1). No statistically significant difference was found between the groups in respect of adverse effects (Table 6). The detected adverse effects were bradycardia, tachycardia, hypotension, hypertension and arrhythmia.

Table 1: The demographic characteristics of the study participants

	Group I	Group II	Group III	Group IV	p
N	24	25	25	25	
Age (year±SD)	34.16±11.19	30.88±11.09	34.96±11.96	33.36±11.59	>0.05
Height(cm±SD)	166.60±9.91	170.36±10.29	162.44±7.14	169.76±11.77	0.035*
Weight(kg±SD)	66.84±9.22	67.64±8.59	63.36±8.65	66.44±11.69	>0.05
BMI(kg.m²±SD)	23.99±2.32	23.26±2.09	23.97±3.07	22.96±3.38	>0.05

Table 2: The changes in mean arterial pressure (MAP) (mmHg±SD)

	Group I	Group II	Group III	Group IV	p
T1	96.64±13.24	91.76±7.93*	94.64±14.02	101.56±11.18*	0.026*
T2	95.88±9.84	93.28±8.51	94.04±12.12	95.96±11.63	>0.05
T3	88.24±11.59	84.24±10.17	83.28±10.95	91.08±15.58	>0.05
T4	110.32±15.50	111.92±9.99	113.48±13.70	117.60±19.92	>0.05
T5	114.33±13.70	111.44±16.38	114.12±20.22	110.44±14.76	>0.05

*p<0.05, T1: when the patient arrived at the operating table, T2: at the end of the preoxygenation period, T3: at the end of mask ventilation, T4: after intubation , T5: when SpO2 was 90%

Table 3: The changes in heart rate (beats.min^{-1}±SD)

	Group I	Group II	Group III	Group IV	p
T1	84.84±17.43	77.08±19.87	82.36±16.87	88.72±17.42	>0.05
T2	84.88±16.01	78.36±17.97*	84.08±15.76	92.56±13.25*	P=0.012*
T3	87.80±11.70	81.52±12.12	88.04±15.10	91.20±16.73	>0.05
T4	97.64±13.41	94.72±9.92	102.48±11.96	98.60±12.85	>0.05
T5	99.83±17.94	91.08±21.21	97.76±20.90	98.64±19.30	>0.05

*p<0.05, T1: when the patient arrived at the operating table, T2: at the end of the preoxygenation period, T3: at the end of mask ventilation, T4: after intubation, T5: when SpO2 was 90%

Table 4: The changes in spO_2 (%±SD)

	Group I	Group II	Group III	Group IV	p
T1	99.16±1.06	98.68±1.06	98.64±1.11	99.24±0.87	>0.05
T2	99.88±0.33	99.24±3.19	99.96±0.20	99.16±3.59	>0.05
T3	99.44±0.50*	99.64±0.49	99.80±0.40*	99.80±0.40*	0.038*
T4	99.92±0.27	100.00±00	99.96±0.20	100.00±00	>0.05
T5	90.00±00	90.00±00	90.00±00	90.00±00	>0.05

*p<0.05, T1: when the patient arrived at the operating table, T2: at the end of the preoxygenation period, T3: at the end of mask ventilation, T4: after intubation , T5: when SpO2 was 90%

Table 5: The time for SpO_2 to decrease to 90% (sec±SD)

	GroupI (n=24)	Group II (n=25)	Group III (n=25)	Group IV (n=25)	p
SpO2 90%	412.50±97.37 *	443.52±88.84 **	415.20±117.45 ***	522.92±83.44	p=0.001* p=0.030** p=0.001***

* p=0.001, Group I-IV; **p=0.030, Group II-IV; ***p=0.001, Group III-IV

Table 6: Adverse effects

	GroupI (+/-) (n=24)	Group II (+/-) (n=25)	Group III (+/-) (n=25)	Group IV (+/-) (n=25)
Tachycardia	5/19	1/24	0/25	2/23
Hypertension	1/23	2/23	3/22	3/22
Hypertension and tachycardia	2/22	3/22	2/23	3/22
Arrhythmia	2/22	2/24	1/24	3/22
Bradycardia	1/23	3/22	1/24	0/25
Hypertension and bradycardia	0/24	0/25	1/24	0/25

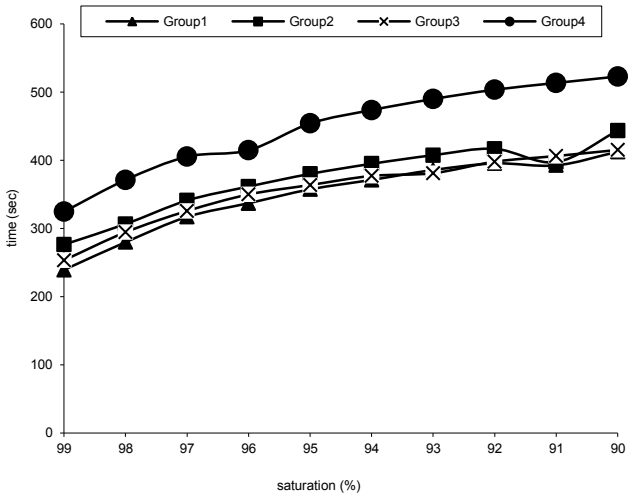


Figure 1: Time to SpO_2 change (p<0.05)

Discussion

During general anesthesia, atelectasis formation with the use of 100% oxygen [11] and thereby an increase in intrapulmonary shunts primarily caused by atelectasis occurs [12]. The formation of atelectasis in patients during general anesthesia was demonstrated on computed tomography imaging in the 1980s [13]. An increase in density in dependent regions of the lungs five minutes after the induction of anesthesia was reported [13]. In animal researches, these densities have been reported as atelectatic lung regions [14].

The most dramatic effect of atelectasis is the impairment of systemic oxygenation [15]. There is a correlation between the impaired gas exchange and atelectasis [11]. A high concentration of inspired oxygen has been found to be related to atelectasis formation. It has been demonstrated that preoxygenation with 100% oxygen is the most important determinant in atelectasis formation [6]. Previous studies have shown that when FiO_2 is decreased or no preoxygenation is performed, atelectasis formation can be minimized [5,16]. In this situation, the safe apnea period shortens. Preoxygenation before anesthesia induction is recommended to increase total body oxygen stores and delay oxyhemoglobin desaturation in the state of apnea [17,18]. In patients at risk of rapid desaturation in particular or in those with no tolerance to a decrease in oxygen content, body oxygen stores must be filled [5,19].

It has been shown that applying CPAP during preoxygenation and PEEP during induction prevents atelectasis formation and improves oxygenation in patients who have been preoxygenated with 100% oxygen [8]. Applying CPAP during preoxygenation and PEEP during mask ventilation has been reported to prolong the duration of non-hypoxic apnea by approximately 2 minutes [9]. Applying 10 cmH_2O CPAP during preoxygenation and 10 cmH_2O PEEP during mask ventilation in

morbidly obese patients has been reported to decrease the amount of atelectasis, improve arterial oxygenation and prolong the duration of the non-hypoxic apnea period [19]. In those studies, CPAP and PEEP were used together and therefore it could not be determined which was effective. In the current study, 4 groups were established to examine which method was more effective on the non-hypoxic apnea period, the application of CPAP during preoxygenation or PEEP during mask ventilation.

The main finding in this study was that using only CPAP during preoxygenation and only PEEP during mask ventilation had no effect on the duration of non-hypoxic apnea, but when CPAP and PEEP were used together, the non-hypoxic apnea period was significantly prolonged.

CPAP causes an increase in thoracic lung volume and functional residual capacity and a decrease in total airway resistance [20], lung compliance [21] and work of breathe [21]. CPAP prevents the collapse of alveoli of borderline stability as the effect is greater in the early period, when the alveoli are already open [22]. Some authors have reported the potential benefits of preoxygenating the patient with CPAP before intubation [23,24]. In contrast, it has been reported that no statistically significant difference was found in the safe apnea period between a group in which CPAP was used in the preoxygenation period and a control group [25]. Using CPAP during the preoxygenation period in morbidly obese patients has been reported to have no effect on the non-hypoxic apnea period. The mechanism of ineffectiveness of CPAP is explained as the regression of FRC to pre-CPAP levels within 1 min once the CPAP mask is removed or an increased activation of expiratory muscles to maintain lung volumes at previous values.

In the current study, no difference was found in the non-hypoxic apnea period between the group to which preoxygenation was administered with CPAP and mask ventilation was applied without PEEP (Group II) and the control group (Group I). This can be explained as the regression of FRC to pre-CPAP levels within 1 min once the CPAP mask was removed and after occurrence of this atelectatic areas as the mask ventilation was applied with 100% oxygen without PEEP.

The application of 10 cmH_2O PEEP has been examined in many studies and has been reported to be successful in re-opening collapsed lung tissue. However, in some patients, small atelectatic areas persist. When PEEP level is increased, shunts do not always decrease and arterial oxygenation is not always improved. It can be explained as the redistribution of blood to the dependent regions of the lung because of the increased intrathoracic pressure. In this case, applying PEEP causes atelectatic lung regions to receive more blood from the pulmonary circulation [27].

To re-open all collapsed lung regions an inflation pressure of 40 cmH_2O must be applied for 15 seconds [28]. This pressure is equal to vital capacity inflation and is therefore called the vital capacity maneuver (VCM). A previous study reported that arterial oxygenation improved in the group to which VCM was applied but showed no difference from the control group of 5cmH_2O PEEP with no VCM [29]. The PEEP applied just after the VCM has been shown to be efficient in the prevention of atelectasis formation despite the use of 100% oxygen [30]. As a result, it has been demonstrated that to correct anesthesia-induced collapse, a pressure higher than the pressure of collapsed alveoli is needed.

In the current study, no difference was found in the non-hypoxic apnea period between the group to which preoxygenation was applied without CPAP and mask ventilation was performed with PEEP (Group III) and the control group (Group I). This situation can be explained by the inadequacy of the level of PEEP applied during the mask ventilation (6 cm H_2O) to re-open the alveoli which had already collapsed during the preoxygenation without CPAP.

When CPAP is applied during the preoxygenation period and PEEP is applied during mask ventilation (Group IV), alveolar collapse is prevented beginning from the preoxygenation period and thus the level of PEEP used in the current study could be enough to keep the alveoli open despite the use of 100% oxygen. In this way the impairment in oxygenation is prevented and the duration of the non-hypoxic apnea period is prolonged.

A potential risk of mechanical ventilation by mask with PEEP is to expose a sedated, paralyzed patient to insufflation of the stomach, thereby, increasing the risk of regurgitation and bronchoaspiration. This risk exists with an insufflation pressure higher than 25 mm Hg. To avoid this complication, the alarm limits of the ventilator are set at 20mmHg, which will prevent the use of higher pressure via the facemask.

Adverse cardiovascular effects have been reported with the use of CPAP and PEEP. In the current study, no significant cardiovascular depressant effects of CPAP were observed in any group in respect of systolic, diastolic and mean arterial pressure. The mean heart rate was lower in Group II compared with Group IV, although in both groups CPAP was used at the end of the pre-oxygenation period. However, the difference was not evaluated as statistically significant. The CPAP mask may not be tolerated by conscious patients but in the current study it was well-tolerated by all patients. No adverse effects or impairment in cognitive functions developed in any patient throughout the follow-up period.

One limitation of the study is the absence of arterial blood gas analysis. Some studies measured paO_2 values of the patients after intubation before lifting the tube at air at atmospheric pressure. In this study paO_2 value at this time was not measured because further focus on the practical result - the safe apnea period is aimed.

The time for SpO_2 to decrease to 90% was statistically significantly longer in the group for which preoxygenation was applied with CPAP and mask ventilation was applied with PEEP. Using only CPAP during preoxygenation and only PEEP during mask ventilation had no significant effect on the duration of non-hypoxic apnea. Therefore, especially for patients with difficult intubation, the application of CPAP during preoxygenation followed by PEEP during mask ventilation is a safe and simple method, which is well accepted by patients.

References

1. Lumb AB. Oxygen. Nunn's Applied Respiratory Physiology Oxford: Butterworth-Heinmann 2000;288-90.

2. Edmark L, Enlund M, Kostova-Aherdan K, Hedenstierna G. Atelectasis formation and apnoea tolerance after pre-oxygenation with 100%, 80%, or 60% oxygen. Anesthesiology. 2001;95:A1330.
3. Lundquist H, Hedenstierna G, Strandberg A, Tokics L, Brismar B. CT-assessment of dependent lung densities in man during general anaesthesia. Acta Radiologica. 1995;36:626–32.
4. Magnusson L, Spahn DR. New concepts of atelectasis during general anaesthesia. British Journal of Anaesthesia. 2003;91:61–72.
5. Rothen HU, Sporre B, Engberg G, Wegenius G, Reber A, Hedenstierna G. Prevention of atelectasis during general anaesthesia. Lancet. 1995;345:1387–91.
6. Joyce CJ, Wıllıams AB. Kinetics of absorption atelectasis during anesthesia: a mathematical model. J Appl Physiol. 1999;86:1116-25.
7. Rusca M, Wicky S, Proietti S. Continuous positive airways pressure prevents atelectasis formation during induction of general anaesthesia. Anesthesiology. 2001;95:AI33I.
8. Rusca M, Proietti S, Schnyder P, Frascarolo P, Hedenstierna G, Spahn DR, Magnusson L. Prevention of atelectasis formation during induction of general anesthesia. Anesthesia & Analgesia. 2003;97:1835–9.
9. Herriger A, Frascarolo Ph, Spahn DR, Magnusson L. The effect of positive airway pressure during pre-oxygenation and induction of anaesthesia upon duration of non-hypoxic apnoea. Anaesthesia. 2004;59:243–47.
10. Gander S, Frascarolo P, Suter M, Spahn D.R, Magnusson L. Positive end-expiratory pressure during induction of general anesthesia increases duration of nonhypoxic apnea in morbidly obese patients. Anesth Analg. 2005;100:580–4
11. Hedenstierna G, Tokics L, Strandberg A, Lundquist H, Brismar B. Correlation of gas exchange impairment to development of atelectasis during anaesthesia and muscle paralysis. Ada Anaesthesiol Scand. 1986;30:183-91.
12. Nunn JF. Factors influencing the arterial oxygen tension during halothane anaesthesia with spontaneous respiration. British Journal of Anaesthesia. 1964;36:327–41.
13. Bendixen HH, Hedley-White J, Laver MB. Impaired oxygenation in surgical patients during general anesthesia with controlled ventilation. A concept of atelectasis. N Engl J Med. 1963;269:991-6
14. Nyman G, Funkquist B, Kvart C, et al. Atelectasis causes gas exchange impairment in the anaesthetised horse. Equine Vet J. 1990;22:317-24.
15. Duggan M, Kavanagh BP. Pulmonary Atelectasis A Pathogenic Perioperative Entity Anesthesiology. 2005;102:838–54.
16. Reber A, Engberg G, Wegenius G, Hedenstierna G. Lung aeration. The effect of pre-oxygenation and hyperoxygenation during total intravenous anaesthesia. Anaesthesia. 1996;51:733-7.
17. Baraka A. Routine preoxygenation. Anesthesia. 2006;61:612-3.
18. Kung MC, Hung CT, Ng KP. Arterial desaturation during induction in healty adults: should preoxygenation be a routine? Anesth Intens Care. 1991;19:192-6.
19. Bell MDD. Routine preoxygenation- a new 'minimum standard of care'. Anaesthesia. 2004;59:943–5.
20. Saunders RA, Milner AD, Hopkins IE. The effects of CPAP on lung mechanics and lung volumes in the neonate. Biol Neonate. 1976;29:178-84.
21. Ahumada CA, Goldsmith JP. Continuous Distending pressure. In: Goldsmith JP, Karotkin EH, editors. Philadelphia: Assisted Ventilation of the Neonate. WB Saunders: p. 151-166.
22. Lawson EE, Birdwell RL, Huang PS. Augmentation of pulmonary surfactant secretion by lung expansion at birth. Pediatr Res. 1979;13:611-4.
23. Benumof J. Preoxygenation: best method for both efficacy and efficiency. Anesthesiology. 1999;9:603–5.
24. Reynolds S, Heffner J. Airway management of the critically ill patient: rapid-sequence intubation. Chest. 2005;127:1397–412.
25. Venkateswaran R, Goneppanavar U, Frenny AP. Preoxygenation with 208 head-up tilt provides longer duration of non-hypoxic apnea than conventional preoxygenationin non-obese healthy adults. J Anesth. 2011;25:189–94.
26. Cressey DM, Berthoud M. C, Reilly CS. Effectiveness of continuous positive airway pressure to enhance pre-oxygenation in morbidly obese women. Anaesthesia. 2001;56:670-89.
27. Xue FS, Huang YG, Tong SY, et al. A comparative study of early postoperative hypoxemia in infants, children, and adults undergoing elective plastic surgery. Anesth Analg. 1996;83:709-15.
28. Rothen HU, Sporre B, Engberg G,Wegenius G, Hedenstierna G. Re-expansion of atelectasis during general anesthesia: A computed tomography study. Br J Anaesth. 1993;71:788-95.
29. Tusman G, Böhm SH, Vazquez de Anda GF, Campo JL, Lachmann B. Alveolar recruitment strategy improves arterial oxygenation during general anesthesia. BJA. 1999;82(1):8-13.
30. Neumann P, Rothen HU, Berglund JE, Valtysson J, Magnusson A, Hedenstıerna G. Positive end-expiratory pressure prevents atelectasis during general anaesthesia even in the presence of a high inspired oxygen concentration. Acta Anaesthesiol Scand. 1999;43:295–301.

J Surg Med. 2018;2(3):315-319.
DOI: 10.28982/josam.421803

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Acute toxicities of three-dimensional conformal radiotherapy in the treatment of gynecological cancer, and retrospective dosimetric comparison of three dimensional conformal radiotherapy and invers intensity-modulated radiotherapy

Jinekolojik kanserlerde retrospektif üç boyutlu konformal radyoterapi ve yoğunluk ayarlı radyoterapinin dozimetrik karşılaştırılması ve üç boyutlu konformal radyoterapinin akut yan etkileri

Halil Sağınç [1], Özgür Yıldırım [2], Bahar Baltalarlı [3]

[1] Department of Radiation Oncology, Denizli State Hospital, Denizli, Turkey
[2] Department of Radiation Oncology, Manisa State Hospital, Manisa, Turkey
[3] Department of Radiation Oncology, School of Medicine, University of Pamukkale, Denizli, Turkey

ORCID ID of the authors
HS: 0000-0002-3269-0267
ÖY: 0000-0003-4547-1669
BB: 0000-0001-5317-3851

Abstract

Aim: The study was designed to compare the critical organ and bone marrow doses with three-dimensional conformal radiotherapy plans and intensity-modulated radiotherapy re-treatment plans and to evaluate acute toxicities of three-dimensional conformal radiotherapy for gynecological cancer.

Methods: Twenty-eight patients who underwent conformal radiotherapy (3D-CRT) were evaluated retrospectively and were re- planned according to IMRT technique. The critical organ and bone marrow doses of patients were compared dosimetrically. Evaluation of early side effects was performed using RTOG toxicity scale and European Organization for Research and Treatment of Cancer (EORTC) QLQ30 side effect evaluation questionnaire.

Results: The assessment of early toxicity revealed Grade 1 lower gastrointestinal (GIS) toxicity in 16 (57.1%) patients, grade 1 upper GIS toxicity in 9 (32.1%) patients, grade 1 hematological toxicity in one (3.6%) patients, grade 1 genitourinary toxicity in 15 (53.6%), grade 1 skin toxicity in (50%) 14 patients . One patient (3.6%) had grade 2 upper GIS toxicity, 11 patients (39.3%) had grade 2-3 hematological toxicity. Bone marrow V20 ($p<0.001$), V95 (%) of bone marrow ($p<0.001$), urinary bladder V40 ($p<0.001$), urinary bladder mean dose ($p<0.001$), rectum V40 ($p<0.001$), rectum mean dose ($p<0.001$), small bowel V40 ($p<0.001$) were received lower doses in the IMRT planning arm than the conformal planning arm.

Conclusion: 3D-CRT is a safe treatment with acceptable low toxicity levels in gynecological cancer patients, and it does not adversely affect quality of life. IMRT reduce dose to the bone marrow and the normal tissues as compared to 3D-CRT.

Keywords: Gynecological cancer, Acute toxicities, Quality of life, Conformal radiotherapy, Intensity modulated radiotherapy

Öz

Amaç: Jinekolojik kanserlerde retrospektif üç boyutlu konformal radyoterapi tedavisine ait akut yan etkileri değerlendirmek ve yoğunluk ayarlı radyoterapinin ve üç boyutlu konformal radyoterapinin kemik iliği ve riskli organların dozimetrik olarak karşılaştırmak amaçlanmıştır.

Yöntemler: Üç boyutlu konformal radyoterapi ile tedavisi tamamlanmış 28 hasta retrospektif olarak değerlendirildi ve hastalar IMRT tekniğine göre yeniden planlandı. Olguların kemik iliği ve kritik organ dozları dozimetrik olarak karşılaştırıldı. Olgularda yan etki değerlendirmesi RTOG toksisite skalası ve yaşam kalitesi Avrupa Kanser Araştırma ve Tedavi Merkezi (EORTC) QLQ30 anketi uygulanarak değerlendirildi.

Bulgular: Akut yan etkiler değerlendirildiğinde grad 1 alt gastrointestinal (GIS) yan etki 16 (% 57,1) olguda, grad 1 üst GIS yan etki 9 (%32,1) olguda, grad 1 hematolojik yan etki 1 (% 3,6) olguda, grad 1 cilt yan etki 14 (% 50) olguda görüldü. Grad 2 üst GIS yan etki 1 (% 3,6) olguda, grad 2-3 hematolojik yan etki 11 (% 39,3) olguda görüldü. Kemik iliği V20 ($p<0,001$), kemik iliği V95 (%) ($p<0,001$) mesane V40 ($p<0,001$), mesane ortalama doz ($p<0,001$), rektum V40 ($p<0,001$), rektum ortalama doz ($p<0,001$), ince barsak V40 ($p<0,001$) yoğunluk ayarlı radyoterapi ile konformal radyoterapiden daha düşük doz aldı.

Sonuç: IMRT reduce dose to the bone marrow and the normal tissues as compared to 3D-CRT. Üç boyutlu radyoterapi jinekolojik kanserlerde düşük yan etki seviyesiyle kabul edilebilir güvenilir bir tedavidir ve yaşam kalitesini olumsuz etkilemez. Yoğunluk ayarlı radyoterapi kemik iliği ve riskli organ dozlarını konformal radyoterapiye göre daha iyi kısıtlar.

Anahtar kelimeler: Jinekolojik kanser, Akut yan etkiler, Yaşam kalitesi, Konformal radyoterapi, Yoğunluk ayarlı radyoterapi

Corresponding author / Sorumlu yazar:
Halil Sağınç
Address / Adres: Denizli Devlet Hastanesi, Radyasyon Onkolojisi Anabilim Dalı, Merkezefendi, Denizli, Türkiye
E-mail: halilsaginc@hotmail.com

Ethics Committee Approval: Ethics committee approval was obtained from Pamukkale University Faculty of Medicine (2013-21).
Etik Kurul Onayı: Çalışma için Pamukkale Üniversitesi Tıp Fakültesinden etik kurul onayı alınmıştır (2013-21).

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 08.05.2018
Accepted / Kabul Tarihi: 16.07.2018
Published / Yayın Tarihi: 20.07.2018

How to cite / Atıf için: Sağınç H, Yıldırım Ö, Baltalarlı B. Acute toxicities of three-dimensional conformal radiotherapy in the treatment of gynecological cancer, and retrospective dosimetric comparison of three dimensional conformal radiotherapy and invers intensity-modulated radiotherapy. J Surg Med. 2018;2(3):315-319.

Introduction

Endometrial cancer is the most common gynecological cancer in the USA and Europe [1,2]. Endometrial cancer is the most common gynecological cancer in developed countries. The number of newly diagnosed cases in Europe was nearly 100,000 in 2012. More than 90% of cases of endometrial cancer occur in women >50 years of age, with a median age at diagnosis of 63 years. Four percent of women with endometrial cancer are younger than 40 years old [3,4]. The majority of endometrial cancers are diagnosed early (80% in stage I), with 5-year survival rates of over 95%. However, 5-year survival rates are much lower if there is regional spread or distant disease 68% and 17%, respectively) [5]. Cervical cancer is the third most common cancer in women. More than 85% of the global burden occurs in developing countries, where it accounts for 13% of all female cancers [6].

The hematopoietic stem cells of the bone marrow are very sensitive to radiation [7]. It is shown that increased dose to the bone marrow and increased volume of the marrow in the field of radiation can proportionately increase the risk of acute hematological toxicities [8]. Addition of chemotherapy along with radiation reduces the tolerance of marrow and increases the acute hematological toxicities. Intensity modulated radiotherapy (IMRT) can give conformal dose distributions while sparing the normal tissues. Hence, it is recommended that sparing bone marrow using IMRT in patients receiving concurrent chemotherapy can reduce the hematological toxicities [9]. The aim of the study was to compare three-dimensional conformal radiotherapy plans and intensity-modulated radiotherapy re-treatment plans in our patients for the normal tissues and to evaluate the treatment-related side effects and the change in quality of life in patients treated with 3D-CRT (three-dimensional conformal radiotherapy) for cervical and endometrial cancer. We created the 3D-CRT plans and IMRT re-treatment plans for our patients who had previously received 3D-CRT, and performed their comparisons dosimetrically.

Materials and methods

Twenty-eight patients who underwent conformal radiotherapy (3D-CRT) were evaluated retrospectively and were re- planned according to IMRT technique by the Department of Radiation Oncology at the University of Pamukkale. Critical organs and bone marrow doses of 28 patients with cervical and endometrial cancer were compared dosimetrically. Evaluation of early side effects was performed using RTOG toxicity scale and European Organization for Research and Treatment of Cancer (EORTC) QLQ30 side effect evaluation questionnaire in patients with cervical and endometrial cancer who had undergone curative pelvic radiotherapy with three-dimensional conformal radiotherapy (3D-CRT) technique.

Details of radiotherapy

All patients underwent aquaplast immobilization in the supine position and contrast-enhanced computed tomography (CT) scan for simulation following a uniform water protocol. Axial CT sections of slice thickness 3-5 mm were taken. The organs at risk (OAR) (urinary bladder, rectum, small bowel, head of femur, and bone marrow) and target volumes were delineated on commercial treatment planning system, Prowess version 4.71. The OARs and the target volumes were delineated based on standard Radiation Therapy Oncology Group guidelines [10,11]. Figure 1 shows the contours of CTV and organs at risk (OARs) in pelvic region on a transverse plane of a typical patient.

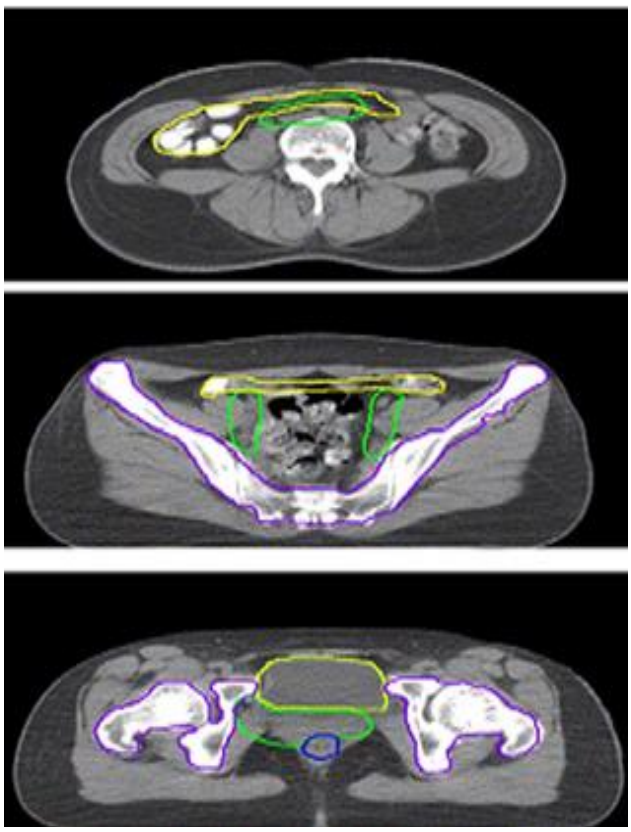


Figure 1: The contour of CTV and organs at risk, including CTV (green), small bowel (yellow), rectum (blue), bladder (yellowish green), pelvic bone marrow (violet)

IMRT plans were made to examine the patient planning system's ability to better cover the target volume and to provide less normal tissue toxicity with IMRT planning. To ensure homogeneity of the comparison, IMRT plans were reconstructed with critical structures and critical normal tissue dose limits for the same target volumes based on volumes of 45 Gy in all patients treated. A 7-field IMRT technique with 6 MV photon energy was used in the IMRT treatment plans. With both technique target organ and critical organ doses were evaluated with DVH. During the planning comparison, in the cases planned using both techniques, V40, rectum mean dose and rectum maximum dose for the rectum; V40 bladder, bladder mean dose and bladder maximum dose for the bladder; V20 and V40 for the small bowel; V40 for the femoral head; V10 and V20 for the bone marrow; V95, V75, V70, V60, V50 and V40 percent doses for the total bone marrow PTV were measured. For dose comparison of 3D-CRT and IMRT, small intestine, urinary bladder, rectum, bone marrow from L4 vertebra to below the trochanter minor, and femoral head were contoured as the organs at risk. 3D conformal therapy plans and inverse intensity-modulated radiotherapy (IMRT) plans were made to ensure that the defined desirable (prescription) dose covered 95% of the PTV.

Chemotherapy

Concurrent weekly 40 mg/m² cisplatin (median 3 weeks cisplatin) was administered to 7 patients.

Statistical analysis

The analysis was made using the SPSS software package. Continuous variables were given as mean ± standard deviation, and categorical variables were given as number (percentage). Mann-Whitney U test, independent samples t- test and Chi-square analysis were used to compare independent groups. Paired samples t-test and Wilcoxon paired two-sample tests were used to compare dependent groups. Pearson correlation analysis and multiple regression analysis were used to examine inter-variable relationships. P <0.05 was considered statistically significant.

Results

Twenty-eight patients were enrolled in this study. Their ages ranged from 34 to 73, with a median age of 60. Among these patients, 23 (82%) were postmenopausal and 5 (18%) were premenopausal. Seventeen patients (61%) had operable and 11 (39%) had inoperable gynecologic tumors. Of the inoperable patients, seven were diagnosed based on cervical biopsy and diagnosed with inoperable cervical cancer after examination and investigation. Two were diagnosed based on Probe / Curatage + cervical biopsy due to systemic diseases and were diagnosed with inoperable cervical cancer, and 2 were diagnosed with inoperable endometrial cancer. Of the patients with operable cancer, 16 were diagnosed with endometrial cancer and 1 with operable cervical cancer. The general characteristics of gynecological cancer patients treated with conformal radiotherapy are given in Table 1.

Table 1: General characteristics of gynecological cancer patients treated with conformal radiotherapy

	Result
Age (Median)	60 years old
General characteristics	Number
Pre-menopausal	5
Post-menopausal	23
Operable uterine tumor	16
Inoperable uterine tumor	2
Operable cervical tumor	1
Inoperable cervical tumor	9
External radiotherapy	19
External radiotherapy and brachytherapy	9
Concomitant Chemotherapy	
Yes	7
No	21
Adjuvant Chemotherapy	
Yes	11
No	17
Lymphovascular invasion	
Yes	7
No	8
Lymph node involvement	
None	20
1-3	1
More than 3	7
Systemic disease	
Yes	16
No	12

External radiotherapy was applied to the patients (range: 45 Gy to 65 Gy; median dose 50.4 Gy). The doses of external radiotherapy were 45 Gy in 13 patients (46.4%), 50.4 Gy in 7 patients (25%), 54 Gy in 1 patient, 59.4 Gy in 3 patients, 46.8 Gy in 1 patient, 61.2 Gy in 1 patient, 45 Gy (45 Gy for first treatment) in 1 patient (due to re- irradiation therapy) and 65 Gy in 1 patient. Intracavitary brachytherapy of median 18 Gy (13-28) was applied to the patients in whom brachytherapy indication was found subsequently, with median 3 fractions (2-4) at another center. Concurrent weekly 40 mg/m² cisplatin (median 3 weeks cisplatin) was administered to 7 patients (25%).

When the side effects and quality of life were assessed, grade 1 lower gastrointestinal (GIS) toxicity was seen in 16 / 28 patients (57.1%). Nine of the patients (32.1%) had grade 1 and 1 (3.6%) had grade 2 upper GIS toxicity. Grade 1 genitourinary (GUS) toxicity was seen in 15 of the patients (53.6%), while 14 of the patients had grade 1 skin toxicity. Hematological toxicity was observed in 12 of the patients (42.8%) of whom 1 (3.6%) had grade 1 and 11 (39.3%) had grade 2-3 hematologic toxicity. Grade 3 hematologic toxicity was seen in 2 patients who received external radiotherapy of 61.2 Gy and 65 Gy. Early toxicities due to conformal radiotherapy in our patients are given in Table 2.

Table 2: Early toxicities of gynecological cancer patients treated with conformal radiotherapy

Early toxicities	Number
Lower GIS	
Grade 0	12
Grade 1	16
Grade 2-3-4	0
Upper GIS	
Grade 0	8
Grade 1	9
Grade 2	1
Grade 3-4	0
GUS toxicity	
Grade 0	13
Grade 1	15
Grade 2-3-4	0
Skin toxicity	
Grade 0	14
Grade 1	14
Grade 2-3-4	0
Hematological	
Grade 0	16
Grade 1	1
Grade 2-3	11
Grade 4	0

In the assessment of quality of life, the results were "good" in all patients except 2 (7.1%) who had "moderate" well-being. The quality of life of patients who received conformal therapy has shown that "mental well-being," "social life," "metabolic status," "general condition assessment" and "physical well-being" of patients in conformal therapy were not adversely affected. The assessment of quality of life is given in Table 3.

Table 3: Quality of life of gynecological cancer patients treated with conformal radiotherapy

	Number of patients
Physical well being	
Good	26
Moderate	2
Poor	0
Mental well being	
Good	28
Moderate-Poor	0
Social well being	
Good	28
Moderate-Poor	0
Metabolic status	
Good	28
Moderate-Poor	0
General condition	
Good	28
Moderate-Poor	0

The total bone marrow V10, V20 values were reduced statistically significant in the IMRT arm (p<0.001). When the planning methods were compared, the bladder V40 values and the bladder mean dose values were found to be lower and statistically significant (p<0.001). When the planning methods were compared, the rectum V40 values and the rectum mean dose values were lower in the IMRT arm, and this difference was statistically significant (p<0.001). The bladder max dose and rectum max dose values were higher in the IMRT arm than in the conformal planning arm, but no statistical significance was found

(p>0.05). The small bowel V40 values were lower in the IMRT arm than the conformal planning arm (p=0.01). When the doses received by 95%, 75%, 70%, 60%, 50% and V 40% of the total bone marrow were compared, it was found that only the 95% values received a lower dose in the IMRT arm than the conformal planning arm (p<0.001). The dosimetric comparison of 3D-CRT and IMRT plans for bone marrow and OAR in patients with gynecological cancer is given in Table 4.

Table 4: Dosimetric comparison of 3D-CRT and IMRT plans for bone marrow and OAR in patients with gynecological cancer

p value	IMRT < 3D-CRT	IMRT > 3D-CRT	IMRT = 3D-CRT
BM V10 (p<0.001)	12	10	6
BM V20 (p<0.001)	28	0	0
BL V40 (p<0.001)	26	1	1
BL MEAN (p<0.001)	28	0	0
BL MAX (p> 0.05)	0	28	0
REC V40 (p<0.001)	28	0	0
REC MEAN (p<0.001)	28	0	0
REC MAX (p>0.05)	28	0	0
SB V40 (p<0.001)	13	6	9
BM V 95 % (p<0.001)	28	0	0
BM V 75 % (p<0.001)	28	0	0
BM V 70 % (p<0.001)	28	0	0
BM V 60 % (p<0.001)	28	0	0
BM V 50 % (p<0.001)	16	12	0
BM V 40 % (p<0.001)	15	12	1

Abbreviations: BM V95 % (Volume) :Radiotherapy dose received by 95% of total bone marrow (BM); Bone Marrow (BM) V10: Volume % of the total pelvic bone that received 10 Gy; Bladder (BL) V40: Volume % of the bladder that received 40 Gy; Rectum (REC) V40: Volume % of the rectum that received 40 Gy; Small bowel (SB) V40: Volume % of the small intestine that received 40 Gy; Bladder mean dose: The average dose received by the bladder; Bladder max dose: The maximum dose received by the bladder; The organs at risk (OAR)

Discussion

In a study conducted by Yamazaki et al. [12] to compare 3D-CRT with 2D conventional therapy in cervical cancer patients in a post-operative setting, it was demonstrated that grade 2-3 small intestine complications were reduced from 17.5% to 2.9% with 3D-CRT. In a study by Mundt et al. [13] acute toxicity was evaluated in 40 patients with gynecologic tumors to whom IMRT planning was applied. Acute toxicities in 35 previously treated conventional pelvic radiotherapy patients were analyzed. IMRT planning resulted in excellent PTV coverage, with considerable sparing of normal tissues. Grade 2 acute GIS toxicity was less common in patients with IMRT (60 vs. 91%, p = 0.00) than in patients with conventional RT. In a study by Liu et al. [14], who published their clinical therapy experiences with 3D-CRT and IMRT in 50 patients with recurrent and metastatic disease, nine patients developed grade 3 leukopenia. No patient developed grade 3 or greater acute gastrointestinal toxicity or GUS toxicity. In a study by Lim et al., 7 patients developed Grade 2 proctitis, 1 patient had Grade 3 proctitis requiring surgical intervention, and 1 patient had Grade 3 intestinal obstruction treated with conventionally fractionated 60 Gy. Grade 2 hematuria was observed in 3 patients. In a study by Brixey et al. [9], grade 2 hematological toxicity was 31.2% in the IMRT arm and 60% in the conventional therapy arm in women with gynecologic tumors (p=0.08). In our study, no grade 3 GIS toxicity was observed. We also found similar grade 1 and 2 GIS toxicities to those found by other investigators in the literature. Sixteen of our patients (57.1%) had grade 1 GIS toxicity, and no serious toxicity of grades 2-3-4 was observed. As for upper GIS toxicity, 9 patients (32.1%) had grade 1 and 1 (3.6%) had grade 2 toxicity, and none had grade 3-4 toxicity. Fifteen of our patients (53.1%) had grade 1 GUS toxicity. None of our patients had grades 2-3-4 toxicity. One patient had grade 1, 9 (32.1%) had grade 2 and 2 (7.2%) had grade 3 hematological toxicity.

The PORTEC–2 study, which was one of the largest studies known in the literature relating to gynecologic tumors, examined 5-year quality of life in patients who underwent post-operative radiotherapy for endometrial cancer. This study investigated the changes in quality of life as assessed by EORTC QLQ-C30 in patients who received brachytherapy and external radiotherapy. Patients who received EBRT showed reduced social well-being compared to the normal population [15]. When we assessed the quality of life in our patients who received 3D-CRT, we observed that the results were “good” in all patients except 2 (7.1%) who had “moderate” well-being. No statistical cause was found in those with moderate physical well-being. The quality of life results obtained for conformal therapy demonstrated that “mental well-being”, “social life”, “metabolic status”, “general condition assessment” and “physical well-being” of patients in conformal therapy were not adversely affected. Physical well-being changes were seen in very few patients, and none was changed to “poor”.

Heron et al. [16] compared 3D-CRT and IMRT therapies dosimetrically in gynecologic tumors. They found that the small intestine, rectum and bladder doses that received 30 Gy were lower by 52%, 66% and 36%, respectively, in the IMRT arm. In a study by Avinash et al. [17], 11 consecutive patients treated with IMRT and 12 patients treated with 3D-CRT to the whole pelvis, along with concurrent chemotherapy, were selected. V10 Gy, V20 Gy, V95%, and mean of bone marrow were recorded. The dose to the bone marrow V20 Gy was 206.78 ± 57.10 cc (75%) and 251.70 ± 40.45 cc (91%) for IMRT and 3D-CRT, respectively (p=0.04), and V95% was 23.30 ± 8.34% and 46.76 ± 6.71% for IMRT and 3D-CRT, respectively (p<0.001). The grade of toxicities each week did not show a difference in either arm. However, the total count and Neutrophil counts during the second week showed statistical significance between IMRT and 3D-CRT. IMRT significantly reduced the dose to the bone marrow as compared to 3D-CRT. In our study, critical organs and total bone marrow (BM) were received lower doses in the IMRT arm than 3D- CRT arm. When the doses received by total bone marrow V20 (p<0.001), bladder V40 (p<0.001), bladder mean dose (p<0.001), rectum V40 (p<0.001), rectum mean dose (p<0.001), small bowel V40 (p=0.01) were compared, statistical significance was found in the IMRT arm.

Conclusion

Based on the results of our study, three-dimensional conformal radiotherapy is a safe treatment with acceptable low toxicity levels in patients and does not adversely affect quality of life. IMRT significantly reduces the dose to the bone marrow and other OARs as compared to 3DCRT. Delineation and avoidance of bone marrow and other OARs with functional imaging will probably result in reduced acute hematological toxicities.

Acknowledgements

We thank the medical staff and the Heads of the Department of Radiation Oncology, School of Medicine, University of Pamukkale for cooperation related to this paper.

References

1. SEER Cancer Statistics Review, 1975–2010 [Internet]. seer.cancer.gov; Apr. 2013 Available from: http://seer.cancer.gov/csr/1975 2010/ based on November 2012 SEER data submission, posted to the SEER web site.
2. Bray F, Loos AH, Oostindier M, Weiderpass E. Geographic and temporal variations in cancer of the corpus uteri: incidence and mortality in pre- and postmenopausal women in Europe. Int J Cancer. 2005;117(1):123–31.
3. WHO.GLOBOCAN 2012: Estimated cancer incidence, mortality and prevalence worldwide in 2012. http://globocan.iarc.fr/Pages/fact_sheets_population.aspx (3 April 2015, date last accessed).
4. Lee NK, Cheung MK, Shin JY, et al. Prognostic factors for uterine cancer in reproductive-aged women. Obstet Gynecol. 2007;109:655–62.
5. National Cancer Institute. Endometrial cancer treatment Physician Data Query (PDQ).2015; http://www.cancer.gov/cancertopics/pdq/treatment/endometrial/healthprofessional (1 April 2015, date last accessed).
6. Ferlay J, Shin HR, Bray F. GLOBOCAN 2008: cancer incidence and mortality Worldwide: IARC Cancer Base No.10. Lyon, France: International Agency for Research on Cancer. 2010; http://globocan.iarc.fr.Google Scholar
7. Mauch P, Constine L, Greenberger J, Knospe W, Sullivan J, Liesveld JL, et al. Hematopoietic stem cell compartment: Acute and late effects of radiation therapy and chemotherapy. Int J Radiat Oncol Biol Phys. 1995;31:1319-39.
8. Mell LK, Tiryaki H, Ahn KH, Mundt AJ, Roeske JC, Aydogan B. Dosimetric comparison of bone marrow-sparing intensity-modulated radiotherapy versus conventional techniques for treatment of cervical cancer. Int J Radiat Oncol Biol Phys. 2008;71:1504-10.
9. Brixey CJ, Roeske JC, Lujan AE, Yamada SD, Rotmensch J, Mundt AJ. Impact of intensity-modulated radiotherapy on acute hematologic toxicity in women with gynecologic malignancies. Int J Radiat Oncol Biol Phys. 2002;54:1388-96.
10. Small W Jr, Mell LK, Anderson P, Creutzberg C, De Los Santos J, Gaffney D, et al. Consensus guidelines for delineation of clinical target volume for intensity-modulated pelvic radiotherapy in postoperative treatment of endometrial and cervical cancer. Int J Radiat Oncol Biol Phys. 2008;71:428-34.
11. Lim K, Small WJ, Portelance L, Creutzberg C, Jürgenliemk-Schulz IM, Mundt A, et al. Consensus guidelines for delineation of clinical target volume for intensity- modulated pelvic radiotherapy for the definitive treatment of cervix cancer. Int J Radiat Oncol Biol Phys. 2011;79:348-55.
12. Yamazaki A, Shirato H, Nishioka T, Hashimoto S, Kitahara T, et al. Reduction Of Late Complications After İrregularly Shaped Four-Field Whole Pelvic Radiotherapy Using Computed Tomographic Simulation Compared With Parallel opposed Whole Pelvic Radiotherapy. Jpn J Clin Oncol. 2000;30:180–4.
13. Mundt AJ, Lujan AE, Rotmensch J, Waggoner SE, Yamada SD, et al. Intensity-modulated whole pelvic radiotherapy in women with gynecologic malignancies. Int J Radiat Oncol Biol Phys. 2002;52:1330–7.
14. Liu SP, Huang X, Ke GH, Huang XW. 3D radiation therapy or intensity-modulated radiotherapy for recurrent and metastatic cervical cancer: the Shanghai Cancer Hospital experience. PLoS One. 2012;7(6):e40299. doi: 10.1371/journal. pone.0040299. Epub 2012 Jun 29.
15. Nout RA, Putter H, Jobsen J, et al. Five-year quality of life of endometrial cancer patients treated in the randomised Post-Operative Radiation Therapy in Endometrial Cancer (PORTEC–2) trial and comparison with norm data. Eur J Cancer. 2012;48(11):1638-48.
16. Heron DE, Gerszten K, Selvaraj RN, et al. Conventional 3D conformal versus intensity- modulated radiotherapy for the adjuvant treatment of gynecologic malignancies: a comparative dosimetric study of dose-volume histograms. Gynecol Oncol. 2003;91(1):39-45.
17. Avinash HU, Arul Ponni TR, Janaki MG, Kirthi Koushik AS, Kumar SM. A prospective dosimetric and clinical comparison of acute hematological toxicities in three-dimensional conformal radiation therapy and intensity modulated radiation therapy with concurrent chemotherapy in carcinoma cervix. J Can Res Ther. 2015;11:837.

J Surg Med. 2018;2(3):320-323.
DOI: 10.28982/josam.429889

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Rare and overlooked two diagnoses in low back pain: Osteitis condensans ilii and lumbosacral transitional vertebrae

Bel ağrısında nadir ve gözden kaçan iki tanı: Osteitis kondensans ilii ve lumbosakral transizyonel vertebra

Elif Gündoğdu [1]

[1] **Department of Radiology, Eskişehir Osmangazi University, Eskişehir, Turkey**

ORCID ID of the authors
EG: 0000-0002-1729-6958

Abstract

Aim: In this study, we investigated the prevelance of osteitis condensans ilii (OCI) and lumbosacral transitional vertebra (LSTV), relationship of these diseases with age and gender, and whether there was a relationship between these two conditions.

Methods: The computed tomography (CT) scans of 599 patients who underwent lumbar CT between January 2016 and March 2016 due to lumbar pain were evaluated retrospectively. All of the CT scans were performed with a 16-slice CT scanner. For each patient; age, gender, LSTV anomaly presence and type (lumbalisation, sacralization), and presence and side information of OCI were recorded.

Results: OCI was not detected in 577 patients (96.3%) and was detected in 22 patients (3.7%). LSTV was not detected in 522 patients (87.2%) and was present in 77 patients (12.8%). The mean age of the patients who detected OCI was 30.7 years (+/- 9.5) while without OCI was 43.1 years (+/- 16.6) . 18 (81.8%) of the 22 OCI detected cases were female while 4 (18.2%) cases were male. OCI was more common in young people and female. LSTV was observed in 41 (16.2%) of the female patients while in 36 of the male patients (10.3%). LSTV was observed more frequently in female patients. There was no statistically significant difference between groups with and without OCI disease in terms of presence of LSVT.

Conclusion: Both OCI and LSVT are situations that cause back pain. These two diagnoses must be taken into account in examinations made with lumbar pain cause.

Keywords: Osteitis condensans ilii, Lumbosacral transitional vertebra, Computed tomography

Öz

Amaç: Bu çalışmada osteitis kondensans ilii (OKİ) ve lumbosakral transizyonel vertebranın (LSTV) sıklığı, bu iki durum arasında ilişki olup olmadığı ve bu durumların yaş ve cinsiyetler arasındaki değişkenliklerinin tespitini amaçladık.

Yöntemler: Ocak 2016 -Mart 2016 tarihleri arasında lomber bel ağrısı nedeni ile lomber bilgisayarlı tomografi (BT) çekilmiş 599 hastanın incelemeleri retrospektif olarak değerlendirildi. Bütün BT çekimleri 16 kesitli BT cihazında gerçekleştirildi. Her hasta için yaş, cinsiyet, LSTV anomalisi olup olmadığı bilgisi ve tipi (lumbalizasyon ve sakralizasyon) ile OKİ varlığı ile taraf bilgisi kaydedildi.

Bulgular: Değerlendirilen hastaların 577'sinde (%96.3) OKİ saptanmazken 22'sinde (%3.7) saptandı. Değerlendirilen hastaların 522'sinde (%87.2) LSTV saptanmazken 77'sinde (%12.8) saptandı. OKİ saptanan hastaların ortalama yaşı 30.7 (+/- 9.5), saptanmayanlarınki 43.1 (+/- 16.6) yıl idi. OKİ saptanan hastaların 18'i (%81.8) kadın, 4'ü (%18.2) erkekti. OKİ kadın hastalarda ve genç yaş grubunda daha sıktı. LSTV kadın hastaların 41'inde (16.2%) erkek hastaların ise 36 'sında (10.3%) gözlendi. LSTV kadın hastalarda daha sık gözlendi. OKİ olan ve olmayan hasta grupları arasında LSTV varlığı ve yokluğu arasında istatiksel fark yoktu.

Sonuç: Hem OKI hem de LSTV bel ağrısına neden olan durumlardır. Lomber bel ağrısı ile tetkik edilen hastalarda bu iki tanı dikkate alınmalı, akılda tutulmalıdır.

Anahtar kelimeler: Osteitis kondensans ilii, Lumbosakral transizyonel vertebra, Bilgisayarlı tomografi

Introduction

Low back pain is observed at least once throughout life at 60-85% of the general population [1-3]. The vast majority of lumbar pain (97%) is mechanically sourced [3]. Mechanical pain develops as a result of overuse, forcing, trauma, or deformation of structures that form the spine [3]. Osteotitis condensans ili (OCI) and lumbosacral transitional vertebra (LSTV) are two entities that can cause mechanical back pain [1,4-6]. The diagnosis of both can be easily determined with typical radiological findings, and it can be possible to distinguish from the inflammatory pain of the back.

Although the mechanism by which LSTV causes back pain is not clearly known, it has been suggested that early degeneration, spinal- extraforaminal stenosis and changes in load distribution caused by instability. Because OCI is often associated with pregnancy and be seen in young female, it has been reported that changes in the distribution of burden of sacroiliac in pregnancy and ligament laxity caused by hormonal factors may play a role in etiology [5-7].

Corresponding author / Sorumlu yazar:
Elif Gündoğdu
Address / Adres: Eskişehir Osmangazi Üniversitesi, Radyoloji Anabilim Dalı, Eskişehir, Türkiye
E-mail: elif_basbay@hotmail.com

Ethics Committee Approval: The Medical Faculty of Gaziantep University Ethics Committe approved the study (decision no: 2017/316 decision date: 02.10.2017).
Etik Kurul Onayı: Gaziantep Üniversitesi Etik Kurulunun Tıp Fakültesi çalışmayı onayladı (karar no: 2017/316 karar tarih: 02.10.2017).

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 02.06.2018
Accepted / Kabul Tarihi: 16.07.2018
Published / Yayın Tarihi: 25.07.2018

How to cite / Atıf için: Gündoğdu E. Rare and overlooked two diagnoses in low back pain: Osteitis condensans ilii and lumbosacral transitional vertebrae. J Surg Med. 2018;2(3):320-323.

In this study, we investigated the prevalence of OCI and LSTV, relationship with age and sex, and the relationship between these two conditions in patients referred to our clinic for lumbar computed tomography (CT) due to low back pain.

Materials and methods

The Medical Faculty of Gaziantep University Ethics Committee approved the study. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patients Selection

In this cross- sectional study, the CT examinations of patients who were referred to the Department of Radiology on 25 December State Hospital between January and March 2016 due to lumbar pain were evaluated retrospectively. Patients with previous history of lumbar surgical operation and acute trauma patients were excluded from the study. The images that were not evaluated due to technical insufficiency, such as artefacts caused by patient movements or images which did not contain the lumbar region completely were removed from study. A total of 599 lumbar CT examinations in the study group were evaluated. The radiological evaluation was conducted by a single senior radiologist.

CT Imaging

No contrast agent was used in CT scans. All of the CT scans were performed using the 16-slices CT device (Toshiba, Activion 16, Toshiba Medical Systems, Otowara, Japan). No preparation was made prior to the examination. All examinations were conducted in the supine position with the arms of the patients above their heads. Sagittal and axial planar sections were taken at the soft tissue and bone window.

The imaging parameters were tube voltage of 120 kV, tube flow of 100 mA. The width and level for the soft tissue window were 400 HU and 40 HU, respectively. For bone window, these values were 2500 HU and 280 HU. For each patient; age, gender, LSTV anomaly presence and type (lumbalisation, sacralization), and OCI presence and side information were recorded.

The diagnosis of OCI was based on the presence of sclerosis in the triangular shape in the inferior part of the iliac bone adjacent to the both sacroiliac joint. The absence of findings to marking sacroileitis such as bone erosion in sacroiliac joint, narrowing of joint space, irregularity of joint surfaces and presence of sclerosis on sacral side were accepted as supportive findings for OCI diagnosis. LSTV evaluation was based on iliolumbar ligament and the ligament-adherent vertebra was considered L5. The relationship of the OCI with age and gender, the relationship of LSTV with gender, and the relationship between OCI and LSTV anomaly were evaluated.

Statistical analysis

Statistical analysis was performed using SPSS 20.0 (Chicago, IL) software. P <0.05 was considered statistically significant. Chi-square test was used to analyze whether there is a significant relationship between the gender and LSTV or OCI. In addition the test was used to analyze whether there is a significant relationship between the LSTV and OCI. Mann-Whitney U Test was used to assess the relationship between age and OCI.

Results

The lumbar CT scans of 599 patients aged between 14 and 98 were evaluated. The mean age of the patients was 42.73±16.23 years.

OCI was not detected in 577 patients (96.3%) and OCI was detected in 22 patients (3.7%) (Table 1). In 2 of OCI detected cases (9%) the disease was unilateral (Figure 1) and in 20 (90%) the disease was bilateral (Figure 2, 3).

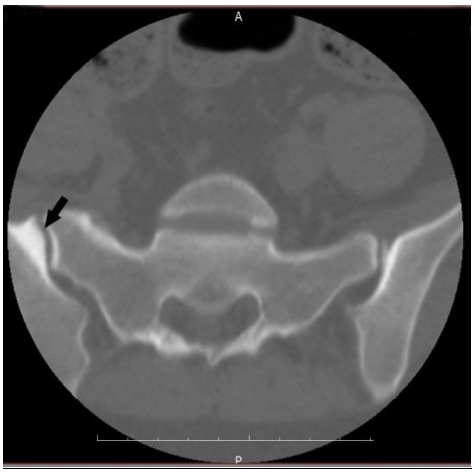


Figure 1: Right sided osteitis condensans ilii in a 18 year old female patient. Computed tomography shows triangular shaped sclerosis around the lower part of the right sacroiliac joint (thick arrow).

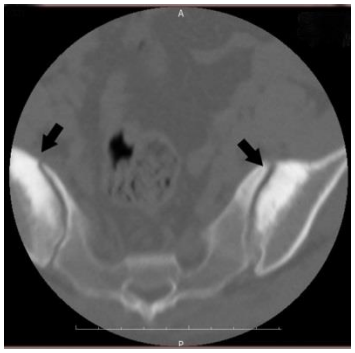


Figure 2: Bilateral osteitis condensans ilii in a 34 year old female patient. Computed tomography shows triangular shaped sclerosis in the inferior part of the bilateral iliac bone adjacent to the both sacroiliac joint (thick arrows).

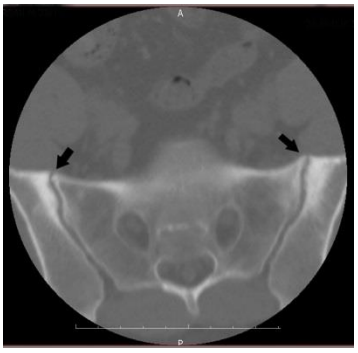


Figure 3: Bilateral osteitis condensans ilii in a 36 year old male patient. Bilateral-symmetrical triangular shaped sclerosis (thick arrows) on the iliac aspect of the sacroiliac joints on the axial computed tomography scan (thick arrow).

LSTV was not detected in 522 patients (87.2%) and LSTV was present in 77 patients (12.8%). 33 (% 5.5) patients had lumbalisation (Figure 4), 44 (% 7.3) patients had sacralisation (Figure 5) (Table 2). The mean age of the patients who detected OCI was 30.7 ± 9.5 years while the mean age of the patients without OCI was 43.1 ± 16.6 years. The age difference between the two groups was statistically significant (Figure 6). OCI was more common in the younger age group (p=0.001).

Table 1: Frequency of osteitis condensans ilii

	Frequency (n)	Percent (%)
OCI +	22	3.7
Bilateral OCI	20	3.3
Unilateral OCI	2	0.3
OCI -	577	96.3
Total	599	100

OCI: Osteitis Condensans Ilii

Table 2: Frequency of lumbosacral transitional vertebra

	Frequency (n)	Percent (%)
LSVT +	77	12.8
Lumbalisation	33	5.5
Sacralisation	44	7.3
LSVT -	522	87.1
Total	599	100

LSVT: Lumbosacral Transitional Vertebra

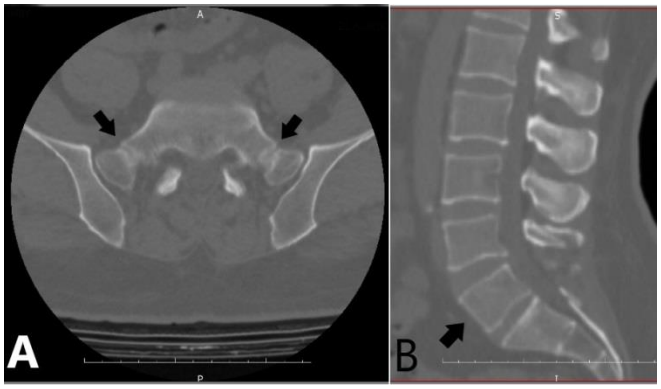


Figure 4: Lumbalisation form of lumbosacral transitional vertebra in a 48 year old male patient on axial (A) and sagittal (B) computed tomography scan (thick arrows).

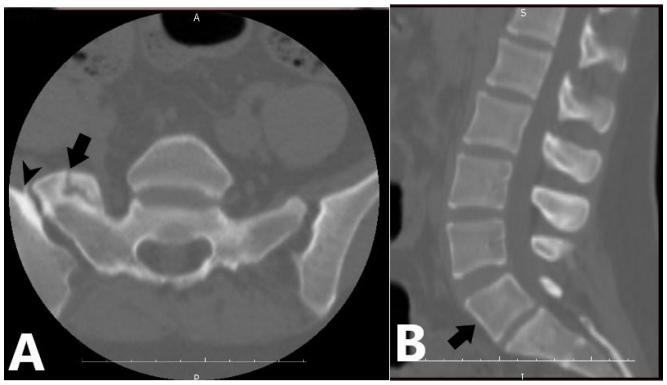


Figure 5: Sacralisation form of lumbosacral transitional vertebra in a 25 year old female patient on axial (A) and sagittal (B) computed tomography scan (thick arrows). Right sided osteitis condensans ilii is also seen on axial (A) computed tomography scan (arrow head).

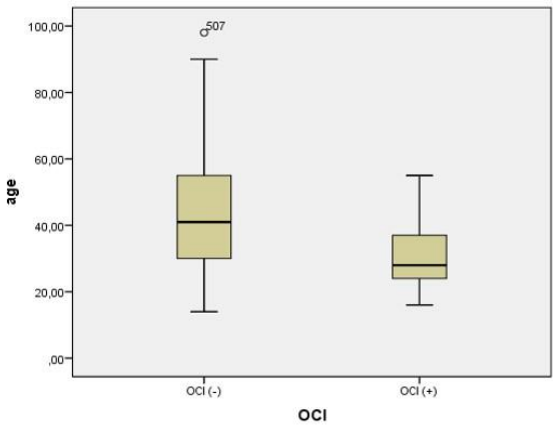


Figure 6: The age difference between the two groups osteitis condensans ilii (OCI) (-) and OCI (+).

18 (81.8%) of the 22 OCI detected cases were female while 4 (18.2%) cases were male. Of the 577 patients without OCI, 329 (57%) were female and 248 (43%) were male (Table 3). The difference was significant for gender in groups which has OCI or not, while OCI was more common in female (p=0.036).

Of the 599 patients, 347 (57.9%) were female while 252 (42.1%) were male. LSTV was observed in 41 (16.2%) of the male patients while LSTV was detected in 36 of the female patients (10.3%). LSTV was observed more frequently in male patients and the difference was statistically significant (p=0.033).

The relationship between LSTV and OCI was investigated. LSTV was observed in 75 (13%) of 577 patients without OCI, while LSTV was observed in 2 (9%) of 22 patients detected OCI (Table 4). There was no statistically significant difference between groups with and without OCI disease in terms of presence of LSTV (p=0.59).

Table 3: Frequency and Distribution of OCI (-) and OCI (+) patients according to the gender

		Frequency (n)	Percent (%)
OCI(-)	Female	329	57.0
	Male	248	43.0
	Total	577	100.0
OCI (+)	Female	18	81.8
	Male	4	18.2
	Total	22	100.0

OCI: Osteitis Condensans Ilii

Table 4: Frequency and Distribution of patients according to the presence or absence of the lumbosacral transitional vertebra

		Frequency (n)	Percent (%)
OCI (-)	LSVT (-)	502	87.0
	LSVT (+)	75	13.0
	Total	577	100.0
OCI (+)	LSVT (-)	20	90.9
	LSVT (+)	2	9.1
	Total	22	100.0

OCI: Osteitis Condensans Ilii LSVT: Lumbosacral Transitional Vertebra

Discussion

OCI is one of the rare causes of low back pain [5,6,8]. It is more common in young age group and female gender [5,6,8]. In the etiology, it is mentioned that OCI may be due to increases of the load to sacroiliac joint and changing distribution of the load especially during pregnancy [5-8]. However, this etiology is controversial because it is seen in nullipars and in male patients [5,6].

OCI is a benign form of low back pain and it is important to distinguish from inflammatory low back pain because of typical radiological findings [5-7]. The sacroiliac joint is usually affected by the inferior segment [5,6,8]. Triangular-shaped sclerosis of the iliac bone adjacent to sacroiliac joint is apparent [5,6,8]. The sacral region is usually protected. The absence of narrowing of the sacroiliac joint space and no irregularity and erosion in adjacent bony structures and also usually be seen bilateral allowing sclerosis to be identified in favor of OCI [5,6,8].

It is estimated that the OCI is seen between 0.9% -2.5% in the general population [5,7]. It is usually reported as a rare disease in the literature and reported as case reports. According to our knowledge, there is no study on prevalence. The OCI prevalence in our patient group was found to be 3.7%. The reason for our finding more frequently than the literature is may be that the patient group we have examined consists of the patients evaluated for lumbar pain etiology. In addition, patient presentations in the literature were mostly evaluated by X-ray findings. In our study, MDCT images of the patients were evaluated. In detecting sclerosis, especially in cases with mild findings, CT is more sensitive than x-ray, which may be reason of finding higher prevalence.

OCI is more frequent in female patients, younger age group and bilaterally [5-8]. However, unilateral cases have been reported rarely [5]. Consistent with the literature, was found a higher prevalence in female patients of our study group. Patients who were diagnosed with OCI were lower mean age than without OCI. The disease was bilateral in 90% of the OCI-detected patients.

LSTV may cause early degenerative changes and back pain by altering the load distribution in the vertebral column [1,4,9]. It was classified by Castvelli in four groups based on radiological findings [1,4,9-11]. However, for correct numbering only the evaluation of the lumbar graphs does not always give the correct results. The most accurate numbering and

classification is achieved by inclusion of the entire vertebral column from C2 to sacral region imaging field [11]. In routinely practice, however, this is usually not possible, and usually only lumbar region images can be obtained. Another method for correct classification is to use other anatomical structures to identify the lumbosacral transitional vertebrae [11,12].

One of the anatomic structures that can be used for this purpose is ililumbal ligament [11,12]. This ligament originates from the transverse process of the L5 vertebrae in 95-100% and adheres to the posterior aspect of the iliac wing [12]. When classifying, accepting the vertebrae L5 attached to this ligament allows enumeration and naming with high accuracy [12]. In our study, was classified LSTV by evaluating the vertebrae attached to the iliolumbar ligament as L5.

Ratios varying from 4 to 35% for the frequency of LSTV in the population were reported according to the number of samples and the diversity of the study population [1,9,12,13].

In our study, the rate was found to be 12.8% similar to the literature. Some studies have found that sacralization is more frequent while lumbalisation is more common in some studies [4, 10-13]. In our case group, the sacralization rate was higher. Again, many studies have found different conclusions about in which gender is more common. In our study group, was higher the prevelance of male cases [11-13].

LSTV is one of the condition that changes the load distribution by causing instability in the lumbosacral region [1,2]. One of the alleged assertions in the etiology of the OCI is the mechanical stress caused by the change of load distribution in the lumbosacral region.

Because of this claim, it is thought that LSTV may be a predisposing factor to OCI, and it is investigated whether there is a relationship between LSTV and OCI. In our study, no statistically significant difference was found between groups of patients with and without OCI in terms of the presence of LSTV. Mechanical stress may be an effective factor in OCI etiology, but it is not a sufficient factor alone. It may contribute to OCI formation when present with other predisposing factors of the patient. According to our knowledge there is no study in the literature about relationship between LSTV and OCI. According to our study, there was no relationship between these two conditions. The result we have obtained should be supported by studies with larger patient groups.

The limitations of this study were due to retrospective nature. Magnetic resonance imaging must be first choice for low back pain due to most common etiology, disc herniation. And also x-ray could be used for bone pathology. We evaluated CT scans for both of them.

Conclusion

OCI and LSTV, which are among the rare causes of mechanical back pain, must be considered in radiologic imaging carried out for this purpose. Radiologically, it is easy and important to distinguish both conditions from inflammatory low back pain. The correct diagnosis avoids aggressive treatments.

References

1. Atıcı Y. Lumbosacral Junction Anomalies and Low Back Pain. TOTBİD. 2015;14:258–61.
2. Kurt EE, Türkyılmaz AK, Dadalı Y, Erdem HR, Tuncay F. Are Transitional Vertebra and Spina Bifida Occulta Related with Lumbar Disc Herniation and Clinical Parameters in Young Patients with Chronic Low Back Pain? Eurasian J Med. 2016;48:177-80.
3. Suyabatmaz Ö, Çağlar NS, Tütün Ş, Özgönenel L, Burnaz Ö, Aytekin E. Assessment of the Effect of Back School Therapy in Patients with Low Back Pain. Istanbul Med J. 2011;12(1):5-10.
4. Baysal Ö, Baysal T, Altay Z, Füdan F. The Relationship Between Types of Transitional Vertebrae and Disc Degeneration. Ege Fiz Tıp Reh Der. 2001;7:45-9.
5. Demirdal ÜS, Haktanır A, Yaman F. Low Back Pain Due to the Osteitis Condensans Ilii. Turkish Journal of Osteoporosis. 2013;19:48-51.
6. Alkan BM, Karaarslan H, Eroğlu E, Alemdar A, Yamçiçi S, Ardıçoğlu S. Osteitis Condensans Ilii: Case Report. Open Journal of Rheumatology and Autoimmune Diseases. 2011;1:1-4.
7. Ayoub MA. Refractory osteitis condensans ilii: Outcome of a novel mini-invasive surgical approach. International Orthopaedics (SICOT). 2013;37:1251–6.
8. Jenks K, Meikle G, Gray A, Stebbings S. Osteitis condensans ilii: a significant association with sacroiliac joint tenderness in women. International Journal of Rheumatic Diseases. 2009;12:39–43.
9. Nardo L, Alizai H, Virayavanich W, Liu F, Hernandez A, Lynch JA, et al. Lumbosacral transitional vertebrae: association with low back pain. Radiology. 2012 Nov;265(2):497-503.
10. Uçar D, Uçar BY, Coşar Y, Emrem K, Gümüşsuyu G, Mutlu S, et al. Retrospective cohort study of the prevalence of lumbosacral transitional vertebra in a wide and well-represented population. Arthritis. 2013;2013:461425.
11. Konin GP, Walz DM. Lumbosacral Transitional Vertebrae: Classification, Imaging Findings, and Clinical Relevance. AJNR Am J Neuroradiol. 2010;31:1778–86.
12. Hughes RJ, Saifuddin A. Numbering of Lumbosacral Transitional Vertebrae on MRI: Role of the Iliolumbar Ligaments. AJR. 2006;187:59-66.
13. Sekharappa V, Amritanand R, Krishnan V, David KS. Lumbosacral Transition Vertebra: Prevalence and Its Significance. Asian Spine J. 2014;8:51-8.

J Surg Med. 2018;2(3):324-329.
DOI: 10.28982/josam.432680

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Clinical outcome of stereotactic ablative radiotherapy with CyberKnife® for lung tumors: A single center experience

Akciğer tümörlerinde CyberKnife® ile stereotaktik ablatif radyoterapi sonuçlarımız: Tek merkez deneyimi

Ebru Atasever Akkaş [1], Ebru Karakaya [1], Gonca Altınışık İnan [2], Yasemin Güzle Adaş [1], Ömer Yazıcı [1], Esra Kekilli [1], Ferhat Kıran [3], Ferihan Ertan [1], Bülent Küçükpilakçı [3], Yıldız Güney [3]

[1] Department of Radiation Oncology, Ankara Dr. Abdurrahman Yurtaslan Oncology Research and Training Hospital, Ankara, Turkey
[2] Department of Radiation Oncology, Ankara Atatürk Education and Research Hospital, Ankara, Turkey
[3] Department of Radiation Oncology, Ankara Memorial Hospital, Ankara, Turkey

ORCID ID of the authors
EAA: 0000-0003-4164-7196
EK: 0000-0001-8970-5186
GAİ: 0000-0002-7385-3480
YGA: 0000-0001-7099-9663
ÖY: 0000-0002-9732-4241
EK: 0000-0001-5112-4175
FK: 0000-0002-0017-177X
FE: 0000-0003-2287-7260
BK: 0000-0001-8280-0244
YG: 0000-0003-2251-3571

Corresponding author / Sorumlu yazar:
Ebru Atasever Akkaş
Address / Adres: Abdurrahman Yurtaslan Onkoloji Araştırma ve Eğitim Hastanesi, Radyasyon Onkolojisi Anabilim Dalı, Ankara, Türkiye
E-mail: ebruataseverakkas@gmail.com

Ethics Committee Approval: Approval was obtained from Clinical Research Ethics Committee of Dr. Abdurrahman Yurtarslan Ankara Onkoloji Research and Training Hospital (date/number: 11.12.2014 / 014/362).
Etik Kurul Onayı: Abdurrahman Yurtarlan Ankara Onkoloji Araştırma ve Eğitim Hastanesi Klinik Araştırma Etik Kurulu'ndan onay alındı (tarih / sayı: 11.12.2014 / 014/362).

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Previous presentation: Presented as a poster in 12th UROK Congress, 20-24 April 2016, Belek, Antalya, Turkey.
Önceki sunum: 12. UROK Kongresi'nde poster olarak sunulmuştur, 20-24 Nisan 2016, Belek, Antalya, Türkiye.

Received / Geliş Tarihi: 10.06.2018
Accepted / Kabul Tarihi: 24.07.2018
Published / Yayın Tarihi: 25.07.2018

Abstract

Aim: To evaluate retrospectively clinical outcomes of treated with stereotactic ablative radiotherapy (SABR) using the CyberKnife® (Accuray, Sunnyvale, CA, USA), for early primary and oligometastatic lung tumors.

Methods: This descriptive study included thirty tumors from 29 patients with primary lung cancer (n=21) or oligometastatic lung tumors (n=9), who underwent SABR with robotic linear accelerator between March 2011 and July2015. Out of the 30 tumors, 21 were NSCLC, 9 were metastatic lung disease. Treatment was given using different tracking methods including fiducial tracking with Synchrony (21 patients), Xsight lung with Synchrony (4 patients) and Xsight spine (5 patients). Treatment was delivered two to three fractions per week and with different fractionations depending on location and other tumor related factors. Factors, potentially effective on local control and overall survival were investigated.

Results: Median follow-up time for local control was 11 months (2.4-39 months). Of 25 patients with known follow-up data, local control (LC) rates for 1, 2 and 3 years were 82.8%, 82.8% and 55.2 %, respectively. Overall survival (OS) rates for primary lung tumor patients 1, 2 and 3 years were 72.2%, 64.2%, 51.4% and metastatic lung tumor patients for 1 year was 71%, respectively. Except for gender, none of the factors were statistically significantly associated with local control in univariate analysis; female gender was associated with worse local control (p=0.001). Also in univariate analysis of overall survival, there was a trend for worse survival in females, too (p=0.07).

Conclusion: This small study may give some idea about utilizing different tracking ways for CyberKnife® with less toxicity.

Keywords: CyberKnife®, Lung tumor, Stereotactic ablative radiotherapy

Öz

Amaç: Primer ve oligometastatik akciğer karsinomu tanısıyla CyberKnife® (Accuray, Sunnyvale, CA, USA) kullanarak stereotaktik ablatif radyoterapi (SABR) ile tedavi edilen olgularımızın tedavi sonuçlarımızı değerlendirmek.

Yöntemler: Bu tanımlayıcı çalışmaya Mart 2011- Temmuz 2015 tarihleri arasında robotik lineer akselatör ile SABR tedavisi alan primer akciğer kanserli (n=21) ve oligometastatik akciğer tümörlü (n=9) 30 hastanın 29'u dahil edilmiştir. 30 tümörden 21'i KHDAK, 9'u metastatik akciğer hastalığı idi. Tüm tedavi adımları aynı doktor tarafından kontrol edildi. Tedavi, Synchrony (21 hasta), Synchrony ile Xsight akciğer (4 hasta) ve Xsight vertebra (5 hasta) ile fidusiyal izleme dahil olmak üzere farklı izleme yöntemleri kullanılarak verildi. Tedavi, lokal ve diğer tümörle ilişkili faktörlere bağlı olarak, haftada iki veya üç farklı fraksiyonlarda verildi. Lokal kontrol ve genel sağkalım üzerinde potansiyel olarak etkili faktörler araştırıldı.

Bulgular: Lokal kontrol için medyan takip süresi 11 ay (2,4-39 ay) idi. Bilinen takip verileri bulunan 25 hastanın 1, 2 ve 3 yıllık lokal kontrol (LC) oranları sırasıyla% 82,8, % 82,8 ve % 55,2 idi. Tüm sağkalım oranları primer akciğer tümörlü hastalar için 1, 2 ve 3 yıllık sırasıyla %72,2, %64,2 ve %51,4 ve metastatik akciğer tümörleri için 1 yıllık %71 idi. Cinsiyet haricinde, tek değişkenli analizde faktörlerin hiçbiri lokal kontrol ile istatistiksel olarak anlamlı bir şekilde ilişkili değildi; kadın cinsiyeti daha kötü lokal kontrol ile ilişkiliydi (p=0,001). Ayrıca genel sağkalımın tek değişkenli analizinde, kadınlarda da daha kötü bir sağkalım eğilimi vardı (p=0,07).

Sonuç: Bu küçük çalışma, CyberKnife® için daha az toksisite ile farklı tedavi takip yöntemlerinin kullanımı hakkında biraz fikir verebilir.

Anahtar kelimeler: CyberKnife®, Akciğer tümörü, Stereotaktik ablatif radyoterapi

How to cite / Atıf için: Akkaş EA, Karakaya E, İnan GA, Adaş YG, Yazıcı Ö, Kekilli E, Kıran F, Ertan F, Küçükpilakçı B, Güney Y. Clinical outcome of stereotactic ablative radiotherapy with CyberKnife® for lung tumors: A single center experience. J Surg Med. 2018;2(3):324-329.

Introduction

Although surgery is the standard treatment for stage I non-small cell lung cancer (NSCLC) [1]. Stereotactic ablative radiotherapy (SABR) is an increasingly used and revolutionary treatment modality for early stage non-small cell lung cancer (NSCLC) with high rates of local control [2]. Conventional radiotherapy was reported to result in much more lower local control and overall survival rates than surgery [3]. However SABR, with reported high rates of local control, can improve survival even in medically inoperable patients having multiple comorbidities [4-7].

In addition to early primary lung cancer patients, SABR is also revealed with favorable results for oligometastatic lung disease [8]. The CyberKnife, frameless stereotactic radiosurgery system, can track the tumour and motion real time via different tracking methods [9-11].

In our institution we use 3 different target tracking methods of CyberKnife® for lung SABR: Fiducial tracking with Synchrony® (FTTS), Respiratory Tracking System (Synchrony), Xsight® Lung Tracking System (XLTS) with Synchrony and Xsight spine.

For fiducial tracking, fiducial markers were implanted inside or near the tumor by CT guidance [9-10]. Whereas XLTS, capable of tracking the tumour directly instead of fiducials is completely uninvasive method [10]. For Xsight spine method, position of the tumor can be evaluated and corrected relative to the spine location [9].

The purpose of the current study is to document our treatment practices on LC, OS and different tracking methods of central and peripheral located early-stage NSCLC and lung metastases from patient undergone to CyberKnife® for lung SABR.

Materials and methods

We reviewed treatment plans and electronic medical database of 29 lung SABR patients with 30 tumors treated between March 2011 and July 2015. Out of 30 tumors, 21 (70%) had been treated for primary lung cancer and 9 (30 %) for metastatic disease. Some patients had recurrent primary lung cancer (7 patients) and had prior thoracic radiation therapy or lung surgery. Patients' characteristics are listed in table 1.

Table 1: Baseline characteristics

Factor	n	%
Total patient number	29	100
Total number of lesions treated	30	100
Age (years)	Median:68	Range:49-82
Gender (male/female)	22/8	73/ 27
Tumor greatest dimension(mm.)	Median:20.7	Range:8-53.4
Tumor volume (mm^3)	Median:6216.5	Range:904-55980
Primary lung cancer/lung metastasis	21/9	70 / 30
Central /peripheral located tumor	7 / 23	23.3 / 76.7
Histology (known/unknown)	19/ 11	63.3 / 36.7
Pretreatment SUVmax	Median:4.96	Range:1-20.90
BED10 (Gy)	Median:105.6	Range: 59.5-180
Fraction numbers	Median:4	Range:3-7
Tumor follow-up method		
Fiducial	21	70
X sight lung	4	13.3
X sight spine	5	16.7

All patients with lung primary were considered inoperable or preferred SABR over surgery. 23 (77%) patients' tumor were considered peripherally located and 7 (23%) were centrally located according to Radiation Therapy Oncology Group (RTOG) 0236 study definition [12].

All patients were treated with SABR via CyberKnife® (Accuray, Sunnyvale, CA, USA) robotic linear accelerator. Patients underwent computed tomography (CT) or 4-dimensional computed tomography (4DCT) scan for treatment planning with 1.5mm slice thickness. In our department we are using 4DCT (Brilliance CT Big Bore, Philips Healthcare, Cleveland, OH) since January 2014. Gross tumor volume (GTV) was delineated on lung window setting. Clinical target volume (CTV) was not used (GTV=CTV). We used 4DCT, just to have an idea about tumor motion and didn't generate an internal target volume (ITV). General margin for PTV was 5 mm. in all dimension. Occasionally, in case of little movement of the tumor we used narrower margin of 1-2mm. The dose was prescribed to isodose line (median: 81.5%; 75%-97%) covering PTV. As a tumor tracking methods; fiducials tracking, Xsight lung and Xsight spine systems (Figure 1) were used for 21 (70 %), 4 (13.3 %) and 4 (13.3 %) tumors, respectively. One week after fiducial placement, planning CT was performed. Depending on the clinician's discretion, dose and fractionation schedules were varied. But all treatment steps, including contouring, dose scheduling, and plan evaluation were checked by the same physician experienced about stereotactic treatment. Median prescribed dose was 48 Gy (35 to 60 cGy) given in median 4 fractions (3 to 7 fractions). Most common fractionation scheme was 48 Gy in 4 fraction (for 17 tumors).

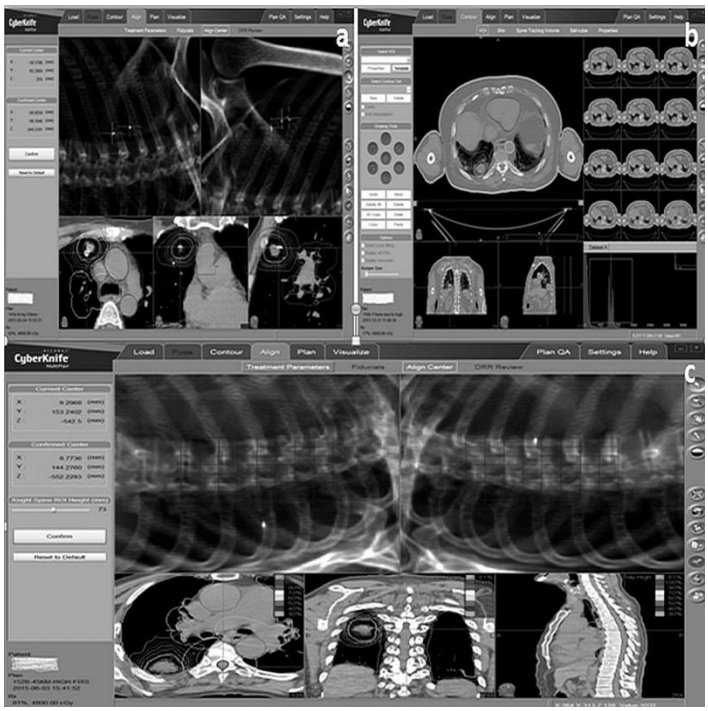


Figure 1: It was shown that the tumor tracking methods as fiducials tracking (a), as Xsight lung (b) and as Xsight spine systems (c)

Follow-up

Follow up data were collected starting from March 2011 to January 2016. Data were obtained from institutional electronic records and via direct/ telephone contact with patient and or family. For the first two years after treatment 3 monthly and every 6 to 12 months visits were planned thereafter. CT scans or PET/CT scans were scheduled initially at 3 to 6 months after treatment and with longer intervals afterwards. Chest x-rays were done more frequently. Treatment response was evaluated

according to Response Evaluation Criteria In Solid Tumors (RECIST) [13].

Statistical analysis

The primary end point of the study was local control and the secondary endpoint was overall survival and also giving an idea about different tracking methods of CyberKnife®. Local failure was defined as disease progression or recurrence in the originally irradiated tumor with SABR. Thus, if the tumor receiving SABR was stable, smaller or disappeared afterwards, it is thought to be locally controlled. Local control and survival analysis were evaluated with Kaplan-Meier for univariate analysis. For multivariate analysis of local control, Cox regression including all the factors in the univariate analysis were carried out. Statistics were analyzed using SPSS version 15 (IBM,USA) software.

Results

All 29 patients were assessed for survival, but 25 patients could be assessed for local control due to lack of follow-up radiologic imaging information. Median follow up time for local control was 11 months (2.4-39 months). Totally 21 (72.4%) male, 8 (27.6 %) female patients with 30 tumors and a median age of 68 (range, 49-82) were included in this study. One male patient with adenocarcinoma of the lung received SABR for two tumors at different sites of the lung with four months break. Out of 30 tumors, 21 (70%) were primary lung cancer and the rest 9 (30%) were lung metastases from different primary sites. 3 (10.4 %) of the patients had received lung radiotherapy for their lung cancers previously. Also 4 (14 %) patients had lung surgery for lung cancer and 2 (7%) two patients had lung surgery for lung metastases, before SABR. Between metastatic tumors, 4 tumors (44.4%) were from colon primary, 1 (11.1 %) tumor was from lung primary and the rest 4 (44.4%) metastatic tumors derived from different primary sites.

For all study population, 21 (70%) of the tumors were treated with fiducial tracking. Xsight spine and Xsight lung tracking systems was preferred for 5 (16.7%) and 4 (13.3%) tumors, respectively. One patient experienced a pneumothorax when fiducial markers were implanted and needed tube placement. After recovering, this patient received treatment without problem and had complete response.

After SABR, one (3.5 %) patient who received 2 SABR for right and left sided tumors received chemoradiotherapy (56 Gy) for progressive right sided lesion, one year later. Another one (3.5%) patient with complete response of the treated tumor, eleven months after treatment, received stereotactic radiotherapy for a new lung lesion, outside of our hospital. One (3.5 %) patient received imatinib for colon primary and 4 patients (14 %) received chemotherapy. Two patients underwent chemotherapy due to progressive metastatic disease although partial response after SABR. Other patient undergoing chemotherapy had progressive tumor at the irradiated site and the new lung lesions. Although progressive disease this patient is alive and has shortness of breath only after serious activity. Remaining one had two primary sites in lung and colon and adjuvant chemotherapy was given.

Mean and median follow-up times for local control were 14.3 months and 11 months, ranging from 2.4 to 39 months, respectively. Of 25 patients with known follow-up data, local control rates for 1, 2 and 3 years were 82.8%, 82.8% and 55.2 %, respectively. Local control for all SABR patients with known local control data is shown figure 2. Crude rate of locally uncontrolled patients was 4/25 (16 %). Remaining 21 patient's tumors was smaller (7/25) accepted as partial response, stabile (7/ 25) or had complete response (7/ 25) after SABR.

Overall survival rates for primary lung tumor patients for 1, 2 and 3 years were 72.2%, 64.2%, 51.4% and patients with lung metastases for 1 year was 71%, respectively. Mean overall survival time for primary lung cancer patients is 34.3 months and for patients with lung metastasis is 19.7 months after SABR until data collection time, respectively. The Kaplan-Meier OS curve is shown in figure 3a and 3b.

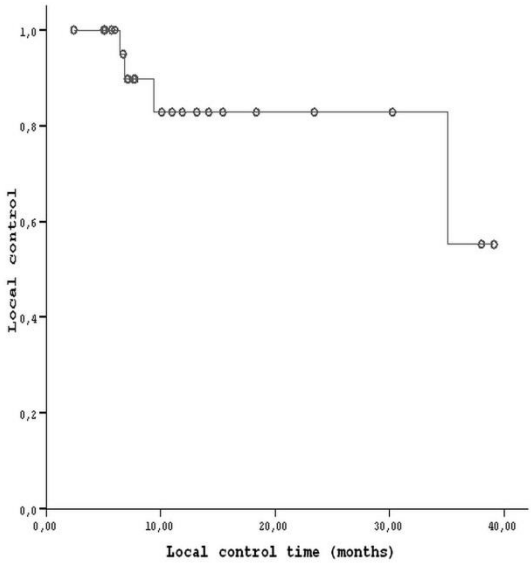


Figure 2: Local control for all SABR patients with known local control data

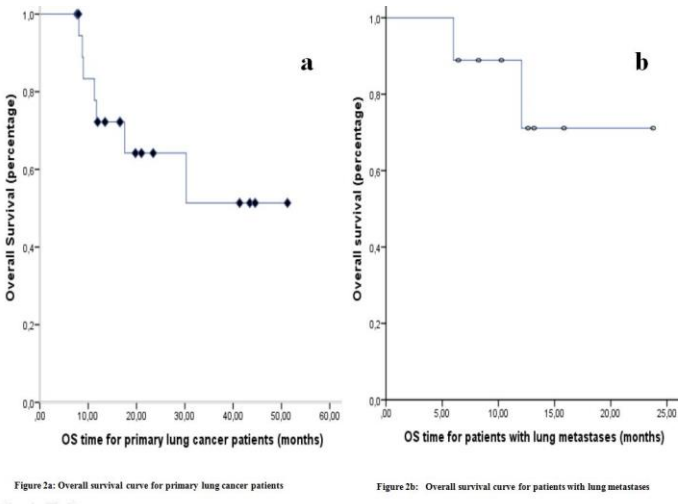


Figure 2a: Overall survival curve for primary lung cancer patients

Figure 2b: Overall survival curve for patients with lung metastases

Figure 3: Overall survival curve for primary lung cancer patients (a), overall survival curve for patients with lung metastases (b)

Table 2 summarizes the univariate analysis of patient, tumor and treatment related characteristics on local recurrence and overall survival. Except gender, none of the factors were statistically significantly associated with local control. Female gender was associated with worse local control (p=0.001) (Table 2). In multivariate analysis for local control including all of the factors, none of the factors was found significantly effective on local control.

Table 2: Results of univariate analysis for local control

Factor	Local Control P value	Overall survival P value
Age (<66 vs.≥66)	0.320	0.841
Gender	0.001	0.073
Tumor greatest dimension (≤24 vs.>24mm.)	0.355	0.307
Tumor volume (≤ 6500mm^{3}vs.>6500mm^3)	0.791	0.922
Pretreatment SUV max. (≤5 vs.>5)	0.333	0.323
Histological diagnosis (yes vs.no)	0.689	0.459
Primary lung cancer vs. lung metastasis	0.651	0.980
PTV dose (BED10, not categorised)	0.340	0.990
Fraction numbers (≤4 vs >4)	0.158	0.182
Tumor follow-up methods(fiducial vs. others)	0.204	0.410
Pretreatment neutrophile/ lymphosite ratio (≤3 vs >3)	0.353	0.794
Peripheral central located	0.464	0.124

Between fiducial implanted patients (21 patients), effect of fiducial numbers on local control was investigated with univariate analysis. There was no relationship between fiducial numbers and local control when categorized (≤3 vs.>3; p=0,547) or not categorized (p=0.983).

We could grade acute side effects retrospectively from patients' records or telephone contact. As an acute side effect we didn't observe Grade 4 or 5 side effects according to Common Toxicity Criteria Version 4. Out of 29 patients, Grade 2 dyspnea was seen in 2 patients (7%) and Grade 3 in 1 patient (3.5%) with all of these patients alive at least 8 months after treatment. One patient (3.5 %) with chronic obstructive lung disease had Grade 2 cough without dyspnea or pain. Apart from these we observed one pneumothorax requiring tube placement at the time of fiducial implanting as mentioned earlier.

Discussion

SABR, with high local control rates, has become a very attractive treatment option not only for early stage primary lung cancer but also for patients having oligometastatic lung tumors [4,5,8]. Due to respiratory motion, conventional radiotherapy has a low conformity and frequently increasing the dose is challenging. CyberKnife®, having ability to tract the tumor and motion is one of the very useful systems for SABR [9-11].

CyberKnife® has a different tumor tracking options. CyberKnife with Synchrony® Tracking System with capacity of real time motion follow-up is capable of delivering high doses of radiation accurately. Compared with linac-based system using breathold technique or respiratory gating, with Synchrony, CyberKnife® gain facility to trace tumour motion in real time which causes reduced margin (typically 3-10 mm.) [14-16]. By means of narrower margins, one can protect adjacent normal tissues more than other systems, resulting in decreased toxicity [17,18].

In our department we use Synchrony® along with Fiducial and Xsight Lung Tracking Systems. For fiducial method, percutaneous transthoracic fiducial implanting by guidance of CT is used [19,20]. Subedi et al. [21] in their phantom study aimed to present data on targeting algorithm accuracy, as a function of image parameters and reported that false locks are more likely to occur with a single fiducial than with multiple fiducials. Therefore, using multiple fiducials helps to be certain about reliable targeting. So, we investigated if the fiducial numbers effect local control or not (≤3 fiducials vs. >3 fiducials) between 16 tumors which treated with fiducial tracking and did not found significant relationship (p=0.547).

Although implanting a gold fiducial allow us to track the tumor accurately, there are some defined side effects related with this intervention like pneumothorax, migration of fiducials and hemorrhage [19,20]. In the current study, out of 21 patients treated with fiducial implanting we saw one pneumothorax requiring tube thoracotomy (5%). This rate is little bit lower than literature as far as we know. Collins et al. reported that after insertion of fiducial markers pneumothorax was seen 25% of the patients [22]. Another stereotactic radiosurgery revealed this rate as 13% [10]. Also, we haven't seen hemorrhage by the time of procedure or afterwards.

For XLTS, similar intensities of digitally reconstructed radiograph (DRR) images match with position of tumor, thus the tumor can be tracked directly. Recently reported lung phantom study from Jung et al. [23], the XLTS was found to have comparable segmentation accuracy with FTTS.

XLTS, is a fully noninvasive method requiring criteria like enough tumor contrast in X-ray images for soft tissue follow up, tumors bigger than 15 mm.in all dimensions and peripheral location of tumor [23].

In the current study XLTS was used for four peripherally located tumors with one of them having a smaller tumor (biggest dimension was 10 mm.) than 15mm. In a study from Korea, done with 58 CyberKnife patients, the authors also reported that they used XLTS for tumors less than 15 mm with high local control rates (1 and 2 years local control rates were 94% and 90.6 %, respectively.) [11].

In our study we have follow-up data for local control for 3 of 4 patients treated with XLTS together with Synchrony. All of these 3 patients were locally controlled at the time of last follow-up.

Another tracking method is Xsight spine by means of which, tumor's position can be assessed based on its location relative to the spine [9]. In Yihang Guo et al.'s study [9] reporting influence of different image guided tracking methods on local control for CyberKnife in lung tumors; they found targets smaller than 15 mL were better controlled with Synchrony than Xsight spine (p=0.038). Whereas in the current study 5 targets between 1.5 and 12.5 mL were treated with Xsight spine tracking and all of them were locally controlled at the end of last control time (3 complete response and 2 partial response).

In this study totally 21 tumors (70%) were treated using Fiducial tracking and we have local control data for 17 of them. 4 tumors were not controlled with SABR and actuarial local control rates for Fiducial tracking ones was 74.6% and 74.6% for 1 and 2 years. Although these were lower than local control rates of tumors tracked with Xsight lung and Xsight spine (all 8 patients were locally controlled), there was not statistically difference between tracking methods.

Between other factors investigated for the effect on local control, only gender was the statistically significantly effective one (p=0.001) and males were doing better than females. In this study we have 6 tumors from female patients and 19 tumors from 18 male patients with known local control follow-up data. Again for overall survival there was a trend towards better survival for males (44.4% vs. 79.4 % at one year) similarly. Whereas in the literature there are studies with both

stereotactic radiotherapy and conventional methods reporting better survival with female patients for lung cancer [24]. In addition, Shibamoto et al. [25], in their multicenter study with stage I NSCLC patients found both overall survival and local control results superior in females. Our study includes not only primary lung cancer but also lung metastatic patients, this heterogeneity and small numbers of patients could be probable explanations for this result. In addition we couldn't see any relationship between tumor's greatest dimension or tumor volume and local control even the fact that we treated tumors with dimension bigger than 50 mm. But there is studies in the literature defining tumor diameter as one of the most significant factors affecting outcome after SABR [26,27].

Dose effect on overall survival and local control was well described in the literature for both early stage primary lung cancer and patients with lung metastasis [24,28]. Onishi et al. in their study with stage I NSCLC patients found that patients receiving a dose greater than BED 10Gy of 100 Gy or more had significantly better overall survival and local control rates than patients receiving lower doses. In our study median BED 10Gy was 105.6 and 4 patients (13.3%) with centrally located tumors had received doses lower than BED 10Gy of 100 Gy. These patients' given doses as BED10Gy were in increasing order; 59.5, 83.3, 86.4 and 94.1 Gy. We couldn't find significant effect of BED10Gy on local control; most probable reason is small sample size.

Due to lower BED10Gy, one can expect lower local control rates with increasing fraction numbers. In our study the most frequently used fraction scheme was 48 Gy in 4 fractions (BED10Gy of 105.6 Gy) with 17 tumors (57%). When we compared patients receiving treatment with bigger than 4 fractions to patients receiving smaller or equal to 4 fractions, although not significant local control rates for 1 year were 62.5% and 92.3%, respectively (p=0.158). A single institution study using CyberKnife® with XLTS from Bibault et al. [10] also showed significantly better local control rates with 3 fractions than with more than 3 fractions (p=0.006).

Treatment was well tolerated and all patients completed the planned course of SABR. Apart from grade 2 and grade 3 dyspnea in 2 and 1 patients, respectively and one pneumothorax we didn't see another severe acute side effect. All of the patients were alive at least 6 months after treatment. Our local control rates for 1,2 and 3 years were 82.8%, 82.8%, 55.2% and overall survival rates for primary lung tumor patients for 1, 2 and 3 years were 72.2%, 64.2%, 51.4% and patients with lung metastases for 1 year was 71%, respectively. First 2 years local control rates look close to literature which is between 83% and 93% while survival rates look fairly well if we take into account the vulnerability of these population and literature again [29-31].

Main limitation of this study was small patient numbers, heterogeneous patient population including both primary lung cancer and lung metastatic patients and retrospective data collection. We thought small patient numbers was the potential main reason for some nonsignificant values of univariate analysis. Otherwise this small study with all patients' treatment procedure checking by the same physician, may give some idea about utilizing different tracking ways for CyberKnife®. As in literature, SABR with CyberKnife® improves survival and local control even for central located and metastatic lung tumors with limited side effects.

Conclusion

Stereotactic ablative radiotherapy with CyberKnife® for the treatment of primary and metastatic lung tumors is a reliable and efficient treatment method for medically inoperable patients. To evaluate tracking methods of CyberKnife® system more comprehensive studies are awaited.

References

1. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer (Version 3.2014) (2014). Availableform: http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf
2. Wu AJ, Williams E, Modh A, Foster A, Yorke E, Rimner A, et al. Dosimetric predictors of esophageal toxicity after stereotactic bodyradiotherapy for central lung tumors. Radiotherapy and Oncology. 2014;112:267-71.
3. Dosoretz DE, Katin MJ, Blitzer PH, Rubenstein JH, Galmarini DH, Garton GR, et al. Medically inoperable lung carcinoma: theroleofradiationtherapy. Semin Radiat Oncol. 1996;98-104.
4. Lagerwaard FJ, Haasbeek CJ, Smit EF, Slotman BJ, Senan S. Outcomes of risk adapted fractionated stereotactic radiotherapy for stage I non-small-cell lung cancer. Int J Radiat Oncol Biol Phys. 2008;70(3):685-92.
5. Hayashi S, Tanaka H, Kajiura Y, Ohno Y, Hoshi H. Stereotactic body radiotherapy for very elderly patients (age, greater than or equal to 85 years) with stage I non-small cell lung cancer. Radiat Oncol. 2014;9:138.
6. Louie AV, Rodrigues G, Hannouf M, Lagerwaard F, Palma D, Gregory S, et al. Withholding stereotactic radiotherapy in elderly patients with stage I nonsmall cell lung cancer and co-existing COPD is not justified: outcomes of a Markov model analysis. Radiother Oncol. 2011;99(2):161-5.
7. Shirvani SM, Jiang J, Chang JY, Welsh JW, Gomez DR, Swisher S, et al. Comparative effectiveness of 5 treatment Phys strategies for early-stage non-small cell lung cancer in the elderly. Int J Radiat Oncol Biol. 2012;84(5):1060-70.
8. Thibault I, Poon I, Yeung L, Erler D, Kim A, Keller B, et al. Predictive Factors for Local Control in Primary and Metastatic Lung Tumours after Four to Five Fraction Stereotactic Ablative Body Radiotherapy: A Single Institution's Comprehensive Experience. Clinical Oncology. 2014;26:713-9.
9. Guo Y, Zhuang H, Zhao L, Yuan Z, Wang P. .Influence of different image-guided tracking methods upon the local efficacy of CyberKnife treatment in lung tumors. Thoracic Cancer. 2015;6:255-9.
10. Bibault JE, Prevost B, Dansin E, Mirabel X, Lacornerie T and Lartigau E. Image-Guided Robotic Stereotactic Radiation Therapy with Fiducial-Free Tumor Tracking for Lung Cancer. Radiation Oncology. 2012;7:102.
11. Jung IH, Song SY, Jung J, Cho B, Kwak J, Je HU et al. Clinical outcome of fiducial-less CyberKnife radiosurgery for stage I non-small cell lung cancer, Radiat Oncol J. 2015;33(2):89-97.
12. Radiation Therapy Oncology Group. RTOG 0236. A phase II trial of stereotactic body radiation therapy (SBRT) in the treatment of patients with medically inoperable stage I/II non-small cell lung cancer. [Internet] 2004 [updated 9 September 2009; cited 2 August2015].Availableat:https://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx? study¼0236.
13. Therasse P, Arbuck SG, Eisenhauer EA, Wanders J, Kaplan RS, Rubinstein L, et al. New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of J. Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. Natl. Cancer Inst. 2000;92:205–16.
14. Collins BT, Vahdat S, Erickson K, Collins SP, Suy S, Yu X, et al. Radical cyberknife radiosurgery with tumor tracking: an effective treatment for inoperable small peripheral stage I non-small cell lung cancer. J Hematol Oncol. 2009;2:1.
15. Hoogeman M, Prevost JB, Nuyttens J, Pöll J, Levendag P, Heijmen B. Clinical accuracy of the respiratory tumor tracking system of the cyberknife: assessment by analysis of log files. Int J Radiat Oncol Biol Phys. 2009;74:297–303.
16. Prevost JB, Voet P, Hoogeman M, Praag J, Levendag P, Nuyttens JJ. Four-dimensional stereotactic radiotherapy for early stage non-small cell

lung cancer: a comparative planning study. Technol Cancer Res Treat. 2008;7:27–33.
17. Derycke S, Van Duyse B, De Gersem W, De Wagter C, De Neve W. Non-coplanar beam intensity modulation allows large dose escalation in stage III lung cancer. Radiother Oncol. 1997;45:253–61.
18. Dong P, Lee P, Ruan D, Long T, Romeijn E, Low DA, et al. 4pi noncoplanar stereotactic body radiation therapy for centrally located or larger lung tumors. Int J Radiat Oncol Biol Phys. 2013;86:407–13.
19. Prevost JB, Nuyttens JJ, Hoogeman MS, Pöll JJ, van Dijk LC, Pattynama PMT, et al. Endovascular coils as lung tumour markers in real-time tumour tracking stereotactic radiotherapy: preliminary results. Eur Radiol. 2008;18:1569-76.
20. Bhagat N, Fidelman N, Durack JC, Collins J, Gordon RL, LaBerge JM, et al. Complications associated with the percutaneous insertion of fiducial markers in the thorax. Cardiovasc Intervent Radiol. 2010;33:1186-91.
21. Subedi G, Karasick T, Grimm J, Jain S, Xue J, Xu Q, et al. Factors that may determine the targeting accuracy of image-guided radiosurgery. Med Phys. 2015; 42(10):6004-10.
22. Collins BT, Erickson K, Reichner CA, Collins SP, Gagnon GJ, Dieterich S, et al. Radical stereotactic radiosurgery with real-time tumor motion tracking in the treatment of small peripheral lung tumors. Radiat Oncol. 2007;2:39.
23. Jung J, Song SY, Yoon SM, Kwak J, Yoon K, Choi W, et al. Verification of accuracy of CyberKnife tumor-tracking radiation therapy using patient-specific lung phantoms. Int J Radiat Oncol Biol Phys 2015;92(4):745-53.
24. Factor OB, Vu CC, Schneider JG, Witten MR, Schubach SL, Gittleman AE, et al. Stereotactic body radiation therapy for stage I non-small cell lung cancer: a small academic hospital experience. Frontiers in Oncology. 2014;(4)287:2-5.
25. Shibamot Y, Hashizume C, Baba F, Ayakawa S, Manabe Y, Nagai A, et al. Stereotactic body radiotherapy using a radi obiology-based regimen for stage I non small cell lung cancer: a multicenter study. Cancer. 2012;118(8):2078–84.
26. Ohri N, Werner-Wasik M, Grills IS, Belderbos J, Hope A, Yan D, et al. Modeling local control after hypofractionated stereotactic body radiation therapy for stage I non-small cell lung cancer: a report from the elekta collaborative lung research group. Int J Radiat Oncol Biol Phys. 2012;84:379-84.
27. Matsuo Y, Shibuya K, Nagata Y, Takayama K, Norihisa Y, Mizowaki T, et al. Prognostic factors in stereotactic body radiotherapy for non-small-cell lung cancer. Int J Radiat Oncol Biol Phys. 2011;79:1104-11.
28. Wang Z, Kong QT, Li J, Wu XH, Li B, Shen ZT, et al. Clinical outcomes of cyberknife stereotactic radiosurgery for lung metastases. J Thorac Dis. 2015;7(3):407-12.
29. Crabtree TD, Puri V, Robinson C, Bradley J, Broderick S, Patterson GA, et al. Analysis of first recurrence and survival in patients with stageI non-smallcell lung cancer treated with surgical resection or stereotactic radiationtherapy. J Thorac Cardiovasc Surg. 2014;147(4):1183–91.
30. Timmerman R, Paulus R,Galvin J, Michalski J, Straube W, Bradley J, et al. Stereotactic body radiationtherapy for inoperable early stage lungcancer. JAMA. 2010;303(11):1070–6.
31. Fakiris AJ, McGarry RC, Yiannoutsos CT Papiez L, Williams M, Henderson MA, et al. Stereotactic body radiation therapy for early-stage non-small-cell lung carcinoma: four-year results of a prospective phase II study. Int J Radiat Oncol Biol Phys. 2009;75(3):677–82.

J Surg Med. 2018;2(3):330-333.
DOI: 10.28982/josam.441711

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

The clinic importance of bilirubin parameters in ankylosing spondylitis: Case control study

Ankilozan spondilitte bilirubin parametrelerinin klinik önemi: Vaka kontrol çalışması

Tuba Tülay Koca [1], Gözde Yıldırım Çetin [2], Hasan Göğebakan [2], Vedat Nacitarhan [1]

[1] Sütçü İmam University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Kahramanmaraş, Turkey
[2] Sütçü İmam University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Kahramanmaraş, Turkey

ORCID ID of the authors:
TTK: 0000-0002-4596-858X
GYÇ: 0000-0001-9680-7535
HG: 0000-0002-3448-4838
VN: 10000-0003-1756-8615

Corresponding author / Sorumlu yazar:
Tuba Tülay Koca
Address / Adres: Sütçü İmam Üniversitesi, Fiziksel Tıp ve Rehabilitasyon Bölümü, Kahramanmaraş, Türkiye
E-mail: tuba_baglan@yahoo.com

Ethics Committee Approval: The local ethic committe approval (No: 178) was taken.
Etik Kurul Onayı: Yerel etik kurul onayı (No: 178) alındı.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 09.07.2018
Accepted / Kabul Tarihi: 26.07.2018
Published / Yayın Tarihi: 27.07.2018

Abstract

Aim: Ankylosing spondylitis (AS) is a chronic disease featuring axial changes, peripheral arthritis and systemic involvement. AS is not only characterized by the strongest genetic contribution for any complex rheumatological disease but is also influenced by environmental and immunological factors. Various proinflammatory cytokines such as tumor necrosis factor (TNF), interleukin- (IL-) 1, IL-6, IL17/28 are probably involved in AS pathogenesis. Recent years IL -23 / IL-17 pathway in the disease pathogenesis has been shown. Bilirubin (Bb) was known to be the end product of hem catabolic pathway, but it was the subject of various studies with antioxidant, anti-inflammatory and immunomodulatory properties in the last decade. Here, the clinic importance of serum Bb parameters in AS patients has been analyzed.

Methods: The study designed as case-control. One hundred (N=100) patients with axial AS diagnosed by 2010 Assesment in Ankylosing Spondylitis International Society (ASAS) Classification Criteria were included to the study. Control group was consisted of 75 patients of similar age, gender and BMI. Participants' age, gender, body mass index (BMI), disease acitivity scores and laboratory data were recorded from the hospital data. Disease activity evaluated by Bath Ankylosing spondylitis disease activity index (BASDAI), Bath Ankylosing spondylitis functional index (BASFI) and Ankylosing spondylitis disease activity score-C-reactive protein (ASDAS_CRP). For these three scores, automatic calculation formulas were used on Internet. ASDAS_CRP>3.5 were accepted as cut-off value for high disease activity. Serum direct Bb, indirect Bb, total Bb, aspartat aminotransferase (AST), alanin aminotransferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), gamma glutamyl transferase (GGT), amylase, lipase, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) values were recorded from the hospital records.

Results: The study included 100 AS patients at mean age of 37.9 ± 12 years, 75 controls at mean age of 39.2 ± 5.2 years. There was no significant difference between the two groups in terms of age ($p = 0.12$), gender ($p = 0.32$), and BMI ($p = 0.067$). In the AS group, ESR ($p< 0.001$), CRP ($p < 0.001$), uric acid ($p<0.001$) was significantly higher whereas direct Bb ($P = 0.016$) were significantly lower than controls. In correlation analysis, Bb parameters and disease activity parameters were negatively correlated with each other. When we divided the group according to ASDAS_CRP> 3.5, direct Bb ($p = 0.020$), total Bb ($p = 0.029$) and AST ($p = 0.004$) were significantly lower in high activity group ($N = 25$) and ESR ($p < 0.001$) was significantly higher.

Conclusion: The direct Bb in patients with AS were found significantly low and negatively correlated with disease activity, this supports the role of oxidative stress in AS disease pathogenesis. Bb can be used as a biomarker in diagnosis and follow up in AS disease.

Keywords: Ankylosing spondylitis, Bilirubin, Inflammation, Oxidative stress

Öz

Amaç: Ankilozan spondilit (AS) aksiyal değişiklikler, periferik artrit ve sistemik tutulum içeren kronik bir hastalıktır. AS herhangi bir komplike romatizmal hastalık gibi sadece en güçlü genetik katkı ile karakterize edilmez, aynı zamanda çevresel ve immünolojik faktörlerden de etkilenir. Tümör nekroz faktörü (TNF), interlökin- (IL-) 1, IL-6, IL17 / 28 gibi çeşitli proinflamatuar sitokinler muhtemelen AS patogenezinde rol oynar. Son yıllarda hastalık patogenezinde IL-23 / IL-17 yolu gösterilmiştir. Bilirubin (Bb) hem katabolik yolun son ürünüdür hem de son on yılda antioksidan, antienflamatuar ve immünmodülatör özellikleri olan çeşitli çalışmaların konusu olmuştur. Burada AS hastalarında serum Bb parametrelerinin klinik önemi analiz edilmiştir.

Yöntemler: Çalışma vaka-kontrol olarak planlandı. Uluslar arası Ankilozan Spondilit Topluluğu 2010 Sınıflandırma Kriterleri'ne göre (ASAS) aksiyal AS tanısı almış 100 hasta (N = 100) çalışmaya dahil edildi. Kontrol grubu benzer yaş, cinsiyet ve VKİ olan 75 kişiden oluşmaktaydı. Katılımcıların yaş, cinsiyet, vücut kitle indeksi (BMI), hastalık skoru puanları ve laboratuvar verileri hastane verilerinden kaydedildi. Hastalık aktivitesi Bath Ankilozan Spondilit Hastalığı Aktivite İndeksi (BASDAI), Bath Ankilozan Spondilit Fonksiyonel İndeks (BASFI) ve Ankilozan Spondilit Hastalığı Aktivite skoru-C-reaktif protein (ASDAS_CRP) ile değerlendirildi. Bu üç puan için, internette otomatik hesaplama formülleri kullanıldı. ASDAS_CRP> 3,5 yüksek hastalık aktivitesi için eşik değer olarak kabul edildi. Serum direkt Bb, indirekt Bb, total Bb, aspartat aminotransferaz (AST), alanin aminotransferaz (ALT), alkalen fosfataz (ALP), laktat dehidrojenaz (LDH), gama glutamil transferaz (GGT), amilaz, lipaz, eritrosit sedimentasyon hızı (ESR) ve C-reaktif protein (CRP) değerleri hastane kayıtlarından kaydedildi.

Bulgular: Çalışmaya yaş ortalaması 37,9 ± 12 yıl olan 100 AS hastası, yaş ortalaması 39,2 ± 5,2 yıl olan 75 kontrol alındı. İki grup arasında yaş ($p = 0.12$), cinsiyet ($p = 0.32$) ve VKİ ($p = 0.067$) açısından anlamlı fark yoktu. AS grubunda ESR ($p < 0.001$), CRP ($p< 0.001$), Bb ($p = 0.016$) anlamlı düşük; ürik asit ($p< 0.001$) kontrollerden anlamlı olarak yüksek bulundu.

Korelasyon analizinde, Bb parametreleri ve hastalık aktivite parametreleri birbirleriyle negatif korelasyon göstermiştir. ASDAS_CRP> 3,5'e göre gruplandırıldığında, direkt Bb ($p = 0,020$), total Bb ($p = 0,029$) ve AST ($p = 0,004$) yüksek aktivite grubunda ($N = 25$) anlamlı düşük; ESR ($p <0,001$) anlamlı olarak daha yüksekti.

Sonuç: AS'li hastalarda direk Bb, hastalık aktivitesi ile negatif ilişkili ve düşük idi, bu sonuç AS hastalık patogenezinde oksidatif stresin rolünü desteklemektedir. Direk Bb, AS hastalığında tanı ve izlemede biyobelirteç olarak kullanılabilir.

Anahtar kelimeler: Ankilozan spondilit, Bilirubin, İnflamasyon, Oksidatif stres

How to cite / Atıf için: Koca TT, Çetin GY, Göğebakan H, Nacitarhan V. The clinic importance of bilirubin parameters in ankylosing spondylitis: Case control study. J Surg Med. 2018;2(3):330-333.

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory arthritis that causes insidious, progressive, axial and peripheral joint involvement lead to physical disability. The presence of genetic predisposition and autoantibodies leads to autoimmune and autoinflammatory etiology. Microbiota and biomechanical stress focus on the initiation and maintenance of inflammation for environmental factors that trigger genetic [1]. Although the underlying mechanism of AS pathogenesis is not yet elucidated, it is known that human leucocyte antigen (HLA)-B27 is responsible for a significant increase in the risk of disease development. Current treatment includes non-steroidal anti-inflammatory drugs (NSAIDs) and disease modifying antirheumatismal drugs (DMARD). In recent years, the prominent effect of interleukin (IL) -23 / IL-17 on the pathogenesis of disease and the use of targeted therapies have been demonstrated [2].

Bilirubin (Bb) is a tetrapyrrole which is the product of hem destruction. Majority of the Bb is obtained from hemoprotein breakdown and a smaller part from the hemoglobin breakdown. In serum, Bb is measured as both direct and total Bb. Excessive production or a defect in the intake or conjugation can lead to a sudden hyperbilirubinemia. In its indirect form, Bb dissolves in water and sticks to the brain, sclera and mucous membranes. Attempts are made to reduce this effect by ensuring the albumin attaches to the plasma. Bb has been shown to be an essential antioxidant both in vitro and in vivo. Bb reacts with reactive oxygen species to form hydrophilic products and they are excreted by the urine. Oxidative metabolites of Bb, biopyrrins are sensitive urinary markers of oxidative stress [3].

The aim of the present study was to examine the clinic importance of Bb parameters and its association with disease activity in AS.

Materials and methods

The study designed as case-control. One hundred (N=100) patients with axial AS diagnosed by 2010 Assessment in Ankylosing Spondylitis International Society (ASAS) Classification Criteria were included to the study. Control group was consisted of 75 patients of similar age, gender and BMI. Participants' age, gender, body mass index (BMI), disease activity scores and laboratory data were recorded from the hospital data.

Disease activity evaluated by Bath Ankylosing spondylitis disease activity (BASDAI), Bath Ankylosing spondylitis functional index (BASFI) and Ankylosing spondylitis disease activity score-C-reactive protein (ASDAS_CRP). For these three scores, automatic calculation formulas were used on Internet. ASDAS_CRP>3.5 were accepted as cut-off value for high disease activity.

Serum direct Bb, indirect Bb, total Bb, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), gamma glutamyl transferase (GGT), amylase, lipase, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) values were recorded from the hospital records. The acute phase reactants (ESR and CRP) were used for disease activity. Patients with other inflammatory rheumatological disease, malignancy, infection, primary liver disease and a history of hepatobiliary surgery were not included in the study.

Statistical analysis

Analyses were performed using Statistical Package for the Social Sciences 22 (IBM SPSS for Windows version 22, IBM Corporation, Armonk, New York, USA). Continuous data were presented as mean±SD and categorical variables were summarized as percentages. Kolmogorov Smirnov test was used for the evaluation of normal distribution. Comparisons between groups were made using Chi-square tests for categorical variables, independent samples Student's t tests for normally distributed continuous variables and Mann-Whitney U tests when the distribution was skewed. Spearman test is used for correlation analysis. A p value <0.05 was considered statistically significant. As a result of the power analysis performed, the minimum number of subjects required in each group was determined as 65 so that the difference of 0.05 units between the two group averages could be meaningful. Type 1 error = 0.01, power of test: 0.08.

Results

The study included 100 AS patients at mean age of 37.9 ± 12 years, 75 controls at mean age of 39.2 ± 5.2 years. There was no significant difference between the two groups in terms of age (p = 0.12), gender (p = 0.32), and BMI (p = 0.067). The descriptive and analytical data for the study are summarized in Table 1. In the AS group, ESR (p <0.001), CRP (p < 0.001), and uric acid (p < 0.001) were significantly higher whereas direct Bb (p = 0.016) was lower than control (Figure 1).

Table 1: Descriptive and analytic data of the groups

	AS (N=100) mean±std	Control (N=75) mean±std	P
Age (year)	37.9±12	39.2±5.2	0.12
Gender (female/male)	29/69	12/63	0.078
BMI (kg/m^2)	27.0±4.5	26.7±6.9	0.08
ESR (mm/h)*	29.5±18.3	12.3±10	<0.001
CRP (mg/dL)*	8.2±9.6	1.1±1.6	<0.001
Direct Bb* (0.1-0.4 mg/dL)	0.166±0.077	0.197±0.061	0.016
İndirect Bb (0.2-0.7 mg/dL)	0.426±0.332	0.339±0.174	0.068
TotalBb (0.2-1.2 mg/dL)	0.594±0.360	0.537±0.226	0.302
Uric acid* (mg/dL)	5.5±1.3	4.2±1.3	<0.001
AST (0-40 UI/L)	25±7.6	23.5±5.3	0.64
ALT (0-56 UI/L)	25.2±17.1	24.4±10.1	0.63
GGT (0-65 UI/L)	28±15.1	27.4±12.3	0.83
ALP (25-100 IU/L)	79.1±20.6	79.2±24.1	0.25
LDH (U/L)	184.1±32.3	167.4±28.1	0.08
Amylase (U/L)	61.8±24.2	60±17.6	0.34
Lipase (U/L)	32.9±12.6	27±15.4	0.06
BASDAI (0-10 cm)	4.1±2.0	-	
BASFI (0-10 cm)	3.5±2.3	-	
ASDAS_CRP	2.7±1	-	

BMI: body mass Index, Bb: bilirubin, ESR: Erythrocytes sedimentation rate, CRP: C-reactive protein, BASDAI: Bath Ankylosing spondylitis disease activity Index, ASDAS_CRP: Ankylosing spondylitis disease activity score-C-reactive protein, BASFI: Bath Ankylosing spondylitis functional index, * statistically significance, p<0.05

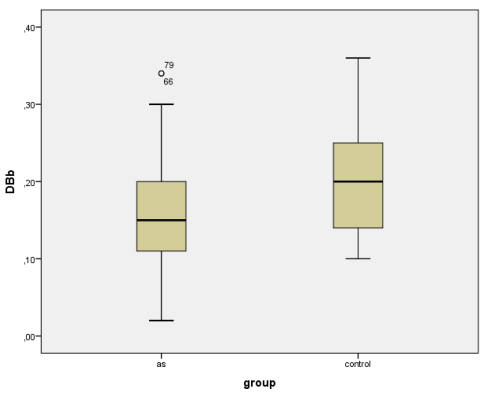


Figure 1: Boxplot of direct Bb (DBb) according to the groups

In correlation analysis, Bb parameters and disease activity parameters were negatively correlated with each other (Table 2). When we divided the group according to ASDAS_CRP> 3.5, direct Bb (p = 0.020) (Figure 2), total Bb (p = 0.029) and AST (p = 0.004) were significantly lower in the high activity group (N = 25); whereas ESR (p < 0.001) was significantly higher than inactive group (N=75).

Table 2: Correlation analysis of bilirubin parameters with disease activity scores

	rho	P
Direct Bb-CRP	-0.299	0.013
Direct Bb-ASDAS_CRP	-0.357	0.020
Direct Bb-BASFI	-0.702	<0.001
Indirect Bb-ESR	-0.315	0.001
Indirect Bb-ASDAS_CRP	-0.312	0.045
Indirect Bb-BASFI	-0.615	<0.001
Total Bb-ESR	-0.214	0.021
Total Bb-ASDAS_CRP	-0.357	0.020
Total Bb-BASFI	-0.684	<0.001

Bb: bilirubin, ESR: Erythrocytes sedimentation rate, CRP: C-reactive protein, BASDAI: Bath Ankylosing spondylitis disease activity index, ASDAS_CRP: Ankylosing spondylitis disease activity score-C-reactive protein, BASFI: Bath Ankylosing spondylitis functional index, * statistically significance, p<0.05.

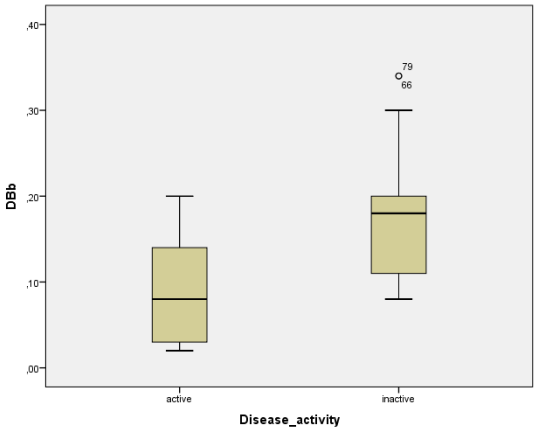


Figure 2: Boxplot of Direct Bb (DBb) according to the disease activity in AS group

Discussion

Spondyloarthropathies (SpA) describe a group of inflammatory diseases characterized by inflammation involving axial joints and / or peripheral arthritis, enthesitis, and dactilitis. Disease development is determined by the presence of genes, especially HLA-B27. In animal models, the direct effect of HLAB27 on disease development has been demonstrated. The propensity of HLAB27 to be expressed in the natural immune system and to form different structural forms that can lead to activation has been discovered [4]. Genetic studies have specifically identified the immunological function associated with gene polymorphism that controls interleukin (IL) -23 / IL-17 pathway. The efficacy of IL-17 inhibitors in SpA patients supports the importance of this pathway [5]. The demonstration of microscopic gout inflammation in the vast majority of SpA patients supports the pathogenic effect of commensal microbiota [6,7].

AS is the prototype of SpA and is characterized by spinal inflammation that starts with sacroiliac joints and results in joint ankylosis. The genetic relationship between HLA-B27 and inflammatory cytokine pathways has been shown in a number of studies. Inflammatory cytokines, tumor necrosis factor (TNF), interleukin- (IL-) 1, IL-6, and IL-23 / IL-17 are prominent. In particular, IL-17 plays a dominant role in the inflammatory and proliferative pathway [8-10]. Early diagnosis of the disease is important in terms of treatment effectiveness. Since 1984 modified New York criteria used in the diagnosis of the disease was unsuccessful in early period of the disease, ASAS developed new criteria: (1) A predominantly axial disease, AS and non-radiographic axial SpA including termed axial SpA; (2) New criteria for peripheral SpA have been developed in 2010. Criteria developed by ASAS for axial SpA are an important step in early diagnosis and disease control, while the non-radiographic axial SpA clinical process is still unclear [11].

Serum total Bb is routinely used in the identification of hepatobiliary and hemolytic diseases. Especially hepatocyte damage including acute hepatitis, cholestatic problems, genetic diseases related to Bb uptake or secretion, hemolytic diseases lead to increase in blood total Bb in adults. In the last decade, Bb, a product of hem degradation, has begun to attract attention. The benefits of increased Bb are supported by antioxidant, anti-inflammatory and immunosuppressive properties in both animal and in vitro experiments. The most well-known immunomodulatory effect that suppresses inflammation is its redox (antioxidative) capacity [12-16]. Clinical trials have been associated high Bb with low risk of myocardial infarction, coronary artery disease, stroke, lung cancer, diabetes, schizophrenia, and chronic obstructive lung disease [17-19]. For the patients with psoriasis, a negative relation was found between total Bb values and inflammatory parameters [20]. Peng et al. [21] detected lower direct Bb values and higher CRP values when assessing neurogenic inflammation in patients with migraine similary with our study. Up to date there is no study examining the Bb parameters in AS in the literature.

Endoplasmic retinaculum (ER) stress, oxidative stress, and inflammatory responses contain common major defense networks for the rescue and adaptation of cells from stressful situations caused by biochemical, physiological and pathological stimuli. In many current publications we see that oxidative stress and inflammation are related to the onset and progression of a wide variety of diseases [22]. In chronic inflammatory rheumatological diseases various biomarkers have been the subjects of clinical trials [23]. New cheap and practical biomarkers which correctly show chronic inflammation are needed in the clinical follow up of the diseases [24]. Liver functional tests in AS have been the subject of some studies. Robinson et al. [25] observed abnormal high GGT and ALP levels as secondary to inflammation in AS patients. İn the study by Seehan et al. [26] they similarly found abnormal high levels of ALP unrelated with drug therapy or disease activity in AS patients. They suggest that bone is the source of the increased ALP. İn our study serum GGT, ALP levels was found similar with control group.

Additionally, we found that direct Bb was significantly lower in AS group. All Bb parameters were negatively correlated with disease activity scores. We can say that the chronic inflammation and oxidative stress involved in the pathogenesis of AS increasing with the severity of the disease. This is supported by the low Bb parameters that are indicative of oxidative stress. Often, even if the disease is active in AS patients, the elevation of acute phase reactants does not correlate with clinical relevance. Measurement of serum Bb parameters can be useful in this case as practical and easy biomarkers. Additionally the serum uric acid level was found significantly

higher in AS as expected. İn most of chronic inflammatory rheumatological diseases we find high uric acid results depending on the high inflammation. Hyperuricemia is not only a risk factor for gout but also an independent determinant of hypertension, diabetes, and chronic kidney diseases. Also low-grade inflammation is found positively associated with hyperuricemia [27].

Limitation of the study

In chronic inflammatory rheumatological diseases the disease itself and the use of NSAIDs, biological and non-biological DMARDs may effect liver enzymes included serum Bb parameters. It is the limit of study not considering the medication used by patients. Smoking, anemia may also affect the Bb values. Additionally we see that the patients in the study group mostly were in inactive period according to ASDAS_CRP results.

Conclusion

The direct Bb in patients with AS were found significantly low and negatively correlated with disease activity, this supports the role of oxidative stress in AS disease pathogenesis. Direct Bb can be used as a biomarker in diagnosis and follow up in AS disease.

References

1. Smith JA. Update on ankylosing spondylitis: current concepts in pathogenesis. Curr Allergy Asthma Rep. 2015 Jan;15(1):489. doi: 10.1007/s11882-014-0489-6.
2. Jethwa H, Bowness P. The interleukin (IL)-23/IL-17 axis in ankylosing spondylitis: new advances and potentials for treatment. Clin Exp Immunol. 2016 Jan;183(1):30-6. doi: 10.1111/cei.12670.
3. Shibama S, Ugajin T, Yamaguchi T, Yokozeki H. Bilirubin oxidation derived from oxidative stress is associated with disease severity of atopic dermatitis in adults. Clin Exp Dermatol. 2018 Jun 4. doi: 10.1111/ced.13674.
4. Vanaki N, Aslani S, Jamshidi A, Mahmoudi M. Role of innate immune system in the pathogenesis of ankylosing spondylitis. Biomed Pharmacother. 2018 May 28;105:130-43. doi: 10.1016/j.biopha.2018.05.097.
5. Chyuan IT, Chen JY. Role of Interleukin- (IL-) 17 in the Pathogenesis and Targeted Therapies in Spondyloarthropathies. Mediators Inflamm. 2018 Feb 12;2018:2403935. doi: 10.1155/2018/2403935.
6. O'Rielly DD, Zhai G, Rahman P. Expression and Metabolomic Profiling in Axial Spondyloarthritis. Curr Rheumatol Rep. 2018 Jun 27;20(8):51. doi: 10.1007/s11926-018-0756-y.
7. Syrbe U, Baraliakos X. [Spondyloarthritis]. Z Rheumatol. 2018 May 16. doi:10.1007/s00393-018-0475-9. [Epub ahead of print] Review.
8. Yeremenko N, Paramarta JE, Baeten D. The interleukin-23/interleukin-17 immune axis as a promising new target in the treatment of spondyloarthritis. Curr Opin Rheumatol. 2014 Jul;26(4):361-70. doi: 10.1097/BOR.0000000000000069.
9. Rabelo CF, Baptista TSA, Petersen LE, Bauer ME, Keiserman MW, Staub HL. Serum IL-6 correlates with axial mobility index (Bath Ankylosing Spondylitis Metrology Index) in Brazilian patients with ankylosing spondylitis. Open Access Rheumatol. 2018 Apr 30;10:21-5. doi: 10.2147/OARRR.S130176.
10. Raychaudhuri SP, Raychaudhuri SK. IL-23/IL-17 axis in spondyloarthritis-bench to bedside. Clin Rheumatol. 2016 Jun;35(6):1437-41. doi:10.1007/s10067-016-3263-4.
11. Raychaudhuri SP, Deodhar A. The classification and diagnostic criteria of ankylosing spondylitis. J Autoimmun. 2014 Feb-Mar;48-49:128-33. doi: 10.1016/j.jaut.2014.01.015.
12. Dani C, Poggi C, Pratesi S. Bilirubin and oxidative stress in term and preterm infants. Free Radic Res. 2018 May 16:1-151. doi: 10.1080/10715762.2018.1478089.
13. Wei J, Zhao H, Fan G, Li J. Bilirubin treatment suppresses pulmonary inflammation in a rat model of smoke-induced emphysema. Biochem Biophys Res Commun. 2015 Sep 18;465(2):180-7. doi: 10.1016/j.bbrc.2015.07.133.
14. Jangi S, Otterbein L, Robson S. The molecular basis for the immunomodulatory activities of unconjugated Bb. Int J Biochem Cell Biol. 2013;45(12):2843-51. doi: 10.1016/j.biocel.2013.09.014.
15. Jangi S, Otterbein L, Robson S. The molecular basis for the immunomodulatory activities of unconjugated bilirubin. Int J Biochem Cell Biol. 2013 Dec;45(12):2843-51. doi: 10.1016/j.biocel.2013.09.014. Epub 2013 Oct 19.
16. Khan NM, Poduval TB. Immunomodulatory and immunotoxic effects of bilirubin: molecular mechanisms. J Leukoc Biol. 2011 Nov;90(5):997-1015. doi: 10.1189/jlb.0211070. Epub 2011 Aug 1.
17. Horsfall LJ, Rait G, Walters K, Swallow DM, Pereira SP, Nazareth I, et al. Serum bilirubin and risk of respiratory disease and death. JAMA. 2011;305(7):691–7.
18. Temme EH, Zhang J, Schouten EG, Kesteloot H. Serum bilirubin and 10-year mortality risk in a Belgian population. Cancer Causes Control. 2001;12(10):887–94.
19. Akboga MK, Canpolat U, Sahinarslan A, Alsancak Y, Nurkoc S, Aras D, Aydogdu S, Abaci A. Association of serum total bilirubin level with severity of coronary atherosclerosis is linked to systemic inflammation. Atherosclerosis. 2015 May;240(1):110-4. doi: 10.1016/j.atherosclerosis.2015.02.051
20. Zhou ZX, Chen JK, Hong YY, Zhou R, Zhou DM, Sun LY, et al. Relationship Between the Serum Total Bb and Inflammation in Patients With Psoriasis Vulgaris. J Clin Lab Anal. 2016;30(5):768-75. doi: 10.1002/jcla.21936. Epub 2016 Apr 7
21. Peng YF, Xie LQ, Xiang Y, Xu GD. Serum Bb and Their Association With C-Reactive Protein in Patients With Migraine. J Clin Lab Anal. 2016;30(6):982-5. doi: 10.1002/jcla.21967.
22. Dandekar A, Mendez R, Zhang K. Cross talk between ER stress, oxidative stress,and inflammation in health and disease. Methods Mol Biol. 2015;1292:205-14. doi: 10.1007/978-1-4939-2522-3_15.
23. Koca T, Arslan A, Çiledağ Özdemir F, Berk E. The importance of red cell distribution width and neutrophil-lymphocyte ratio as a new biomarker in rheumatoid arthritis. The European Research Journal, 2018. doi: 10.18621/eurj.376346
24. Koca TT. Does obesity cause chronic inflammation? The association between complete blood parameters with body mass index and fasting glucose. Pak J Med Sci. 2017 Jan-Feb;33(1):65-69. doi: 10.12669/pjms.331.11532.
25. Robinson AC, Teeling M, Casey EB. Hepatic function in ankylosing spondylitis. Ann Rheum Dis. 1983;42(5):550-552.
26. Sheehan NJ, Slavin BM, Kind PR, Mathews JA. Increased serum alkaline phosphatase activity in ankylosing spondylitis. Ann Rheum Dis. 1983;42(5):563–565.
27. Kim Y, Kang J, Kim GT. Prevalence of hyperuricemia and its associated factors in the general Korean population: an analysis of a population-based nationally representative sample. Clin Rheumatol. 2018 May 23. doi:10.1007/s10067-018-4130-2.

J Surg Med. 2018;2(3):334-336.
DOI: 10.28982/josam.429206

Review
Derleme

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Ethics education during medical residency training and biopsychosocial approach

Tıpta uzmanlık eğitiminde etik eğitimi ve biyopsikososyal yaklaşım

Mehmet Ziya Gençer [1], Seçil Arıca [2], Ege Ağırman [2]

[1] Ankara Province Public Health Center, Çankaya Primary Care Clinic Nr.2, Ankara, Turkey
[2] University of Health Sciences, Department of Family Medicine, Istanbul, Turkey

ORCID ID of the authors
MZG: 0000-0003-0937-2778
SA: 0000-0003-0135-6909
EA: 0000-0001-5361-184X

Abstract

While a rapid specialization process has started within the field of medicine along with the rapid advancement in technology, particularly for the last bicentenary, the significance of an integrated approach towards the patient in that process has been realized once again. Medical ethics and ethics education have appeared as two interconnected notions from ancient times to present that each new specialization area integrates idiosyncratic ethical priorities into the field of medicine with the advancement in information. Even if ethics courses given during basic medical education list the core values, it is not all that wrong to say that the ethical approach has kind of a perpetual structure shaped by the practices within the physician-patient relationships. Moreover, different notions and values exist in different specialties. However, the ideal approach in a physician-patient relationship which has been recognized in the world today is a patient-centered approach apart from the emergency cases in which patients have a risk of death.

Keywords: Ethics, Medical ethics, Residency training, Medical education, Biopsychosocial approach

Öz

Teknolojinin özellikle son iki yüzyıldır hızlı bir şekilde gelişmesiyle birlikte tıp alanında hızlı bir uzmanlaşma süreci başlamış olup bu süreçte hastaya bütüncül yaklaşımının önemi bir kez daha anlaşılmıştır. Antik çağlardan günümüze değin tıp etiği ve tıp eğitimi birbirinden ayrılmaz iki kavram olarak karşımıza çıkmaktadır ki bilginin artmasıyla karşımıza çakın her yeni uzmanlık alanı kendine özgü etik öncelikleri tıp alanına sokmaktadır. Temel tıp eğitimi esnasında alınan etik dersleri temel değerleri listelemekte olsa da etik yaklaşımın hasta-hekim ilişkisinde uygulamalar ile şekillenen süreğen bir yapıya sahip olduğunu söylemek pekte yanlış olmaz. Öyle ki farklı uzmanlık dallarında farklı kavramlar ve değerler göz önünde bulundurulmaktadır bununla birlikte günümüzde dünyada kabul gören hasta-hekim ilişkisinde ki ideal yaklaşım, hastanın hayati tehlikesinin bulunduğu acil durumlar haricinde, hasta merkezli yaklaşımdır.

Anahtar kelimeler: Etik, Tıbbi etik, Uzmanlık eğitimi, Tıp eğitimi, Biyopsikososyal yaklaşım

Corresponding author / Sorumlu yazar:
Mehmet Ziya Gençer
Address / Adres: Ankara Halk Sağlığı Kurumu, Çankaya 2 nolu Aile Sağlığı Merkezi, Ankara, Türkiye
E-mail: mehmetziyagencer@hotmail.com

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 31.05.2018
Accepted / Kabul Tarihi: 19.07.2018
Published / Yayın Tarihi: 25.07.2018

How to cite / Atıf için: Gençer MZ, Arıca S, Ağırman E. Ethics education during medical residency training and biopsychosocial approach. J Surg Med. 2018;2(3):334-336.

Introduction

Education of medical ethics in Turkey has been offered previously under the name of 'Vezaif-i Etibba, (The Science of Ethics and the Duties of Physicians) and then 'Deontology' [1]. Medical ethics keeps its actuality owing to technological innovations and alternations of organizational forms of healthcare, social perceptions and sources of finance, and leads new discussions [2]. Medical discipline is related to the bodies which are the basic means of self-actualization for the individuals in this world. However; human being makes sense not only with his/her body but also his/her values and that makes the human concept meaningful. Medical specialization is getting improved day by day, and sociocultural shifts and the rise in the accumulation of knowledge cause new disciplines and specialties to emerge. Herein, different perspectives and paths are followed in respect of approaches to patient and gaining patient's trust within different specialties, and different concepts are questioned by both the patient and the physician. Many different topics like values evolving out of gender, the authenticity of death concept or what has been changed actually when outer view changes are evaluated differently by various medical disciplines.

Respect for individuals

Medicine field has always remained on the agenda of humankind with its numerous different dimensions in its scope for ages. Although daily physician practices come to mind instantly, when the subject is medicine, a description of both an enormous accumulation of knowledge on the ground and a scientific activity area constructed on upper floors should be included under that head as well [3]. Medical ethics is always open to dispute with its content in consequence of technological and sociological improvements and alternations of civilization, and showing no similarity along with the perceptions and judgments of people from different socio-economical classes and varied cultures. On the other hand, diversified specialties have emerged associated with the increase in medical knowledge and development of medical technology since the beginning of 1900's, and so these specialties differ in their priorities and the populations they serve [4]. While ethical priorities vary by specialties, a patient-centered biopsychosocial approach applied in situations when there is no need for a physician-centered approach is effective in both true diagnoses made by physician owing to overall anamnesis and building trust between the patient and well-humored physician asking open-ended questions. The aim of this article is to touch upon the significance of biopsychosocial approach based on the establishment of patient's trust while evaluating approaches to ethics education in different residency training.

Origin of medical ethics

The basic reason of specialization in medicine is that scientific and technological innovations in medicine and medicine which is certain fields oriented in the 20th century were not learnable and applicable from the ground up by a single person. The argument supporting that the disease called as a mechanical model or biomedical model today arises from impairment of cells underlies the medicine model of industrial society in the 20th century. That model describes the disease by grounding on cellular and chemical instabilities. However, it does not identify the roles of social and psychological processes in sickness. Being patient is not only a medical case but also includes a social dimension. Thereby, besides his/her perceptions and reactions towards the disease, treatment setting, and crew, approaches and the attitudes of the treatment crew towards the patient have a profound effect during the treatment procedure. Descartes prioritized the mind over the body in mind-body dualism. Thus, 'mankind' is defined with his mind which is capable of dominating the nature. Mind-body dualism has been handled and discussed in pretty different ways throughout the history of thought. This dualism has come up within divisions like soul-body, sometimes as mind-body or conscious-material. Yet the most distinct division was lived through in the 17th century when the Cartesian thinking was dominant. Cartesian system of thought by Descartes considerably influenced the field of medicine, and disease-oriented mechanical approach gained acceptance widely through industrialization [5-7]. However, the biopsychosocial model proposed by George Engel was a milestone in reaching the 'whole' in medicine [8] The significance of interpersonal relationships for the recovery of the patient was verbalized even in the Archaic Age. By pointing out the importance of human concept within a patient-physician relationship in treatments, Hippocrates, who has been considered as the father of medicine, asserted that a patient pleased with the goodness of his/her doctor could recuperate [9,10]. Although ethical values are evaluated differently in different specialties and subjects during treatment processes, the significance of integrated biopsychosocial approach to the patient is incontrovertible.

Healthcare is constitutively a system which is in need of the guidance of ethos and values, and complex and unsteady, and characterized by dynamic interaction networks including figures and factors influencing one another. Behaviors of the professionals working in this system are under the influence of organizational and circumferential context directly or indirectly, and their behaviors affect the circumference as well [11]. Human being is so complete in himself with his environment, cultural values, and body that those concepts cannot be evaluated separately [12].

Biopsychosocial approach

Specialization in the field of medicine is increasing each day within the age of information and causes new specialties to emerge. Each specialty becomes different disciplines in itself with its sub-branches. While physicians who are getting residency training obtain new information related to their field, they reshape their relations with the patients within the context of their field. Within this context, the reality we have come across can bring different values and worries within the patient-physician relationships in various specialties, the scope of the patient-physician relationship can differ even in different disease types in the same medical discipline. Even if ethics courses given in the course of basic medical education list the core values, it is not all that wrong to say that the ethical approach has kind of a perpetual structure shaped by the practices within the physician-patient relationships. Moreover, different notions and values exist in different specialties [13,14].

To give examples from different specialties, an oncologist may need to probe the death concept while in an interaction with his/her patient who is on his/her end-stage and edit his/her relations with the patient and his/her relatives according to that reality. At the same time, s/he may need to consider the perceptions of the patients with malignant disease who will receive a long-term treatment at different stages that can change by way of the course of treatments of treatment and other factors. While a gynecologist needs to consider sociocultural values rooted in sex and social perceptions, a dermatologist may need to assess how various diseases can affect patient's social and individual relationships [15]. While physicians in the field of internal medicine may need to consider the concepts of living with the illness and accepting it, a plastic surgeon may need to consider how the surgeries s/he has done will change the patient's life later. It is an accepted truth that today's ideal approach in a patient-physician relationship is the patient-centered approach apart from acute clinical situations that the patient has a risk of death [16-18]. To make the patient-centered approach that evaluates the patient's worries along with a holistic view, identifies the main problem, improves treatment plans, and trains and motivates the patient [19]. Successful, trust building is compulsory, and at the same time ethical values cannot be ignored. It is known that two out of three diagnoses are still made by anamnesis. In addition to that, an effective anamnesis requires a lot of self-sacrifices. Studies have shown that doctors are not good listeners and interrupt the patients frequently during the first 18 seconds [7]. Within the scope of the patient-physician relationship, there are many interconnected components in an effective treatment and the significance of ethical approaches is quite extensive in point of identifying borders and priorities while providing a channel between patient and physician and confidence.

Conclusion

It is significant to give ethics education like the one given throughout the basic medical education by considering different approaches for different specialties during medical residency training. Besides being a different topic which is about how to carry out that kind of a study which will possibly be pretty extensive, it is surely beyond doubt that medical ethics form a part of the integrated and patient-centered approach. As Dr. Richard Cabot said in the 19th century, what makes a physician wise, sophisticated and to have a sensitive foresight is medical ethics education. Vocational competence does not only comprise scientific mastership but also personal and social needs of the patient. One of the important properties of a clinician is his or her interest and care towards the humanity since the secret of providing a good service to the patient is all about caring him/her. Humanitarian qualifications of a clinician are not just a decorative dimension of clinical skills, in fact, it's the entity underlying clinical skills [20,21].

In our age, information has never been as easily accessible as it used to be throughout history while interaction between different cultures and thoughts across the world has speeded up. This situation has resulted in unprecedented diversification of sociocultural segments and faiths. The biopsychosocial approaches of doctors in different specialties to their patients should be diversified without ignoring the diverse human thoughts in this changing world.

References

1. Erdemir AD, Oncel O. Education of medical ethics at istanbul and uludag universities, turkey. Eubios Journal of Asian and International Bioethics. 2001;11:189-91.
2. Fox RC. Advanced medical technology-social and ethical implications. Annual Review of Sociology. 1976;2(1):231-68.
3. Kavas MV, Arda B. Tıpta uzmanlık eğitiminde etiğin yeri. Xii. Tıpta Uzmanlık Eğitimi Kurultayı. 2006:20-3.
4. Miles SH, Lane LW, Bickel J, Walker RM, Cassel CK. Medical ethics education: coming of age. Academic Medicine. 1989;64(12):705-14.
5. Timurturkan MG. Felsefi bedenden sosyolojik bedene. Ethos. 2008;1(4):1-14.
6. Damasio AR. Descartes'in yanılgısı duygu, akıl ve insan beyni. İstanbul: Varlık Yayınları; 1994:254-5.
7. Güleç H, Yavuz A, Topbaş M, Ak İ, Kaygusuz E. Psikiyatri hastalarında tıp dışı çare arama davranışı: Türkiye'de ve Almanya'da yaşayan türkler arasında karşılaştırmalı bir ön çalışma. Klinik Psikiyatri. 2006;9:36-44.
8. Engel GL. The clinical application of the biopsychosocial model. Journal of Medicine and Philosophy. 1981;6(2):101-24.
9. Tekiner AS, Ceyhun AG. Sağlığa Biyopsikososyal Yaklaşım. Aile Hekimliği Dergisi. 2008;2(1):52-8.
10. Bernard L, Krupat E. The patient and practitioner relationship. In: E. Krupat (Ed) Psychology Is Social. New York: Harper Collin Publishers. 1994:18-47.
11. Lesser CS, Lucey CR, Egener B, Braddock CH, Linas SL, Levinson WA. Behavioral and systems view of professionalism. The Journal of The American Medical Association. 2010;304(24):2732-7.
12. Gillon R. Philosophical Medical Ethics. British Medical Journal (Clinical Research Ed.) 1986;292(6519):543.
13. Hafferty FW, Franks R. The hidden curriculum, ethics teaching, and the structure of medical education. Academic Medicine. 1994;69(11):861-71.
14. Eckles RE, Meslin EM, Gaffney M, Helft PR. Medical ethics education: where are we? Where should we be going? A review. Academic Medicine. 2005;80(12):1143-52.
15. Clouser KD. Medical ethics: some uses, abuses, and limitations. New England Journal of Medicine. 1975;293(8):384-7.
16. Borrell-Carrió F, Suchman AL, Epstein RM. The biopsychosocial model 25 years later: principles, practice, and scientific inquiry. The Annals of Family Medicine. 2004;2(6):576-82.
17. Engel GL. The clinical application of the biopsychosocial model. Am J Psychiatry. 1980;137(5):535-44.
18. Engel GL. The biopsychosocial model and the education of health professionals. General Hospital Psychiatry. 1979;1(2):156-65.
19. Larivaara P, Kiuttu J, Taanila A. The patient-centred interview: the key to biopsychosocial diagnosis and treatment. Scandinavian Journal of Primary Health Care. 2001;19(1):8-13.
20. Civaner M, Sarıkaya Ö, Balcıoğlu H. Uzmanlık eğitiminde tıp etiği. Anadolu Kardiyoloji Dergisi. 2009;9:132-8.
21. Cabot RC. The use of truth and falsehood in medicine. Connecticut Medicine. 1978;42(3):189.

J Surg Med. 2018;2(3):337-338.
DOI: 10.28982/josam.402775

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Kounis syndrome as a result of anaphylactic reaction to diclofenac sodium: A case report

Diklofenak sodyum kullanımı sonrası anafilaktik reaksiyon sonucu gelişen Kounis sendromu: Olgu sunumu

Abdullah İbrahim [1], Şahin Çolak [1], Mehmet Özgür Erdoğan [1], Mustafa Ahmet Afacan [1], Ayhan Sarıtaş [2], Hayati Kandiş [2]

[1] Haydarpaşa Numune Training and Research Hospital, Emergency Medicine Clinic, Istanbul, Turkey
[2] Düzce University, School of Medicine, Department of Emergency Medicine, Düzce, Turkey

ORCID ID of the authors
Aİ: 0000-0002-7952-8953
ŞÇ: 0000-0001-8192-9652
MÖE: 0000-0003-2494-4244
MAA: 0000-0003-1045-0681
AS: 0000-0002-4878-8840
HK: 0000-0001-9151-6050

Abstract

Kounis syndrome refers to acute coronary syndromes of varying degrees (myocardial ischaemia to infarction) induced by mast cell activation as a result of allergic and anaphylactic reactions. Following subclinical, acute or chronic allergic reactions, it has a clinical spectrum ranging from chest pain to ST segment elevated myocardial infarction. The trigger of the allergic reaction can be drugs, food, environmental factors (insect bite, bee sting, pollen, latex contact). We present a case of a patient who developed Kounis syndrome as a result of anaphylactic reaction to Voltaren (Diclofenac sodium) which is one of the drugs widely used in the emergency departments as intramuscular pain killer.

Keywords: Kounis syndrome, Diclofenac sodium, Hypersensitivity, Anaphylaxis

Öz

Kounis sendromu mast hücrelerinin etkinleşmesi ile seyreden alerji, hipersensitivite, anaflaksi veya anaflaktoid reaksiyonlarla ilişkili olarak akut koroner sendromun değişik derecelerini ifade eder. Subklinik olarak akut veya kronik alerjik reaksiyona eşlik eden ve göğüs ağrısından başlayıp ST elavasyonlu miyokard enfarktüsü kadar uzanan bir klinik spektruma sahiptir. İlaçlar, yiyecekler, çevresel etkenler (böcek ısırması, arı sokması, polenler, lateks teması gibi) alerjik reaksiyonu tetikleyen neden olabilir. Burada, acil servislerde yaygın olarak kullanılan Voltaren'e (Diklofenak sodyum) bağlı gelişen anafilaktik reaksiyonu olan bir Kounis sendromu vakasını sunuyoruz.

Anahtar kelimeler: Kounis sendromu, Diklofenak sodyum, Aşırı duyarlılık, Anafilaksi

Introduction

Kounis syndrome was first described by Kounis and Zarvas in 1991 [1]. The reaction may be triggered by drugs, food, environmental factors such as insect bite, bee sting, pollens, or latex contact. It is common in Europe, especially in countries like Spain, Italy, Greece, and Turkey. It is sometimes referred to "Allergic Angina syndrome" or "allergic myocardial infarction".

Kounis syndrome has been classified into two main types depending on the pathophysiology or presence of coronary artery disease (CAD). In type I the patients have no signs of arteriosclerotic CAD and symptoms develop as a result of vasospasm triggered by allergic mediators, but in type I there is no increase in cardiac enzymes and troponin. Type II patients are those with CAD in whom the allergic mediators trigger coronary vasospasm or plaque rupture, and they have associated rise in cardiac enzymes and troponin [1-3].

In our case report we present a patient who developed Kounis syndrome after anaphylactic shock as a result of intramuscular injection of diclofenac sodium (DS) which is widely used in emergency department for pain management.

Corresponding author / Sorumlu yazar:
Abdullah İbrahim
Address / Adres: Haydarpaşa Eğitim ve Araştırma Hastanesi, Acil Tıp Kliniği, İstanbul, Türkiye
e-Mail: abdullahibrahim@hotmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 07.03.2018
Accepted / Kabul tarihi: 16.04.2018
Published / Yayın tarihi: 16.04.2018

How to cite / Atıf için: İbrahim A, Çolak Ş, Erdoğan MÖ, Afacan MA, Sarıtaş A, Kandiş H. Kounis syndrome as a result of anaphylactic reaction to diclofenac sodium: A case report. J Surg Med. 2018;2(3):337-338.

Case presentation

A 54 year old man with severe back pain was admitted to our emergency department. The patient had history of CAD and hypertension. He had no history of allergy to any drug. The findings in his physical examination on arrival were: the blood pressure was 140/90 mmHg (no difference between right and left side), pulse: 95 beat/min. temperature: 37 degrees centigrade, respiratory rate: 18/min, oxygen saturation: 98%. Apart from tenderness in intrascapular region, his other physical examinations were normal. The electrocardiography (ECG) and laboratory tests were also normal. The patient was diagnosed as myalgia and hence DS 75mg (Voltaren ® 75 mg/3 mL IM; Novartis, Stein-AG, Swiss) was administered intramuscularly for pain management. Immediately after the injection the patient collapsed. His blood pressure fell to 50/30 mmHg, pulse was 145 beats per minute, his Glasgow Coma Scale was 10 and he developed urticaria and edema of mucous membrane. He was diagnosed as having anaphylactic shock as a result of DS injection. İntramuscular adrenaline 0.3mg and pheniramine maleate 45.5mg (Avil ® 45.5 mg/2ml: Sandoz, Kurtkoy, Istanbul, Turkey) were administered. 80 mg Methylprednosolone (Prednol-l ® 40mg, Mustafa Nevzat, Istanbul, Turkey) and intravenous fluid administration was started and vasopressor support was given. In his new laboratory results after the incident the troponin level that was in normal range on arrival (0.02 ng/ml) showed a seven fold increase to 1.40 ng/ml, also an increase in CK-MB from 15 ng/ml to 68 ng/ml, and aspartate transaminase levels (from 16 U/L to 44 U/L). There were no changes in his ECG findings. Cardiology consultation was performed immediately. His echocardiography showed an ejection fraction of 25% and global hypokinesia of the left ventricle. The patient was diagnosed as Kounis Syndrome resulting from anaphylaxis to DS. Emergency cardiovascular percutaneous intervention was not found necessary and he was put on medical treatment. After 36 hours of hospitalization the patient was discharged with normal vital signs.

Discussion

"Kounis syndrome" is a condition that occurs by coincidence, accompanied by the classical angina pectoris' clinic and laboratory results that is caused by the inflammatory mediators resulting from allergic reaction [2]. Depending on the underlying pathophysiology or presence of CAD, Kounis syndrome has been classified into two main types [3,4]. In type I the patients have no signs of arteriosclerotic CAD risk and symptoms develop as a result of vasospasm triggered by allergic mediators, but in type I there is no increase in cardiac enzymes and troponin. Type II patients are those with CAD in whom the allergic mediators trigger coronary vasospasm or plaque rupture, and they have associated rise in cardiac enzymes and troponin levels as seen in our case.

The underlying pathology in Kounis syndrome is coronary artery vasospasm due to release of vasoactive mediators secondary to mast cell degranulation. The mast cells in heart tissue play a great role in anaphylaxis. They may trigger tachycardia, change ventricular contractility and cause block antihistaminic and corticosteroid treatment should start immediately and preparation for coronary intervention should be ready. In our case adrenalin, antihistaminic and corticosteroid treatment was given. His syndrome has also been referred to as "cardiac anaphylaxis" [3,4]. This has been used to explain the functional and metabolic changes occurring in the heart following an allergic reaction, caused by the release of histamine and metabolites of the arachidonic acid cascade. The most important step in the diagnosis of Kounis syndrome is to suspect it in patients with allergic symptoms accompanied by chest pain [5]. The ECG changes seen may include ST elevation or depression, heart block of varying degrees or cardiac arrhythmias. There were no ECG changes in our case, but an increase in troponin levels was detected. Ordering of ECG and cardiac enzymes in patients with hypersensitive reactions, as seen in our case, is important in the diagnosis of Kounis syndrome.

Fox DJ et al have reported a case of Myocardial infarction after aspirin treatment [6]. Non-steroidal anti-inflammatory drugs have been reported to be one of the most common classes of medications causing anaphylaxis [7-10].

In conclusion, because of extensive use of in the emergency departments, physicians should have enough knowledge about this syndrome and be aware of its complication to make a prompt diagnosis and initiate an early treatment. As seen in our case, non-steroidal anti-inflammatory drugs should be used carefully in those with type II Kounis syndrome, and if the syndrome occurs, acute coronary syndrome protocols should be activated and early anaphylaxis treatment should be given without hesitation.

References

1. Kounis NG, Zavras GM. Histamine-induced coronary artery spasm: the concept of allergic angina. Br J Clin Pract. 1991;45(2):121-8.
2. Gazquez V, Dalmau G, Gaig P, Gomez C, Navarro S. Kounis syndrome: Report of 5 cases. J Investig Allergol Clin Immunol. 2010;20(2):162-5.
3. Kounis NG. Kounis syndrome (allergic angina and allergic myocardial infarction): A natural paradigm? Int J Cardiol 2006;110(1):7-14.
4. Nikolaidis LA, Kounis NG, Gradman AH. Allergic angina and allergic myocardial infarction: a new twist on an old syndrome. Can J Cardiol. 2002;18(5):508-11.
5. Tok D, Özcan F, Şentürk B, Gölbaşı Z. Parenteral penisilin kullanımını takiben gelişen akut koroner sendrom olgusu: Kounis sendromu. Arch Turk Soc Cardiol. 2012;40(7):615-9.
6. Fox DJ, Gray TP, Fath-Ordoubadi F. Myocardial infarction after aspirin treatment. J R Soc Med. 2005;98(1):21-3.
7. Brown AF, McKinnon D, Chu K. Emergency department anaphylaxis: A review of 142 patients in a single year. J Allergy Clin Immunol. 2001;108(5):861-6.
8. Hadar A, Holcberg G, Mazor M. Anaphylactic shock after diclofenac sodium(Voltaren)]. Harefuah. 2000 Feb 1;138(3):211-2.
9. Colak S, Gunes H, Afacan MA, Kandis H, Erdoğan MO,Ayrancı M. Anaphylaxis after intramuscular injection of diclofenak sodium. Am J Emerg Med. 2014 Jan 3. pii: S0735-6757(13)00908-X. doi: 10.1016/j.ajem.2013.12.049.
10. Tiwari AK, Tomar GS, Ganguly CS, Kapoor MC. Kounis syndrome resulting from anaphylaxis to diclofenac. Indian J Anaesth. 2013 May;57(3):282-4.

J Surg Med. 2018;2(3):339-341.
DOI: 10.28982/josam.412354

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Oral hairy leukoplakia in the buccal mucosa of a healthy, HIV-negative patient

Sağlıklı, HIV negatif bir hastada bukkal mukozada oral kıllı lökoplaki

Gülhan Gürel [1], Sevinç Şahin [2], Betül Aytekin [2], Emine Çölgeçen [1]

[1] Department of Dermatology, Bozok University School of Medicine, Yozgat, Turkey
[2] Department of Pathology, Bozok University School of Medicine, Yozgat, Turkey

ORCID ID of the authors
GG: 0000-0001-5716-8750
SŞ: 0000-0002-9409-8138
BA: 0000-0002-2120-6855
EÇ: 0000-0001-9651-6068

Abstract
Oral hairy leukoplakia (OHL), first described in 1984, is an Epstein-Barr virus lesion located laterally in the tongue and manifesting as a white, asymptomatic mucosal plaque which cannot be removed by scraping. OHL is more commonly observed in HIV-positive patients, in immunosuppressed patients after kidney, heart, liver and bone marrow transplantation, in hematological malignancies such as multiple myeloma, and in patients undergoing systemic or topical steroid therapy. OHL has rarely been reported in healthy patients who are not immunosuppressive. The case of an otherwise healthy, HIV-negative 24 year-old woman with OHL lesions in the buccal mucosa is presented here because of its rarity.
Keywords: Oral hairy leukoplakia, HIV-negative patient, Buccal mucosa

Öz
İlk olarak 1984'te tanımlanan oral kıllı lökoplaki (OKL), sıklıkla dil lateralde yerleşen kazımakla çıkarılamayan beyaz renkli, asemptomatik mukozal plak olarak kendini gösteren bir Epstein-Barr virüsü lezyonudur. OKL daha çok HIV pozitif hastalarda bulunurken, böbrek, kalp, karaciğer ve kemik iliği transplantasyonu sonrası immünsüpresif hastalarda, multipl miyelom gibi hematolojik malignitelerde ve sistemik veya topikal steroid tedavisi altındaki hastalarda da tanımlanmıştır. Literatürde OKL, nadiren immünsüpresif olmayan sağlıklı hastalarda da bildirilmiştir. Burada, 24 yaşında diğer açılardan sağlıklı, HIV negatif, bukkal mukozada OKL lezyonu olan kadın hasta nadir görülmesi nedeniyle sunulmaktadır.
Anahtar kelimeler: Oral kıllı lökoplaki, HIV-negatif hasta, Bukkal mukoza

Corresponding author / Sorumlu yazar:
Gülhan Gürel
Address / Adres: Bozok Üniversitesi, Tıp Fakültesi, Dermatoloji Bölümü, 66200, Yozgat, Türkiye
e-Mail: gulhanozturkgurel@hotmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 04.04.2018
Accepted / Kabul tarihi: 19.04.2018
Published / Yayın tarihi: 19.04.2018

Introduction

Oral hairy leukoplakia (OHL), first described in 1984 in homosexual male patients by Greenspan et al. [1], is an Epstein-Barr virus (EBV) lesion located laterally in the tongue and manifesting as a white, asymptomatic mucosal plaque which cannot be removed by scraping [2]. The prevalence of OHL reported among human immunodeficiency virus (HIV) positive individuals is as high as 53% [3]. Despite being mostly observed in HIV-positive patients, OHL has also been described in immunosuppressive patients after renal, heart, liver and bone marrow transplantation, in hematological malignancies such as multiple myeloma, and in patients undergoing systemic or topical steroid therapy [2,4]. OHL has rarely been reported in healthy patients who are not immunosuppressive. In these reports, the definition of healthy includes patients with no history of underlying medical illness or immunosuppressive treatment [4,5].

We describe a case of an otherwise healthy, HIV-negative 24 year-old woman with OHL lesions in the buccal mucosa because of its rarity.

Case presentation

A 24-year-old female patient was admitted to our clinic due to white spots in her mouth for about 3 years. Her history revealed that these white spots never resolved entirely and caused no symptoms other than a mild burning sensation. She had no history of disease other than hypothyroidism. The patient was receiving levothyroxine sodium medication, and did not smoke or drink alcohol. There were no reports of previous use of immunosuppressive drugs or steroids. Dermatologic examination revealed slightly elevated, linear white plaques on the bilateral buccal mucosa, which could not be removed by scraping (Figure 1).

How to cite / Atıf için: Gürel G, Şahin S, Aytekin B, Çölgeçen E. Oral hairy leukoplakia in the buccal mucosa of a healthy, HIV-negative patient. J Surg Med. 2018;2(3):339-341.

Incisional biopsy specimens were taken from the lesions. Histopathological examination revealed hyperkeratosis and paracetatosis in the keratin layer (Figures 2-3). Papillomatosis in the squamous epithelium, evident pseudoepitheliomatous hyperplasia, and balloon-like cells with large vacuolar cytoplasm were also observed (Figure 2-3). No evidence of dysplasia or malignancy was present. Diffuse nuclear positivity in squamous epithelium was observed at immunohistochemical examination using EBV antibody (Figure 4), while HPV and p16 were negative. No fungal microorganisms were observed at histochemical examination with PAS staining.

The patient was assessed by the Department of Internal Medicine in terms of possible underlying immunosuppressive diseases. General physical examination revealed no pathological findings. Laboratory tests were within normal limits. The serological test for HIV antibody was negative. The patient was started on 2 x 500 mg valaciclovir with a diagnosis of OHL. At follow-up after 1 week, the lesions appeared completely regressed (Figure 5). The current treatment was maintained for 3 more weeks and then terminated. There was no recurrence in the first month of follow-up. The patient is still attending regular follow-ups.

Figure 1: Slightly elevated, linear white plaques on the bilateral buccal mucosa, which could not be removed by scraping.

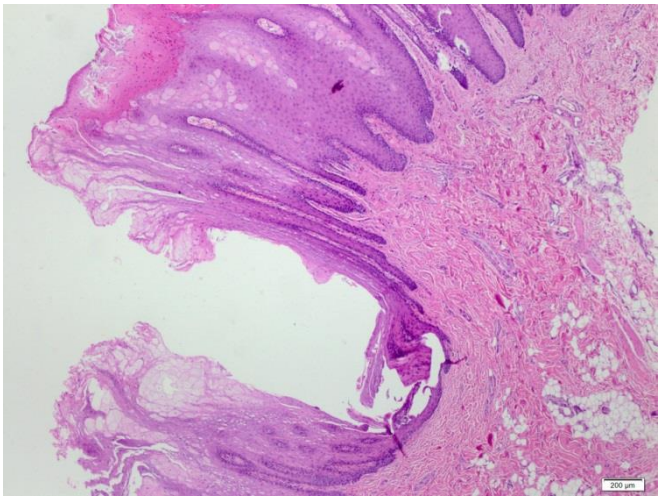


Figure 2: Light microscopic image of the lesion with hyperkeratosis and parakeratosis in the keratin layer, papillomatosis in the squamous epithelium, evident pseudoepitheliomatous hyperplasia and balloon-like cells with large vacuolar cytoplasm (hematoxylin-eosin staining, original magnification x40).

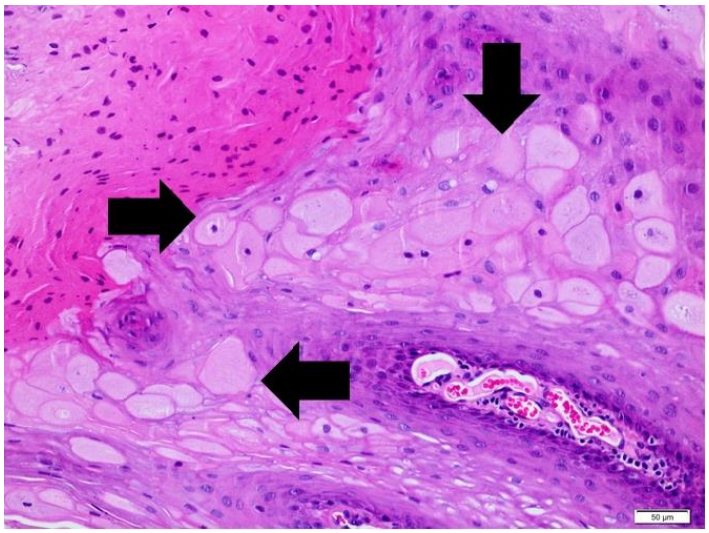


Figure 3: A light microscopic image under higher magnification of the balloon-like cells (arrows) in the squamous epithelium (hematoxylin-eosin staining, original magnification x200).

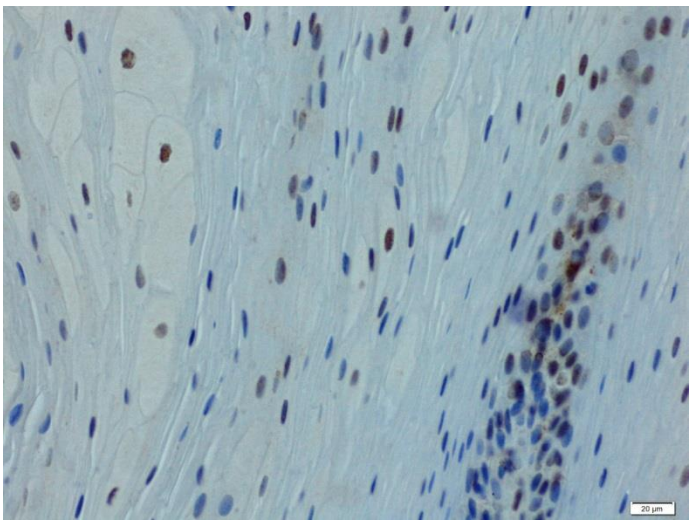


Figure 4: Diffuse nuclear positivity (brown staining) in the squamous epithelium at immunohistochemical examination using EBV antibody (The avidin-biotin-peroxidase method, original magnification x400).

Figure 5: Appearance of the lesions 1 week after oral valaciclovir treatment.

Discussion

Although buccal mucosal involvement has been reported in a few OHL cases, the lesion is generally observed on the lateral edges of the tongue. Although OHL has a characteristic appearance on the tongue, it can be confused with other white lesions when located on the buccal mucosa (such as

candidiasis, idiopathic or smoking-related leukoplakia, frictional keratosis, carcinoma, idiopathic lichen planus and medication related lichenoid reactions). Biopsy may therefore be required to confirm the clinical diagnosis [6]. Histopathological findings in our case were compatible with OHL, and no pathological skin findings were observed except for the oral mucosa.

EBV is a ubiquitous human herpesvirus that affects approximately 90-95% of the adult population worldwide and that primarily infects B-lymphocytes. The virus causes a wide spectrum of mucocutaneous and systemic illnesses, ranging from self-limiting diseases to aggressive malignancies [7]. The virus lives in peripheral blood memory B lymphocytes, which are cellular reservoirs of permanent latent EBV infection. Virus infiltration occurs by secretion of EBV-infected oropharyngeal cells during viral reactivation [2]. EBV can be detected in 10 to 90% of healthy adults using the polymerase chain reaction in the normal lingual epithelium, although it is very rare in healthy non-HIV infected individuals [8]. Other factors may thus be involved in the pathogenesis of OHL, including systemic immunosuppression and persistent EBV replication, as well as suppression of EBV virulence and local host immunity [2].

OHL is usually asymptomatic, but patients may report pain, taste sensation changes, or a burning sensation. Cosmetic concerns can also lead to some psychological distress [7]. White spongiform nevus, lichen planus, idiopathic leukoplakia and oral candidiasis should be considered at differential diagnosis of OHL. Unlike OCL, the oral candidiasis plaque can easily be removed with a tongue depressor, and an erythematous area appears at the base [6,7]. Our patient's lesion could not be removed by scraping.

While OHL is considered a benign condition, definite diagnosis is nevertheless important, since the clinical appearance may mimic a premalign lesion and because the lateral margin of the tongue is a high-risk site for squamous cell carcinoma. This is especially important if there are no underlying predisposing factors in HIV-negative patients or for OHL [4]. OHL treatment should be considered in patients with symptoms or cosmetic concerns. Treatment options include systemic antiviral therapy (acyclovir, valaciclovir), topical podophylline, topical retinoids, gentian violet, surgical excision and cryotherapy [9-13]. Regardless of the type of treatment, OHL often recurs after termination [7]. Our patient was started on 2 x 500 mg valaciclovir. At follow-up after 1 week, the lesions appeared completely regressed. There was no recurrence in the first month of follow-up.

In conclusion, we present this case of a healthy, HIV-negative female patient with no underlying predisposing factors, due to the rarity of the location of the OHL lesion on the buccal mucosa.

References

1. Greenspan D, Greenspan JS, Conant M, et al. Oral "hairy" leukoplakia in male homosexuals: evidence of association with both papillomavirus and a herpes-group virus. Lancet. 1984;2:831-4.
2. Piperi E, Omlie J, Koutlas IG, Pambuccian S. Oral hairy leukoplakia in HIV-negative patients: report of 10 cases. Int J Surg Pathol. 2010;18:177-83.
3. Bravo IM, Correnti M, Escalona L, et al. Prevalence of oral lesions in HIV patients related to CD4 cell count and viral load in a Venezuelan population. Med Oral Patol Oral Cir Bucal. 2006;11:E33-E39.
4. Prasad JL, Bilodeau EA. Oral hairy leukoplakia in patients without HIV: presentation of 2 new cases. Oral Surg Oral Med Oral Pathol Oral Radiol. 2014;118:e151-60.
5. Felix DH, Watret K, Wray D, Southam JC. Hairy leukoplakia in an HIV-negative, nonimmunosuppressed patient. Oral Surg Oral Med Oral Pathol. 1992;74:563-6.
6. Ficarra G, Romagnoli P, Piluso S, et al. Hairy leukoplakia with involvement of the buccal mucosa. J Am Acad Dermatol. 1992;27:855-8.
7. Hall LD, Eminger LA, Hesterman KS, Heymann WR. Epstein-Barr virus: dermatologic associations and implications: part I. Mucocutaneous manifestations of Epstein-Barr virus and nonmalignant disorders. J Am Acad Dermatol. 2015;72:1-19.
8. Scully C, Porter SR, Di Alberti L, et al. Detection of Epstein-Barr virus in oral scrapes in HIV-infection, in hairy leukoplakia, and in healthy non-HIV-infected people. J Oral Pathol Med. 1998;27:480-2.
9. Walling DM, Flaitz CM, Nichols CM. Epstein-Barr virus replication in oral hairy leukoplakia: response, persistence, and resistance to treatment with valacyclovir. J Infect Dis. 2003;188:883-90.
10. Moura MD, Guimar~aes TR, Fonseca LM, et al. A random clinical trial study to assess the efficiency of topical applications of podophyllin resin (25%) versus podophyllin resin (25%) together with acyclovir cream (5%) in the treatment of oral hairy leukoplakia. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;103:64-71.
11. Schöfer H, Ochsendorf FR, Helm EB, Milbradt R. Treatment of oral 'hairy' leukoplakia in AIDS patients with vitamin A acid (topically) or acyclovir (systemically). Dermatologica. 1987;174:150-1.
12. Bhandarkar SS, MacKelfresh J, Fried L, Arbiser JL. Targeted therapy of oral hairy leukoplakia with gentian violet. J Am Acad Dermatol. 2008;58:711-2.
13. Goh BT, Lau RK. Treatment of AIDS-associated oral hairy leukoplakia with cryotherapy. Int J STD AIDS. 1994;5:60-2.

J Surg Med. 2018;2(3):342-343.
DOI: 10.28982/josam.409227

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Simultaneous dorsal dislocation of the proximal interphalangeal joints in two digits: A case report

Ardışık iki el parmağında proksimal interfalangeal eklem çıkığı: Olgu sunumu

Suavi Aydoğmuş [1], Can Emre Baş [2], Tahir Mutlu Duymuş [3], Adnan Behçet Kafadar [4]

[1] Istanbul Maltepe State Hospital, Department of Orthopedics, Maltepe, Istanbul, Turkey
[2] Mersin University, Faculty of Medicine, Department of Hand Surgery, Mersin, Turkey
[3] Saygı Hospital, Department of Orthopedics, Istanbul, Turkey
[4] Haydarpasa Numune Education and Research Hospital, Department of Orthopedics, Istanbul, Turkey

ORCID ID of the authors
SA: 0000-0002-8844-9536
CEB: 0000-0002-2254-547X
TMD: 0000-0002-9610-2188
ABK: 0000-0003-4098-7826

Abstract
Majority of proximal interphalangeal (PIP) joint dislocations are dorsal dislocations but multıple PIP dislocations of the adjacent digits is very rare. This study presents a very rare case of a 82-year-old man who had two PIP dislocations in the same hand. He was successfully treated by closed reduction and he had no loss of function at final follow-up. Multiple PIP dislocations in the same hand are seen rarely, when treated properly, outcome is excellent even in elderly.
Keywords: Finger dislocation, Trauma, Reduction

Öz
Proksimal interfalangeal (PIF) eklem çıkıklarının çoğu dorsal çıkıklar olmakla beraber ardışık parmaklarda nadiren gözlenmektedir. Bu çalışma 82 yaşında bir erkek hastanın aynı elindeki iki adet proksimal interfalangeal eklem çıktığını sunmaktadır. Hasta kapalı redüksiyon ile başarılı şekilde tedavi edilip son takiplerinde tamamen iyileşme gözlenmiştir. Çoklu PIF eklem çıkıkları aynı elde nadiren görülmekle beraber uygun tedavi edildikten sonra sonuçları oldukça iyidir.
Anahtar kelimeler: Parmak çıkığı, Travma, Redüksiyon

Introduction

The proximal interphalangeal (PIP) joint is prone to injury because of its long lever arm but the prognosis is mostly excellent [1]. The majority of PIP joint fracture dislocations are dorsal dislocations. Injuries may be stable or unstable, which helps to decide to proceed to nonsurgical versus surgical treatment [2]. Achievement of a concentric reduction with early motion is the key to successful treatment of the PIP joint injuries and also edema control is important to reduce stiffness and contracture [1].

Case presentation

A 82-year-old man who had admitted Emergency department following unwitnessed injury to his two fingers of right hand. The mechanism of injury was pivoting his right hand on the floor during falling from his bed. His examination revealed a swollen and deformed second and third fingers at his right hand. Distally sensations and capillary refill was normal. X-rays showed dislocations of second and third PIP joints (Figure 1).

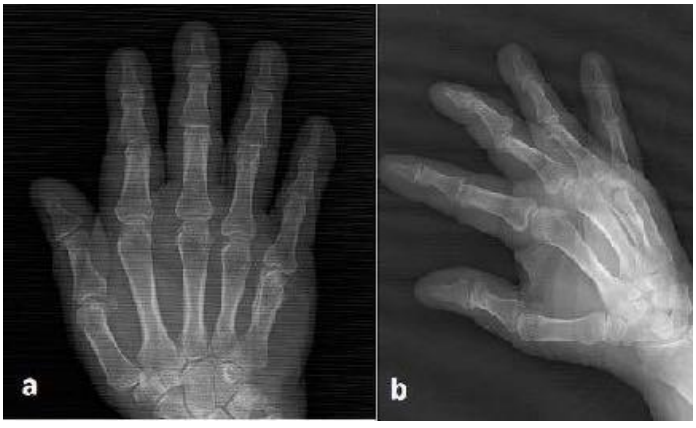


Figure 1: Prereduction x-rays

Corresponding author / Sorumlu yazar:
Suavi Aydoğmuş
Address / Adres: Maltepe Devlet Hastanesi, Ortopedi Bölümü, İstanbul, Türkiye
e-Mail: saydogmus@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 24.03.2018
Accepted / Kabul tarihi: 21.04.2018
Published / Yayın tarihi: 21.04.2018

How to cite / Atıf için: Aydoğmuş S, Baş CE, Duymuş TM, Kafadar AB. Simultaneous dorsal dislocation of the proximal interphalangeal joints in two digits: A case report. J Surg Med. 2018;2(3):342-343.

The joints were reduced by longitudinal traction after digital block. The joints were both stable in full extension and flexion after reduction. Early range of motion was applied and the patient was evaluated every week for 6 weeks postreduction. He had full range of motion and showed no instability (Figure 2).

Figure 2: Final follow-up x-rays

Discussion

The PIP joints' stability is mostly dependent on its bony articular contours, the collateral ligaments, and the volar plate. The boxlike complex well secured laterally by the collateral ligaments and volarly by the volar plate is the most important contributor to the PIP joint stability. For displacement of the middle phalanx to occur, this complex must be disrupted in at least two planes. Typically, collateral ligaments fail proximally, and the volar plate avulses distally [3,4]. If the dislocation is stable, usually nonoperative treatment is enough. Dislocations that are tenuously stable (subluxate only near full extension) may be treated with a figure of eight splint as well [1,3]. The most common complications after PIP dislocation are: Stiffness and flexion contracture, chronic swelling, swan neck deformity, redislocation and subluxation [1]. Early active motion after dorsolateral dislocation of the PIP joint produces significantly superior results regarding the active range of motion and pinch power than static splinting [5]. There are case reports for multiple joint dislocations in the same digit but PIP dislocations of the adjacent digits is not seen often [6,7]. The potential mechanism for dislocation of adjacent PIP joints is probably the same as the case report of Gonzalez and Elhassan: volar surface of the injured digits were the contact points on the floor during falling down from the bed and hyperextension of the PIP joints damaged the capsule and/or the collateral ligaments sufficient enough to dislocate the joint [7].

During the visits the patient was evaluated about hyper laxity but there was no finding suggesting this pathology. Early range of motion prevented contracture and swelling. Considering our patient's age achieved range of motion and stability is excellent. Multiple PIP dislocations in the same hand are seen rarely, when treated properly, outcome is excellent even in elderly.

References

1. Mangelson JJ, Stern P, Abzug JM, Chang J, Osterman AL. Osterman. Complications Following Dislocations of the Proximal Interphalangeal Joint. J Bone Joint Surg Am. 2013;95:1326-32.
2. Calfee RP, Sommerkamp TP. Fracture–Dislocation About the Finger Joint. J Hand Surg. 2009;34A:1140–7.
3. Bot AG, Bekkers S, Herndon JH, Mudgal CS, Jupiter JB, Ring D. Determinants of disability after proximal interphalangeal joint sprain or dislocation. Psychosomatics. 2014 Nov-Dec;55(6):595-601.
4. Scott WW. Dislocations and Ligament Injuries in the Digits. Green's Operative Hand Surgery, Sixth Edition pp292.
5. Arora R, Lutz M, Fritz D, Zimmermann R, Gabl M, Pechlaner S. Dorsolateral dislocation of the proximal interphalangeal joint: closed reduction and early active motion or static splinting; a retrospective study. Arch Orthop Trauma Surg. 2004;124:486–8.
6. Eglseder W, Andrew Jr, Gens DR, Burgess A. Multiple Ipsilateral Dorsal Metacarpophalangeal and Proximal Interphalangeal Joint Dislocations: A Case Report. The Journal of Trauma: Injury, Infection, and Critical Care. 1995;38(6):955-7.
7. Gonzalez M, Elhassan BT. Multiple Dislocations of the Proximal Interphalangeal Joint Dislocations in Three Adjacent Digits. Journal of Surgical Orthopaedic Advances. 204;13:44-6.

J Surg Med. 2018;2(3):344-346.
DOI: 10.28982/josam.410144

Case report
Olgu sunumu

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Rare and challenging two complications after prostate biopsy of an older man

Yaşlı bir erkekte prostat biyopsisi sonrası gelişen zor ve nadir iki komplikasyon

Tuğba Turgut [1], Deniz Mut Sürmeli [1], Remzi Bahşi [1], Hande Selvi Öztorun [1], Murat Varlı [1], Sevgi Aras [1]

[1] Department of Geriatrics, Faculty of Medicine, Ankara University, Ankara, Turkey

ORCID ID of the authors
TT: 0000-0001-6479-8857
DMS: 0000-0002-3913-1046
RB: 0000-0003-1715-6856
HSÖ: 0000-0003-0343-8510
MV: 0000-0003-0144-9646
SA: 0000-0002-5356-303X

Corresponding author / Sorumlu yazar:
Tuğba Turgut
Address / Adres: Hacettepe, Talatpaşa Bulvarı, No:82, 06230, Altındağ, Ankara, Türkiye
Tel: +90312 5083333
e-Mail: drtugbaonacan@hotmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 28.03.2018
Accepted / Kabul tarihi: 24.04.2018
Published / Yayın tarihi: 24.04.2018

Abstract

Although prostate cancer is the second most common cancer type in men, its mortality rate is lower. Despite European Randomized Study of Screening for Prostate Cancer study reported that screening with prostate-specific antigen made a substantial reduction in prostate cancer mortality at 13 years of follow-up; they do not recommend population screening with prostate specific antigen because of the uncertain balance between benefits and harms. In our case, prostate biopsy was performed because of urinary symptoms but two severe operation planned due to infective endocarditis and spondylitis, a long and serious antibiotherapy process and its side effects were occurred after prostate biopsy. In light of this case, clinicians should consider that prostate biopsy may cause serious complications when they are screening asymptomatic men for prostate cancer or deciding whether or not to have a prostate biopsy.

Keywords: Older patient, Prostate cancer, Infective endocarditis

Öz

Prostat kanseri erkeklerde ikinci sıklıkta görülen kanser tipi olmasına rağmen mortalite hızı düşüktür. Avrupa Randomize Prostat Kanser Tarama çalışmasında; prostat spesifik antijen ile taramada 13 yıllık takipte mortalitede belirgin düşüş sağlanmasına rağmen fayda ve zararları arasındaki belirsiz denge nedeniyle prostat spesifik antijen ile genel toplum taraması önerilmemiştir. Vakamızda; üriner semptomlar nedeniyle prostat biyopsisi yapıldıktan sonra enfektif endokardit ve spondilodiskit gelişti ve bu komplikasyonlara yönelik iki ciddi operasyon planlandı, uzun ve ciddi bir antibiyoterapi süreci ile antibiyoterapiye bağlı yan etkiler ortaya çıktı. Bu vaka ışığında, klinisyenlerin asemptomatik erkeklerde tarama yaparken veya prostat biyopsisi kararı verirken bu komplikasyonları göz önünde bulundurmaları önerilir.

Anahtar kelimeler: Yaşlı hasta, Prostat kanseri, İnfektif endokardit

Introduction

Although prostate cancer is the second most common cancer type in men, its mortality rate is lower [1]. Despite European Randomized Study of Screening for Prostate Cancer study reported that screening with prostate-specific antigen (PSA) made a substantial reduction in prostate cancer mortality at 13years of follow; they do not recommend population screening with PSA because of the uncertain balance between benefits and harms [2]. The European Association of Urology guidelines recommend PSA-based screening for men aged between 55 and 69, although PSA testing may result in over diagnosis and overtreatment of prostate cancer particularly in men under 50 and over 69 years. In addition, routine PSA screening is not recommended for males older than 70 years and whose life expectancy is less than 10-15 years [3]. We wanted to show that even some simple diagnostic procedures can leave the clinician in a difficult situation due to the age and comorbidities of patient.

How to cite / Atıf için: Turgut T, Sürmeli DM, Bahşi R, Öztorun HS, Varlı M, Aras S. Rare and challenging two complications after prostate biopsy of an older man. J Surg Med. 2018;2(3):344-346.

Case presentation

77-year-old male patient with history of hypertension, mitral valve prolapse and benign prostate hypertrophy was admitted to geriatric outpatient clinic with complaints of fatigue, loss of appetite, pollakiuria, nocturia and urinary incontinence. His physical examination was normal except mild rhonchi and 2/6 cardiac murmurs on mitral focus. We investigated PSA and urine culture because of urinary complaints. PSA value was 16.01 ng/mL and urine culture was positive for Enterococcus faecalis. Oral levofloxacin was started according to antibiogram.

He was referred to urology department because of sudden acute urinary retention and urinary catheter was applied to the patient when he was on antibiotherapy. In rectal examination, his prostate was found stiff and prostate biopsy was performed. Pathological examination of the biopsy specimen revealed adenocarcinoma of the prostate.

One month after prostate biopsy, he admitted to our clinic with complaints of fatigue, severe back pain, fever and night sweats. Transthoracic echocardiography (ECO) was performed because of fever and murmurs and revealed slightly thicker aortic valves prolapse with proliferation of tissue in mitral anterior leaflet and moderate to severe mitral insufficiency. Second echocardiography was performed because of Enterococcus faecalis growth in 4 consecutive blood cultures and 1 urine culture in fever periods and found similar with the previous one. Brucella agglutination test, tuberculin skin test and bone scintigraphy were negative which were done for fever and back pain. Oral levofloxacin treatment was completed to 14 days and patient was discharged from hospital.

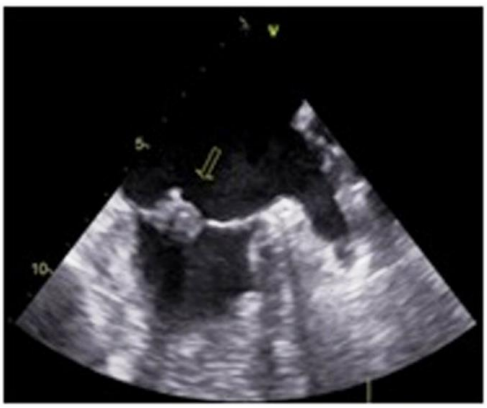


Figure 1: Vegetation on mitral valve

Figure 2: Spondylitis and paravertebral abscess on L3 vertebra

Patient was re-admitted to hospital due to fever, severe back pain and abdominal pain two months later. Enterococcus faecalis was isolated from his blood culture and intravenous ampicillin treatment was started. Thoracic and abdominal computerized tomography revealed an abscess primarily in the anterior paravertebral region and the right psoas muscle and spondylodiscitis at L3-4 level (Figure 1). Patient was consulted to the neurosurgery department and operation was planned. An echocardiography was performed for preoperative evaluation and seen vegetation of 1.4x0.9 cm in diameter on the mitral valve (Figure 2). Spondylodiscitis operation was delayed and intravenous gentamicin was added to ampicillin treatment for infective endocarditis.

Because of acute renal failure, gentamicin was changed with ceftriaxone and then azotemia regressed. After 6 weeks of antibiotherapy, mitral valve replacement operation was recommended but the patient did not accept. Control echocardiography 3 months after discharge revealed 1.2x0.8 cm diameter calcified vegetation on the mitral valve.

Discussion

European Society of Medical Oncology guideline for prostate cancer does not recommend population-based PSA screening because of risk of over-diagnosis and overtreatment, though reducing prostate cancer mortality [4]. The guideline recommends deciding whether or not to perform prostate biopsy in the light of digital rectal examination findings, ethnicity, age, comorbidities, PSA values and history of previous biopsy [4]. For our patient, prostate biopsy was necessary because of having common urinary tract symptoms, suspicious digital rectal examination and elevated PSA.

Infective endocarditis is a serious disease associated with significant morbidity and mortality. American College of Cardiology/ American Heart Association (ACC/AHA) recommended prophylaxis for mitral valve prolapse (MVP) with regurgitation and/or valve thickening in endocarditis prophylaxis recommendations in 2006 [5]; but the updated guide does not include this recommendation. Also new guideline recommends that eradication with antibiotics before the procedure will be a rational approach if there is enterococcal urinary infection or colonization in high-risk patients who will undergo elective cystoscopy or other urinary maneuvers [6]. Likewise, the European Society of Cardiology guidelines for the management of infective endocarditis, published in 2015, recommended prophylaxis against enterococci (ampicillin, amoxicillin, or vancomycin) to protect against wound infection or septicemia due to genitourinary maneuver in high-risk patients. The high-risk patients described as; patients with prosthetic valves, those with previous infective endocarditis, and those with congenital heart disease [7].

Because of the patient did not accept any operational procedure, we could not collect diagnostic samples anymore. However, as same pathogen growth in blood culture samples which were taken after prostate biopsy and in urine culture taken during prostate biopsy; it is believed that the source of abscess, vegetation and spondylodiscitis were also the same pathogen.

In our case, prostate biopsy was performed within the indications but two severe operations were planned, a long and

serious antibiotherapy process and its related side effects were occurred because of prostate biopsy. In a study of Hiyama et al. [8], they reported a 59-year-old patient who underwent prostate biopsy because of high PSA values found in checkup without any symptoms. Aortic valve replacement was performed due to acute heart failure because of infective endocarditis and in this patient there was vegetation in echocardiography and positive blood cultures in which Enterococcus faecalis was responsible.

As far as we know, our case is second in which these two important complications were seen together after prostate biopsy. In light of these two cases, clinicians should consider that prostate biopsy may cause serious complications when they are screening asymptomatic men for prostate cancer or deciding whether or not to have a prostate biopsy.

References

1. Center MM, Jemal A, Lortet-Tieulent J, Ward E, Ferlay J, Brawley O, et al. International variation in prostate cancer incidence and mortality rates. European Urology. 2012;61(6):1079-92.
2. Schroder FH, Hugosson J, Roobol MJ, Tammela TL, Zappa M, Nelen V, et al. Screening and prostate cancer mortality: results of the European Randomised Study of Screening for Prostate Cancer (ERSPC) at 13 years of follow-up. Lancet. 2014;384(9959):2027-35. doi: 10.1016/S0140-6736(14)60525-0. PMID: 25108889; PMCID: PMC4427906.
3. Carter HB, Albertsen PC, Barry MJ, Etzioni R, Freedland SJ, Greene KL, et al. Early detection of prostate cancer: AUA Guideline. The Journal of Urology. 2013;190(2):419-26.
4. Parker C, Gillessen S, Heidenreich A, Horwich A. Cancer of the prostate: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2015;26(suppl 5):v69-v77.
5. Bonow RO, Carabello BA, Chatterjee K, de Leon AC, Faxon DP, Freed MD, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing Committee to Revise the 1998 guidelines for the management of patients with valvular heart disease) developed in collaboration with the Society of Cardiovascular Anesthesiologists endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. Journal of the American College of Cardiology. 2006;48(3):e1-e148.
6. Antman EM, Hand M, Armstrong PW, Bates ER, Green LA, Halasyamani LK, et al. 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: developed in collaboration With the Canadian Cardiovascular Society endorsed by the American Academy of Family Physicians: 2007 Writing Group to Review New Evidence and Update the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction, Writing on Behalf of the 2004 Writing Committee. Circulation. 2008;117(2):296-329. doi: 10.1161/CIRCULATIONAHA.107.188209. PMID: 18071078.
7. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta J-P, Del Zotti F, et al. 2015 ESC Guidelines for the management of infective endocarditis. European Heart Journal. 2015:ehv319.
8. Hiyama Y, Takahashi S, Uehara T, Ichihara K, Hashimoto J, Masumori N. A case of infective endocarditis and pyogenic spondylitis after transrectal ultrasound guided prostate biopsy. J Infect Chemother. 2016;22(11):767-9. Epub 2016/10/26. doi: 10.1016/j.jiac.2016.05.002. PMID: 27374863.

J Surg Med. 2018;2(3):347-349.
DOI: 10.28982/josam.413987

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Cytomegalovirus myocarditis with rapid response to intravenous immunoglobulin therapy

İntravenöz immünoglobulin tedavisine hızlı yanıt veren Sitomegalovirüs miyokarditi

Mehmet Türe [1], Hasan Balık [1], Meki Bilici [1], Alper Akın [1], Savaş Mert Darakci [2], Sercan Yücel Yanmaz [2]

[1] Dicle University Hospital, Department of Pediatric Cardiology, Diyarbakır, Turkey
[2] Dicle University Hospital, Department of Pediatric, Diyarbakır, Turkey

ORCID ID of the authors
MT: 0000-0002-8167-4714
HB: 0000-0002-3373-1585
MB: 0000-0001-8316-7102
AA: 0000-0003-1587-9559
SMD: 0000-0001-7788-9248
SYY: 0000-0002-2930-2817

Abstract

Myocarditis is an inflammatory disease of the heart muscle. Most cases are caused by viral agents such as enteroviruses and adenoviruses. Cytomegalovirus is one of the more rare causes of viral myocarditis. In this article, case is reported of viral myocarditis diagnosed due to Cytomegalovirus infection and which then responded very rapidly to intravenous immunoglobulin treatment. This case report can be considered to contribute to literature as there are not enough data about intravenous immunoglobulin treatment results in Cytomegalovirus myocarditis.

Keywords: Cytomegalovirus, Myocarditis, Intravenous immunoglobulin therapy

Öz

Miyokardit; kalp kasının enflamatuar bir hastalığıdır. Olguların çoğunda etken enterovirüsler ve adenovirüsler gibi viral ajanlardır. Sitomegalovirüs viral miyokarditin daha nadir görülen nedenlerinden biridir. Bu makalede Sitomegalovirüs enfeksiyonuna bağlı viral miyokardit tanısı konulan ve intravenöz immunglobulin tedavisine çok hızlı yanıt veren bir olgu sunuldu. Sitomegalovirüs miyokarditinde intravenöz immunglobulin tedavisi sonuçları ile ilgili yeterli veri olmaması nedeniyle bu olgu sunumunun literatüre katkıda bulunacağını düşünüyoruz.

Anahtar kelimeler: Sitomegalovirüs, Miyokardit, İntravenöz immunglobulin tedavisi

Introduction

Myocarditis is a disease progressing with inflammatory cell infiltration of the myocardium, caused primarily by viral infections. Cytomegalovirus (CMV), which is a member of the herpes virus family, is one of the more uncommon agents of myocarditis [1]. Cardiac complications associated with CMV infection are rarely seen and only a few cases have been reported. Primary cardiac involvement is pericarditis and/or myocarditis [2]. The first stage of treatment in myocarditis is supportive treatment. Although studies have reported positive effects of intravenous immunoglobulin (IVIG) treatment in acute viral myocarditis, the use of immunosuppressive agents remains controversial. Antiviral treatment has been used in some cases of viral myocarditis associated with CMV infection. However, there have been insufficient studies related to IVIG treatment efficacy in these patients [3]. We aimed to present a successful treatment of CMV myocarditis with IVIG therapy.

Corresponding author / Sorumlu yazar:
Mehmet Türe
Address / Adres: Dicle Üniversite Hastanesi, Çocuk Kardiyoloji Bölümü, Diyarbakır, Türkiye
e-Mail: drture21@gmail.com

Informed Consent: The author stated that the written consent was obtained from the parent of the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastanın ailesinden yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 09.04.2018
Accepted / Kabul tarihi: 25.04.2018
Published / Yayın tarihi: 25.04.2018

How to cite / Atıf için: Türe M, Balık H, Bilici M, Akın A, Darakci SM, Yanmaz SY. Cytomegalovirus myocarditis with rapid response to intravenous immunoglobulin therapy. J Surg Med. 2018;2(3):347-349.

Case presentation

A 3-month old male infant presented at our center because of discomfort and on determination of cardiomegaly, was referred to the Pediatric Cardiology Polyclinic. In the physical examination, the general status was fair, with agitation and discomfort. Body weight was 4.2 kg, body temperature 36.4°C, respiratory rate 46/min and arterial blood pressure 64/43 mmHg. In the cardiac examination, there was determined to be tachycardia (heart rate 154 bpm), heart sounds were normal and there was no murmur. Findings of the 12-derivation surface electrocardiograph were consistent with sinus tachycardia. On telegraphy, the cardiothoracic ratio was measured as 63%. On transthoracic echocardiography (ECO), the left ventricle was determined to be wider than normal, left ventricle diastole end diameter (LVEDd) was 27 mm (Z score 4.18), left ventricle systole end diameter (LVESd) was 20 mm (Z score 4.84), left ventricle ejection fraction (LVEF) was 50%, left ventricle shortening fraction (LVSF) was 24% and there was a mild level of mitral failure. CK-MB (Creatinine kinase myocardial isoenzyme) was determined as 8.8 ng/ml (normal: 0.6-6.3), troponin I 0.06 ng/ml (normal 0-0.04), C-reactive protein 0.02 mg/dl (normal: 0-0.5), and white blood cell as 9.8 K/uL. Liver and kidney function test results and thyroid functions were normal. There was no production in blood, urine or feces cultures. Tandem mass, and amino acid levels in the blood and urine, antinuclear antibodies (ANA) and anti-dsDNA and blood gas values were normal. Anti CMV IgM was determined as 45.1 % (normal <22%), anti CMV IgG 48.1 UA/ml (normal <14 UA/ml), CMV IgG avidity <0.3 UA/ml (low avidity), and CMV PCR 1.58x 102 cp/ml (positive). When these results were evaluated together with the ECO findings, viral myocarditis associated with active CMV infection was considered. Treatment of furosemide, captopril and low-dose digoxin was started. On the third day of hospitalization, as the discomfort of the patient increased and the ECO findings and clinical findings continued, IVIG of 1gr/kg/day (48 hours) was started. The changes in the ECO and laboratory findings from before and after the IVIG treatment are shown in Table 1. On the thirteenth day of hospitalization, the general status was good so the patient was discharged with digoxin, captopril and furosemide. At the first and sixth month follow-up examinations, the left ventricular systolic and diastolic functions on ECO were determined to be normal. The written consent was obtained from the parent of the patient presented in the study.

Table 1: Laboratory and ECO findings before and after IVIG treatment (Note: IVIG treatment was given on the 3rd day of hospitalization)

	At the time of diagnosis	1st Day	3rd Day	1st Week	1st Month	6th Month
LVEF (%)	50		51	65	71	69
LVSF (%)	24		25	34	39	37
LVEDd (mm)	27		28	24	25	25
LVESd (mm)	20.5		21	16	15	16
Troponin I (ng/ml)	0.06	0.05		0.04	0.01	0.02
CK-MB (ng/ml)	9.9	8.8		7.1	5	6

LVEF: left ventricle ejection fraction LVSF, left ventricle shortening fraction, LVEDd: left ventricle diastole end diameter, LVESd: left ventricle systole end diameter, CK-MB: Creatinine kinase myocardial isoenzyme

Discussion

It has been reported that the myocardial damage seen in myocarditis could be related to immunological mechanisms rather than the direct effect of viral infections. Therefore, there are studies supporting the use of IVIG, which is an immunomodulator, in the treatment of viral myocarditis in children [4]. IVIG treatment increases the plasma level of the anti-inflammatory mediator, IL-10, IL-1 receptor antagonist and tumor necrosis factor receptors. It also reduces the N-terminal pro-atrial natriuretic peptide level. The use of IVIG in viral myocarditis has been reported to decrease cardiac inflammation and pro-inflammatory cytokines [5]. Nevertheless, as the efficacy of IVIG in viral myocarditis patients has not been proven in studies, its use in the treatment of myocarditis remains controversial [6].

In a randomized study of 62 patients with dilated cardiomyopathy, no effect of IVIG treatment was seen on ventricular ejection fraction. This showed that there was no positive effect on cardiac functions and life expectancy [6]. However, there are also studies of patients with myocarditis showing that IVIG was effective in children by regulating left ventricular function and increasing survival [4]. High-dose IVIG treatment has been shown to correct newly-developed dilated cardiomyopathy and increase ejection fraction by 17 units [7]. Although the definitive diagnosis of myocarditis is made from endomyocardial biopsy, definitive diagnosis cannot be made in some patients despite the biopsy and when this procedure is applied in only a few selected patients because of the risk of biopsy, the treatment decision including IVIG is made based on the laboratory, ECO and clinical findings of the patient.

In the current study as viral myocarditis associated with CMV was supported by the clinical, laboratory and ECO findings and the left ventricle systolic functions were impaired, IVIG was started. Although there are publications related to antiviral treatment or the use of IVIG in CMV myocarditis [3,8], there are insufficient data of the results of IVG use in these patients. As a CMV myocarditis patient who improved following IVIG, although this has been rarely reported in literature, the echocardiographic and clinical recovery in this patient was considered to be associated with the IVIG treatment.

Conclusion

Although there are studies in literature that have shown the efficacy of IVIG in the treatment of viral myocarditis in children, as there are also studies showing no effect, the use of IVIG in treatment is still a matter of debate. However, as seen in the current patient, it is possible to achieve a rapid recovery in cardiac functions with this treatment. As there are insufficient studies related to the response to IVIG in CMV myocarditis, there is a need for the evaluation of many more patients to confirm the positive effects of IVIG treatment on cardiac functions.

References

1. Cohen JI, Corey GR. Cytomegalovirus infection in the normal host. Medicine (Baltimore). 1985;64:100-14.
2. Campbell PT, Li JS, Wall TC, O'Connor CM, Van Trigt P, Kenney RT, et al. Cytomegalovirus pericarditis: a case series and review of the literature. Am J Med Sci. 1995;309:229-34.

3. Fernández-Ruiz M, Muñoz-Codoceo C, López-Medrano F, Faré-García R, Carbonell-Porras A, Garfia-Castillo C, et al. Cytomegalovirus Myopericarditis and Hepatitis in an Immunocompetent Adult: Successful Treatment with Oral Valganciclovir. Intern Med. 2008;47:1963-6.
4. Amarendra N Prasad, Sanjay Chaudhary. Intravenous Immunoglobulin in Children with Acute Myocarditis and/or Early Dilated Cardiomyopathy Indıan Pedıatrıcs Volume 51-july 15, 2014.
5. Finkel MS, Oddis CV, Jacob TD, SC Watkins, BG Hattler, RL Simmons. Negative inotropic effects of cytokines on the heart mediated by nitric oxide. Science. 1992;257:387-9.
6. McNamara DM, Holubkov R, Starling RC, Dec GW, Loh E, Torre-Amione G, et al. Controlled trial of intravenous immune globulin in recent-onset dilated cardiomyopathy. Circulation. 2001;103:2254-9.
7. McNamara DM, Rosenblum WD, Janosko KM, Trost MK, Villaneuva FS, Demetris AJ, et al. Intravenous immune globulin in the therapy of myocarditis and acute cardiomyopathy. Circulation. 1997;95:2476-8.
8. Partanen J, Nieminen MS, Krogerus L, Lautenschlager I, Geagea A, Aarnio P, et al. Cytomegalovirus myocarditis in transplanted heart verified by endomyocardial biopsy. Clin Cardiol. 1991 Oct;14(10):847-9.

J Surg Med. 2018;2(3):350-352.
DOI: 10.28982/josam.408634

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Mesenteric panniculitis: Case report

Mezenterik pannikülit: Olgu sunumu

Eddy Oleko Ekuke [1], Fatoumata Djouldé Diallo [2], El Bachir Benjelloun [1], Benajah Dafr-Allah [2]

[1] Department of Visceral Surgery, Hassan II University Hospital, Fez, Morocco
[2] Department of Gastroenterology and Hepatology, Hassan II University Hospital, Fez, Morocco

ORCID ID of the authors
EOE: 0000-0003-0381-4870
FDD: 0000-0003-0053-1920
EBB: 0000-0002-3176-6899
BD: 0000-0002-1815-1080

Abstract

Rare and poorly documented, mesenteric panniculitis (MP) is characterized by nonspecific inflammation affecting adipose tissue of the mesentery. Modern imaging, computed tomography and especially magnetic resonance imaging can be very useful in the workup thus reducing unnecessary laparotomy hitherto required for the positive diagnosis of this affection. Pathology examination still remains necessary as it eliminates key differentials notably liposarcoma. This could be achieved through imaging-guided biopsy. We hereby report a case of sclerosing mesenteritis in a 43 years old patient.

Keywords: Mesenteric panniculitis, Sclerosing mesenteritis

Öz

Nadir ve az belgelenmiş mezenterik pannikülit (MP), mezenterlerin yağ dokusunu etkileyen spesifik olmayan inflamasyon ile karakterizedir. Modern görüntüleme, bilgisayarlı tomografi ve özellikle manyetik rezonans görüntüleme, işte çok faydalı olabilir ve bu nedenle bu affinasyonun pozitif teşhisi için gerekli olan gereksiz laparotomiyi azaltır. Patoloji incelemesi, özellikle liposarkom başta olmak üzere önemli farklılıkları ortadan kaldırdığı için hala gereklidir. Bu, görüntüleme kılavuzluğunda biyopsi ile sağlanabilir. Bu yazıda, 43 yaşında bir hastada sklerozan mezenterit vakası sunulmuştur.

Anahtar kelimeler: Mezenterik pannikülit, Sklerozan mezenterit

Corresponding author / Sorumlu yazar:
Eddy Oleko Ekuke
Address / Adres: Department of Visceral Surgery, Hassan II University Hospital, Fez, Morocco
e-Mail: olekoekuke20121982@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 22.03.2018
Accepted / Kabul tarihi: 26.04.2018
Published / Yayın tarihi: 26.04.2018

Introduction

Mesenteric panniculitis (MP) is a rare condition defined as an acute or subacute inflammation of the bowel mesentery characterized by fibrosis and peritoneal retraction as it progresses to chronicity hence the name sclerosing mesenteritis (SM) [1]. It is a non-specific inflammatory disorder of the adipose tissue of the mesentery. Before the advent of modern imaging technics, definite diagnosis was often achieved through laparotomy or incidentally made on pathology specimens. Thus we deem interesting to report a case of SM in a 43 year old male, for which diagnosis was suspected on imaging and confirmed by pathology findings.

Case presentation

Patient, 43-year-old male with no significant clinical history presented with moderate left upper quadrant pain accompanied by intermittent vomiting which worsened a few hours prior to his admission with incomplete bowel obstruction. Physical examination found a conscious patient, stable vitals, with a slightly distended abdomen, tympanitic with no palpable mass. Abdominal computed tomography (CT) showed several dilated bowel loops with thickening of the wall. There was a partially calcified tissue mass of the mesentery with localized fibrosis, responsible for retraction of the adjoining ileal loops. Well defined hypodense nodules were also found in segment IV and segment V of the liver that faded on contrast injection (Figure 1, 2). Magnetic resonance imaging (MRI) came back for sclerosing mesenteritis. The presence of bowel abnormalities in the form of sclerosing mesenteritis with localized GI wall thickening and calcifications should point to carcinoid tumor of the small intestine especially. The case was discussed at a multidisciplinary cancerology meeting were surgery was indicated.

How to cite / Atıf için: Ekuke EO, Diallo FD, Benjelloun EB, Dafr-Allah B. Mesenteric panniculitis: Case report. J Surg Med. 2018;2(3):350-352.

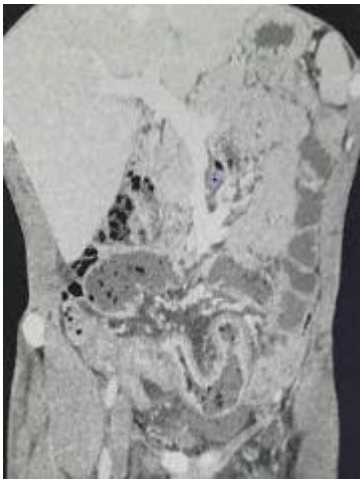


Figure 1: Abdominal computed tomography sagittal showing aspect of mesenteric panniculitis

Figure 2: Abdominal computed tomography axial section showing aspect of mesenteric panniculitis

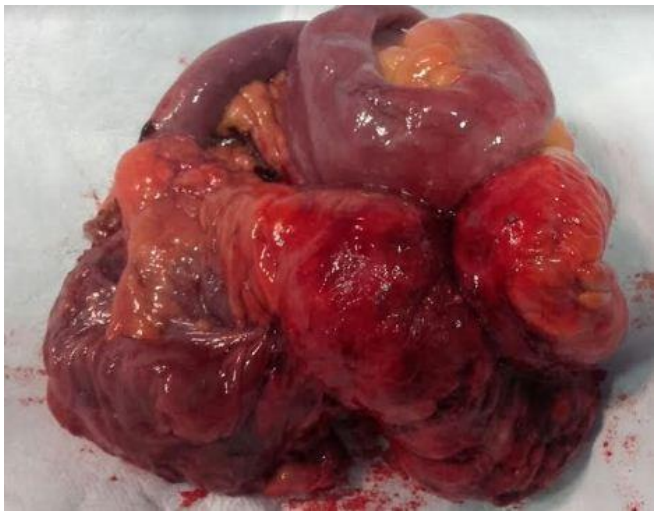


Figure 3: Operational view

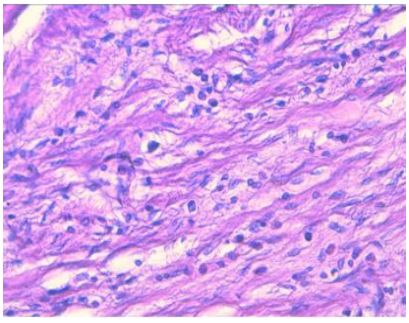


Figure 4: The histological image showing the proliferation of fibroblastic cells without atypiesfrays with an inflammatory infiltrate rich in plasmocytes (HESx400)

The patient underwent surgery with peroperative discovery of a mesenteric mass measuring about 10 cm in diameter invading the last ileal loop and coming into close contact with the bladder, mesosigmoid and even part of the sigmoid colon (Figure 3). An ileocecal resection taking up the mass was undertaken with subsequent mechanical ileo-colic latero-lateral anastomosis. Postoperative recovery was unremarkable. Pathology examination of surgical specimen came back for an inflammatory pseudo-tumor of the mesentery (Figure 4). The case was further discussed at the cancerology meeting in the light of the latest developments where monitoring was prescribed. The evolution was simple.

Discussion

SM is a rare disorder in adults first described in 1994 by Juraz. The highest prevalence is around sixth and seventh decade with a slight male predominance and a sex ratio of 1.8 / 1. In 1 out of 2 cases, it is asymptomatic and of fortuitous discovery. Pain is the main symptom, sometimes associated with gradual weight loss, diarrhea or vomiting or even present in a setting of incomplete bowel obstruction. Fever may also be observed [1,2]. It is characterized by variable associations of inflammatory lesions, necrosis and fibrosis of mesenteric fat tissue. Its pathogenesis remains unclear although associations with inflammatory and other neoplasms, in particular lymphomas have been suggested. The condition can remain asymptomatic in 30 to 50% of cases. In cases where the affection is symptomatic, abdominal pain (70%), an abdominal mass (40 to 70%) of variable location and rarely tender (33%) can usually be observed [3,4].

Asthenia and fever are almost constant in the latter stages of SM: constipation and bowel obstructions are usually observed. The general state is often altered. An abdominal mass can be observed [1]. The etiology of this condition remains unclear. Several predisposing factors have been mooted notably previous abdominal surgery [2,5] or trauma, retention of surgical equipment or bacterial infection. This benign condition may be associated with other diseases such as non-Hodgkin's lymphoma or Hodgkin's disease [5], yet the reason for this association is yet to be explained .Although the pathogenesis of mesenteric panniculitis remains unclear: the possibility of excessive enzymatic degradation due to an inherent a1-antitrypsin deficiency is largely considered as one of the major causes of panniculitis [6,7]. CT is often the first line imaging tool in the diagnosis and allows to rule out other differential diagnoses. CT is very relevant as it shows a marked attenuation of the adipose tissue of the mesentery which is a specific to SM. The fat density of the mesentery (-40 to -60 HU) is higher than that of the subcutaneous fat or normal peritoneal fat (-100 to -160 HU) [8]. CT features, as well as MRI findings, are not specific and thus exploratory laparotomy with multiple biopsies is sometimes required [2]. Modern imaging (CT and MRI) have been useful identifying macroscopic forms including multilocular pseudo cystic forms [6,8]. These are in fact nodular forms associated with partitioned fluid collections containing chylous liquid secondary to extrinsic compression of lymphatic vessels. MRI features vary according to the intensity of the inflammatory component [9,10]. As a general rule, it presents as mass with

intermediate signal on T1 and slightly hyper intense on T2, slightly enhanced after gadolinium injection. Dynamic sequences (FMPSPGR: Fast multiplanar spoiled gradient-recalled) in apnea cover the entire abdomen and allow the study of contrast medium enhancement. Sequences obtained after saturation of fat make it possible to better discern the links of the fat-like inflammatory pseudo-tumor of the mesentery with the surrounding adipose tissue. MP is characterized by multiple relapses with complete remission in more than 50% of cases. An association with lymphoma has been largely reported. In some cases, it may evolve towards SM with its associated complications among others bowel obstruction, superior mesenteric vein thrombosis, anasarca and / or cachexia. The clinical course of mesenteric panniculitis is often favorable. No treatment, surgery in particular, is generally necessary as the mass is indestructible. Symptoms regress, in most cases, without treatment but intermittent pain could sometimes persist [2]. Only one (01) case of fatal evolution with extensive acute necrosis has however been reported in recent literature [11] .The most common complications are extrinsic compression of the bowel lumen, especially the ileal loops by the mesenteric mass, lymphatic compression with formation of chylous ascites and cystic masses, vascular compression and in particular venous compression with thrombosis of the superior mesenteric vein and finally evolution towards sclerosing mesenteritis with formation of diffuse fibrosis. Corticosteroids are useful in subacute episodes whereas azathioprine is effective as maintenance therapy. A recent study reported favorable outcomes with thalidomide in early stages of PM [1]. Surgery is only deemed necessary in the event of complications. As SM lesions are often unresectable, surgical treatment is reserved for the treatment of obstructive or vascular complications and generally consists of digestive bypass with segmental resection.

Conclusion

Mesenteric panniculitis (MP), also known as sclerosing mesenteritis (SM), is a rare disease that causes thickening and shortening of the mesentery. Its etiology and pathogenesis remain unclear, although several predisposing factors and its associations with inflammatory and neoplasms, particularly lymphomatous, have been largely reported. Pain is the most commonly encountered clinical symptom, even though one out of every two cases is incidental and completely asymptomatic. CT and MRI currently allow positive diagnosis in the presence of suggestive yet non-specific signs. This condition poses a great diagnostic challenge to radiologist and surgeons at large as it constitutes a major differential with GI malignancies like liposarcoma in its lipogenic form which has similar imaging features on CT and MRI. Imaging guided percutaneous biopsy could be necessary in the workup of MP as it avoids invasive laparotomy. Surgery is sometimes useful in the management of complications such as acute bowel obstruction.

References

1. Gu G-L, Wang S-L, Wei X-M, Ren L, Li D-C, Zou F-X. Sclerosing mesenteritis as a rare cause of abdominal pain and intraabdominal mass: a cases report and review of the literature. Cases Journal. 2008;1:242.
2. MacVicar D, Husband JE, Taylor R, Menzies-Gow N, Cunningham D. Intra-abdominal panniculitis can mimic recurrent stomach carcinoma. Clinical Oncology. 1992;4:194-5.
3. Jerraya H, Khalfallah M, Nouira R, Dziri C. Mesenteric Panniculitis: An Unusual Cause of Epigastric Pain. Journal of Clinical and Diagnostic Research. 2015;9:PJ01.
4. Kipfer RE, Moertel CG, Dahlin DC. Mesenteric lipodystrophy. Annals of Internal Medicine. 1974;80:582-8.
5. Cooper CJ, Silverman PM, Forer L, Stull MA. Mesenteric panniculitis. American Journal of Roentgenology. 1990;154:1328-9.
6. Sauvaget F, Piette JC, Galezowski N, Jouanique C, Chapelon C, Blétry O, Herreman G, Godeau P. Polychondrite atrophiante et panniculite mésentérique : à propos de 2 cas. Rev Med Interne. 1993;14:253-6.
7. Daskalogiannaki M, Voloudaki A, Prassopoulos P, Magkanas E, Stefanaki K, Apostolaki E, et al. CT evaluation of mesenteric panniculitis: prevalence and associated diseases. American Journal of Roentgenology. 200;174:427–31.
8. Kawashima A, Fishman EK, Hruban RH, Kuhlman JE, Lee RP. Mesenteric panniculitis presenting as a multilocular cystic mesenteric mass: CT and MR evaluation. Clinical Imaging. 1993;17:112-6.
9. Badiola-Varela CM, Sussman SK, Glickstein MF. Mesenteric panniculitis: findings on CT, MRI, and angiography: Case report. Clinical Imaging. 1991;15:265-67.
10. Kakitsubata Y, Umemura Y, Kakitsubata S, Tamura S, Watanabe K, Abe Y, Hatakeyama K. CT and MRI manifestations of intraabdominal panniculitis. Clinical Imaging. 1993;17:186-8.
11. Andersen JA, Rasmussen NR, Pedersen JK. Mesenteric panniculitis: a fatal case. Am J Gastroenterol. 1982 Jul;77(7):523-5.

J Surg Med. 2018;2(3):353-355.
DOI: 10.28982/josam.412609

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Syringomatous adenoma of the nipple: Case report

Meme başının siringomatöz adenomu: Olgu sunumu

Şirin Yaşar [1], Nurhan Döner Aktaş [2], Ayşegül Sevim Keçici [1], Pembegül Güneş [3], Güldehan Atış [1]

[1] Haydarpaşa Numune Training and Research Hospital, Department of Dermatology, Istanbul, Turkey
[2] Katip Çelebi University Training and Research Hospital, Department of Dermatology, Izmir, Turkey
[3] Haydarpaşa Numune Training and Research Hospital, Department of Pathology, Istanbul, Turkey

ORCID ID of the authors
ŞY: 0000-0002-5973-2068
NDA: 0000-0003-2381-3824
ASK: 0000-0002-1569-9198
PG: 0000-0003-2698-2180
GA: 0000-0001-5069-044X

Corresponding author / Sorumlu yazar:
Şirin Yaşar
Address / Adres: Tıbbiye Caddesi, Haydarpaşa Numune Eğitim ve Araştırma Hastanesi, Dermatoloji Bölümü, İstanbul, Türkiye
e-Mail: drsirin@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 04.04.2018
Accepted / Kabul tarihi: 26.04.2018
Published / Yayın tarihi: 26.04.2018

Abstract

Syringomatous adenoma is a rare disease of the nipple that was mostly easily confused nipple eczema or erosive nipple adenoma. Although, mammographic findings indicate carcinoma, this condition has benign, locally infiltrative characteristics. Herein, a patient with complaints of pruritus and minimal enlargement of right nipple was firstly evaluated as nipple eczema or erosive adenoma of nipple, but no response was detected with topical treatments. Patient was diagnosed with syringomatous adenoma of nipple with histopathologic examination findings that were double layered epithelial ductus proliferations which some of them had tear-drop, comma-like appearance and nipple area was excised. This rare condition is discussed with literature.

Keywords: Breast, Nipple, Syringomatous adenoma

Öz

Siringomatöz adenom, çoğunlukla meme başı ekzeması ya da meme başının eroziv adenomu ile kolayca karışabilen, meme başının nadir görülen bir hastalığıdır. Mammografik bulgular karsinomu düşündürmesine rağmen, bu tablo lokal infiltratif özellik taşımaktadır. Burada 1 yıldır sağ meme başında kaşıntı ve hafif büyüme şikayeti olan hasta öncelikle "nipple ekzema" ya da "meme başının eroziv adenomu" olarak değerlendirilmiş, ancak topikal tedavilere yanıt alınamamıştır. Hastaya, histopatolojik incelemede dermiste iki sıra epitel ile döşeli, bazıları "gözyaşı damlası - tear-drop" ve "virgül şeklinde - comma-like" görünümde duktus proliferasyonu ile meme başının siringomatöz adenomu tanısı konuldu ve meme başı eksize edildi. Bu nadir olgu literatürler eşliğinde tartışıldı.

Anahtar kelimeler: Meme, Meme başı, Siringomatöz adenom

Introduction

Syringomatous adenoma of the nipple (SAN) is a very rare benign tumor that was first reported by Rosen in 1983 [1]. SAN is originated from eccrine sweat glands and usually located over the areola area or more specifically nipple. It is histologically similar to a syringoma, a benign tumour originating in the ducts of the dermal sweat glands, and importantly needs to be distinguished from a tubular carcinoma [2]. Tumoral lesions of the nipple area accompanying bleeding, discharge or ulceration are common in female patients. Unilaterally located SAN usually shows locally infiltrating growth but does not metastasize. Nonetheless, in some cases, this tumor may be misdiagnosed as a malignancy owing to its locally aggressive infiltrating growth pattern. Best treatment option is local excision of the tumor [2.3].

Case presentation

A 38-year-old woman presented with a 1-year history of mild itching sensation on her right nipple. She has been previously given various treatments; however her symptoms did not improve. Both her past personal and family medical history was unremarkable, excluding any history of breast cancer.

How to cite / Atıf için: Yaşar Ş, Aktaş ND, Keçici AS, Güneş P, Atış G. Syringomatous adenoma of the nipple: Case report. J Surg Med. 2018;2(3):353-355.

On physical examination, there was an induration over the right nipple area, together with 4 or 5 millia like white papules and desquamation. No discharge or nipple retraction was detected. She was diagnosed as having nipple eczema and started on mid-potent topical corticosteroid ointments and moisturizers. In two weeks follow-up, symptoms improved markedly. Three months later, the signs and symptoms recurred and a biopsy was planned, however the patient did not consent the procedure. Thus physical and mammography exams were performed and fibrocystic changes were detected. Seven months later, she was in 28 weeks of her pregnancy and was admitted with similar complaints together with enlargement of the lesion on her right nipple (Figure 1).

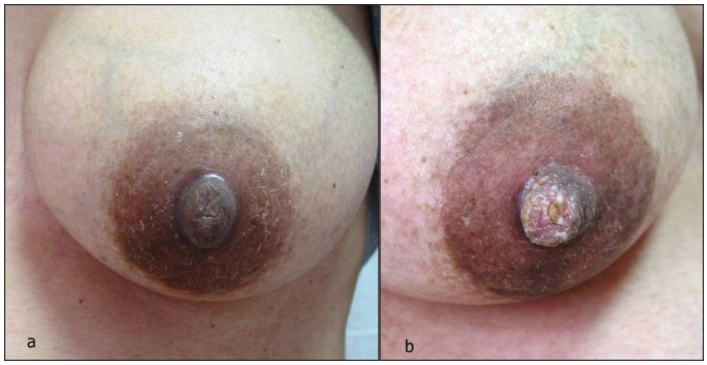


Figure 1: a: Left nipple areolar complex was nonpathological appearance, b: There was an induration over the right nipple area, together with 4 or 5 millia like white papules and desquamation.

A biopsy with a suspicion of nipple eczema, Paget disease, Bowen disease and erosive adenoma of the breast was performed. Histopathological examination showed tear-drop or comma-like ductal proliferation in dermis, lined by double-layered epithelia, consistent with SAN (Figure 2). There were no atypical mitosis or necrosis and estrogen receptors were negative. At the end of the pregnancy period, local excision of the lesion was performed. The written consent was received from the patient who was presented in this study.

Discussion

SAN is a rare, locally aggressive benign tumor of the nipple and subareolar region. These tumors commonly manifest as solitary firm masses in the subareolar or nipple region of the unilateral breast, and may also occur within the breast parenchyma [2-6].

Lesions are generally 1-3 mm in size and they may be clinically asymptomatic, tender and painful on palpation, and/or present with itching and ulceration. Nipple inversion or discharge is noted on occasion [2].

Upon mammographic imaging, SAN generally appears as a high-density mass in the subareolar region with an irregular outline, spicule formation, and microcalcification foci, while ultrasonography shows an ill-defined mass with heterogeneous internal echoes [2,7]. Imaging findings of SANs resemble those of malignant tumors, and, therefore, they may be indistinguishable from carcinoma with mammography, ultrasonography, and MRI. Fine needle biopsy examination of the lesions may not be adequate to fully understand the locally aggressive growth pattern of the lesion and thus may lead to unnecessary mastectomies or axillary dissections [2,5,6]. Incisional or excisional biopsies have been helpful for the diagnosis of 31 patients, with ages ranging between 11 and 76 [2].

In most of the cases, making the diagnosis of syringomatous adenoma clinically is difficult and pathological examination is essential. Histologically, the lesion is composed of tubules, ductules, and strands of small, uniform, generally basophilic cells infiltrating the dermis of the surrounding skin and the stroma of the nipple. Proliferating ducts, which are lined by a single or multiple layers of metaplastic squamous cells, may be present. These double-layered cell nests have a specific teardrop, comma-shaped or tad-pole appearance, and the tumor cells can infiltrate the stroma between the smooth muscle bundles, and even in the perineural region [2,3,8]. Hyperplastic changes can be detected in the breast tissue surrounding the tumoral lesion. While making the histopathological diagnosis of syringomatous adenoma; 1- tumoral invasion of the dermis and subcutaneous tissue around the nipple or areola region 2- Comma-shaped tubular proliferation infiltrating smooth muscle or neural bundles 3- Presence of myoepithelial cells around the tubules 4- Stratified squamous epithelia lining cysts, filled with keratinous material 5- Absence of mitotic activity or necrosis should be considered [2]. In our case, the dermis of the tumor was typically lined with double layered epithelia, together with tear-drop and comma-shaped ductal proliferation. Absence of mitosis and necrosis also supported the diagnosis.

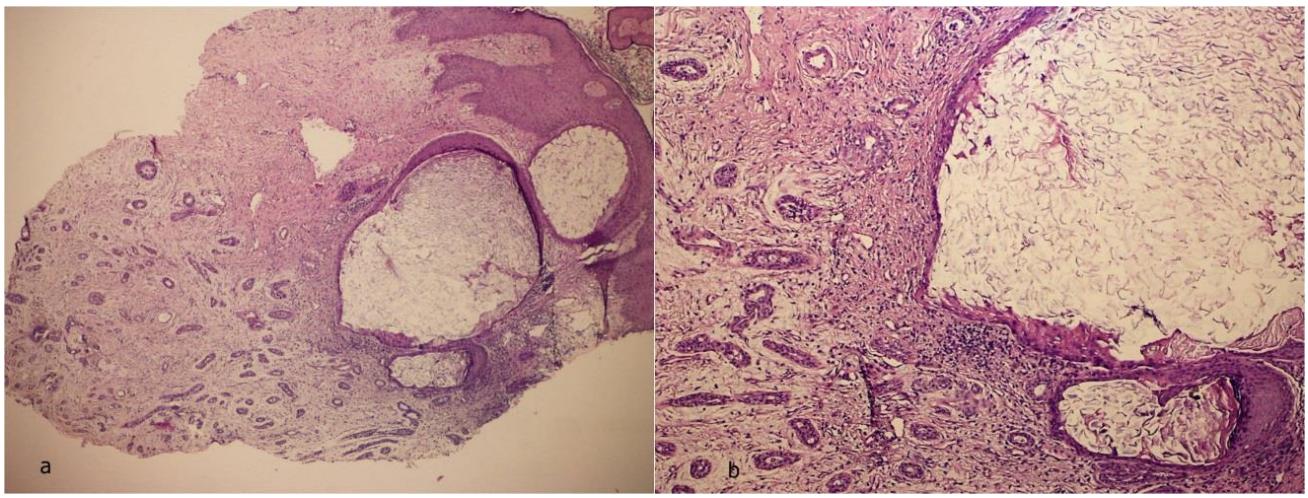


Figure 2: Histopathological examination showed tear-drop or comma-like ductal proliferation in dermis, lined by double-layered epithelia, consistent with syringomatous adenoma of the nipple (H&E x40, x100)

Nipple duct adenoma and well-differentiated tubular carcinoma or low-grade adenosquamous carcinoma are often confused with SAN. These entities, however, exhibit some distinctive characteristics. Nipple duct adenoma often ulcerates the skin, is usually better circumscribed, and does not invade the perineural region or smooth muscle bundles. It consists of epithelial hyperplasia of the lactiferous ducts and does not show stromal invasion, unlike syringomatous adenoma.

Tubular carcinoma tends to occur deeper in the breast with positive estrogen receptors and is commonly located in the upper outer quadrant or away from the nipple. On the other hand, low-grade adenosquamous carcinoma tends to metastasize with both glandular and squamous differentiation. Syringoma, a benign tumor of the eccrine glands, also exhibits clinical features that distinguish it from SAN, including presentation as a solitary lesion in the nipple. Itching and ulceration of the nipple could also be observed in case of Paget's disease. However, histopathological examination of these lesions reveals large and clear cells, also known as Paget cells, with wide, oval shaped nucleus and edematous cytoplasm. Histopathological examination is the gold standard method for the differentiation of all these entities [2-6,8,9].

SAN has a tendency to show local recurrence when resected incompletely. Thus optimal initial management demands complete resection with histologically negative margins [2,3]. There was no recurrence of the lesions with histologically negative margins, for 1-6 years of follow-up periods [2]. There have been no reports of SAN with distant metastasis, so mastectomy or axillary dissection is not routinely performed. For better cosmetic outcomes, tumor resection with nipple preservation should be considered [2,3,10].

In the literature, there have been 3 cases of SAN during pregnancy and lactation, one case during lactation period and 4 cases as soon as the lactation period finishes [8,10-12]. These findings may suggest the possible relation of the tumor and maternal hormonal effects [10]. Increase in the size of the tumor during pregnancy in our case can also support this hormonal influence. In routine practice, local excision of the tumor is the treatment of choice. However, there is not a consensus in the literature about the approach during pregnancy, thus local nipple excision after pregnancy period was preferred in this case.

In conclusion, every chronic lesion of the nipple or subareolar region deserves to be examined histopathologically. Based on the features of this case and a review of the literature, infiltrating SA of the nipple is a rare benign but locally invasive tumor which importantly needs to be distinguished from malignant tumors. Appropriate management involves a consideration of the tendency to recur locally when incompletely excised. Instead of radical approaches, optimal surgical management involves complete excision of the lesion and confirmation of histologically negative margins.

References

1. Rosen PP. Syringomatous adenoma of the nipple. Am J Surg Pathol. 1983;7:739–45.
2. Oo KZ, Xiao PQ. Infiltrating syringomatous adenoma of the nipple: clinical presentation and literature review. Arch Pathol Lab Med. 2009;133:1487-9.
3. Carter E, Dyess DL. Infiltrating syringomatous adenoma of the nipple: a case report and 20-year retrospective review. Breast J. 2004;10:443-7.
4. Sarma DP, Stevens T. Infiltrating syringomatous eccrine adenoma of the nipple: a case report. Cases J. 2009;2:9118.
5. Hwang TS, Ham EK, Kim JP. Syringomatous adenoma of nipple--a case report. J Korean Med Sci. 1987;2:263-5.
6. Toyoshima O, Kanou M, Kintaka N, Miyashita M, Shigematsu S, Sano J. Syringomatous adenoma of the nipple: report of a case. Surg Today. 1998;28:1196-9.
7. Coulthard D, Liston J, Young JR. Case report: infiltrating syringomatous adenoma of the breast—appearances on mammography and ultrasonography. Clin Radiol. 1993;47(1):62–4.
8. Jones MW, Norris HJ, Snyder RC. Infiltrating syringomatous adenoma of the nipple: a clinical and pathological study of 11 cases. Am J Surg Pathol. 1989;13:197–201.
9. Ward BE, Cooper PH, Subramony C. Syringomatous tumor of the nipple. Am J Clin Pathol. 1989;92:692–6.
10. Oliva VL, Little JV, Carlson GW. Syringomatous adenoma of the nipple--treatment by central mound resection and oncoplastic reconstruction. Breast J. 2008;14(1):102-5.
11. Slaughter MS, Pomerantz RA, Murad T, et al. Infiltrating syringomatous adenoma of the nipple. Surgery. 1992;111:711–3.
12. Pernick N. Pathology Outlines. Bringham Falls: Michigan by Pathology Outlines.com, Inc., 2007.

J Surg Med. 2018;2(3):356-358.
DOI: 10.28982/josam.415187

Case report
Olgu sunumu

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Klippel-Trenaunay syndrome in a patient presenting with venous stasis ulcer

Venöz staz ülseri olan bir hastada Klippel Trenaunay sendromu

Kevser Tural [1], Zeynep Bilgi [2], Ceyhun Coşkun [3]

[1] Kafkas University, Faculty of Medicine, Department of Cardiovascular Surgery, Kars, Turkey
[2] Kars Harakani State Hospital, Department of Thoracic Surgery, Kars, Turkey
[3] Yalvaç State Hospital, Department of Cardiovascular Surgery, Isparta, Turkey

ORCID ID of the authors
KT: 0000-0003-4490-037X
ZB: 0000-0003-4981-047X
CC: 0000-0001-9106-1113

Corresponding author / Sorumlu yazar:
Kevser Tural
Address / Adres: Kafkas Üniversitesi, Tıp Fakültesi, Kardiyovasküler Cerrahi Bölümü, Kars, 36100, Türkiye
e-Mail: ktrl2011@hotmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 13.04.2018
Accepted / Kabul tarihi: 11.05.2018
Published / Yayın tarihi: 11.05.2018

Abstract

Klippel-Trenaunay syndrome is a congenital capillary-venous vascular malformation characterized by malformation of the capillaries, soft tissue and bone hypertrophy and atypical varicosities. Klippel-Trenaunay syndrome often affects the lower extremity but can also involve arms, trunk, head, neck, abdominal and pelvic organs, and central nervous system. Deep venous system anomalies are important in directing the treatment of these cases. In cases of deep vein hypoplasia, marginal vein can be resected since hypoplastic deep veins can spontaneously dilate to almost normal dimensions after marginal vein resection. In cases of deep venous aplasia, the embryonal vein can be the main drainage vein of the leg and the resection is unlikely. In this article, we present a case of a 20-year-old male with Klippel-Trenaunay syndrome who had right leg diameter increase, port-wine stain appearance, and venous ulcer.
Keywords: Klippel-Trenaunay syndrome, Port-wine stain, Venous ulcer, Limb hypertrophy

Öz

Klippel-Trenaunay sendromu kapiller malformasyon, yumuşak doku ve kemik hipertrofisi ve atipik varikoziteler ile karakterize edilen konjenital bir kapiler venöz vasküler malformasyondur. Klippel-Trenaunay sendromu genellikle alt ekstremiteyi etkiler; ancak kollar, gövde, baş, boyun, abdominal ve pelvik organlar ve santral sinir sistemini de etkileyebilir. Derin venöz sistem anomalileri, bu vakaların tedavisinin yönlendirilmesinde önemlidir. Derin ven hipoplazisi olan olgularda marjinal ven rezeke edilebilir çünkü rezeksiyondan sonra hipoplastik derin venler kendiliğinden dilate olurlar. Derin venöz aplazisi olan olgularda ise embriyonal ven bacağın ana drenaj veni olabilir ve rezeksiyonu olası değildir. Bu yazıda, sağ bacak çapında artış, port-wine lekesi görünümü ve venöz ülseri bulunan, Klippel-Trenaunay sendromu olan 20 yaşında erkek olgu sunulmuştur.
Anahtar kelimeler: Klippel-Trenaunay sendromu, Şarap lekesi görünümü, Venöz ülser, Bacak hipertrofisi

Introduction

Klippel-Trenaunay syndrome (KTS) was described as a syndrome characterized by limbic capillary nevi, leg hypertrophy and varicose veins [1]. With the addition of significant arteriovenous fistulas, Klippel-Trenaunay-Weber syndrome was also described later [2]. KTS often affects the lower extremity [1] but also can involve arms, trunk, head, neck [3], abdominal and pelvic organs [4,5] and central nervous system [6]. The ethio-pathogenesis of KTS has not been fully elucidated. Although it is mostly seen as sporadic, it has been reported to be inherited, autosomal dominant and originating from the genetic defects [7, 8]. Syndrome equally affects men and women [9]. Treatment of KTS is usually conservative, but surgical procedures for complications are required [10,11].

Case presentation

A 20-year-old male patient was referred to our clinic due to recurrent venous ulceration and swollen right leg. Clinical examination further revealed port wine stain of the right lower extremity covering an area from right foot to hip. The right ankle had a 1 cm venous ulcer scar in the lateral upper part (Figure 1). Both the port wine stain and increased right leg diameter were present since childhood (Figure 2). There was no functional loss. There was no clinical evidence of AV macrofistula.

How to cite / Atıf için: Tural K, Bilgi Z, Coşkun C. Klippel-Trenaunay syndrome in a patient presenting with venous stasis ulcer. J Surg Med. 2018;2(3):356-358.

Figure 1: Venous ulcer in the lateral upper part of the right ankle of the patient

Figure 2: Port-wine stain and right limb hypertrophy of right leg of the patient

Doppler ultrasonography (USG) showed perforating venules 7.2 mm and 6.2 mm in diameter and dilated superficial varicose veins associated with those were observed at the Cockett levels 2 and 3 with reflux flow with proximal compression. The right vena saphena magna diameter was 5.7 mm and there was no reflux in the right saphenofemoral junction. There was no deep venous insufficiency or deep venous thrombus.

Decision for surgical repair was made after appropriate informed consent. Two perforating venules were ligated surgically. At 3rd month follow up, complete healing of the chronic venous ulcer was observed.

Discussion

KTS is a rare form of capillary-venous malformation [12]. Klippel-Trenaunay-Weber syndrome should be considered in cases with significant arteriovenous malformation due to poor prognosis and different treatment approaches [13].

Clinical features occur at birth or during childhood [9,14,15]. KTS is clinically characterized by capillary malformation, soft tissue/bone hypertrophy and atypical varicosities (often lateral superficial) are cardinal features. Two cardinal features are enough for the diagnosis [1,16].

Deep venous anomalies such as hypoplasia, atresia, aneurysmal dilatation, valve hypoplasia and lymphedema can also be identified [12,14]. In the study conducted by Browse et al., hypoplasia/aplasia of the deep venous system was detected in 18% of patients with KTS [17]. In the study reported by Berry et al, deep venous hypoplasia was detected in 35 of 79 patients [3]. Deep venous malformations frequently associated with the preservation of embryonic venues such as lateral marginal vein (vein of Servelle) and sciatic veins [10]. Persistence of lateral marginal vein was found in 68% of KTS cases [11]. The most common lymphatic anomaly is lymphatic aplasia and hypoplasia, which results in lymphedema [11].

In KTS, macular vascular nevus, lymphangioma, longer extremity, swollen extremity, venous varicosities, pain, thrombophlebitis, dislocation of joints, ulcers, gangrene of the affected extremity can be seen [18]. KTS can cause stasis dermatitis, cellulitis, thrombosis, coagulopathy and pulmonary embolism [3,4,9]. KTS may cause macrocephaly, deep venous hypoplasia in the jugular system and varicosities in the facial veins [3]. Intracerebral hemorrhage may develop due to intracerebral involvement [12]. Congenital bone anomalies such as syndactyly, spina bifida occulta, coxa vara can be seen in the KTS [15]. Capillary malformations can be identified in the gastrointestinal tract, liver, spleen, bladder, kidney, lung and heart [9]. Kasabach-Merritt syndrome was found in 45% of cases and high-output heart failure in 13% of cases [18].

Chronic venous hypertension during childhood may be a cause of leg growth [10,11]. Extreme enlargement of the involved extremity may be in the form of bone elongation or soft tissue hypertrophy [3,9]. Significant leg extension discrepancy is defined and can require orthopedic intervention [3].

KTS is a clinical diagnosis. Doppler USG is used for evaluation of venous structures and assesses patency [4]. Computed tomography, magnetic resonance imaging, lymphangiography, sigmoidoscopy and etc. are used for detection of multi-systemic involvement (pelvic and abdominal visceral involvement, intestinal capillary malformations etc) [4,5,10,15,19].

In KTS, treatment is usually conservative. Surgical treatment is recommended for complications [10,11]. In patients with deep vein thrombosis, inferior vena cava filtration or anticoagulant therapy is used to prevent venous thromboembolism [12]. Varicose veins caused by venous insufficiency are treated with compression stockings and lymphatic edema with intermittent pneumatic compression pumps. Surgery is considered for cases where skin ulcers are persistent and cause recurrent bleeding [11].

Deep venous system anomalies are important in directing the treatment of these cases [4,14,19,20]. In cases of deep vein hypoplasia, marginal vein can be resected since hypoplastic deep veins can spontaneously dilate to almost normal

dimensions after marginal vein resection. In cases of deep venous aplasia, the embryonal vein can be the main drainage vein of the leg and resection is unlikely [11,21]. In cases with arteriovenous fistula, venous stasis increases in vessels causing valvular atresia. In these cases, venous skeletonisation may be performed by completely tying up the arterial inflow vessel [21]. Catheter-directed embolization using coils, particulates, or sclerotherapy may be performed in small arteriovenous fistulas [3]. Foam sclerotherapy and endovenous radiofrequency ablation may be performed for perforating venous insufficiency [22].

Osteotomy, epiphysiodesis, and epiphyseal stapling may be performed if a leg is overgrown [23]. Amputation may be required when leg sizes are large enough to affect daily activities [11,15]. Reducing operations may be performed for soft tissues [18].

The diagnosis of KTS was established clinically in our case (venous insufficiency, port wine stain and increased extremity diameter). Surgical repair was seen fit due to the non-healing ulcer. Awareness of the particular syndrome led us to conduct a thorough examination to rule out other abnormalities such as absence of certain venous structures and AV malformations which would cause other complications. Also the surgical approach was also tailored to fit the situation, with specific identifications of venules leading to the leg ulcer and ligation of those.

KTS should be considered for patients with treatment resistant venous insufficiency and exhibiting other characteristics of the syndrome (port wine stain etc.) Careful evaluation of the venous system should be made to refrain from unnecessary or harmful surgical interventions. Once diagnosed, KTS patients should undergo multi-systemic screening to detect further vascular malformations that may be life endangering.

References

1. Klippel M, Trenaunay P. Du naevus variquex osteohypertrophique. Arch Genet Med Paris. 1900;3:11-72.
2. Weber FP. Angioma formation in connection with hypertrophy of limbs and hemi-hypertrophy. Brit J Derm. 1907;19:231-5.
3. Berry SA, Peterson C, Mize W, Bloom K, Zachary C, Blasco P, et al. Klippel-Trenaunay syndrome. Am J Med Genet. 1998;79:319-26.
4. Al-Salman MM. Klippel-Trenaunay syndrome: clinical features, complications, and management. Surg Today. 1997;27:735-40.
5. Ghahremani GG, Kangarloo H, Volberg F, Meyers MA. Diffuse cavernous hemangioma of the colon in the Klippel-Trenaunay syndrome. Radiology. 1976;118:673-8.
6. Meier S. Klippel-Trenaunay syndrome. Advances in Neonatal Care. 2009;9:120-4.
7. Whelan AJ, Watson MS, Porter FD, Steiner RD. Klippel-Trenaunay-Weber syndrome associated with a 5:11 balanced translocation. Am J Med Genet. 1995;59:492-4.
8. Aelvoet GE, Jorens PG, Roelen LM. Genetic aspect of the Klippel-Trenaunay syndrome. Br J Dermatol. 1992;126:603-7.
9. Jacob AG, Driscoll DJ, Shaughnessy WJ, Stanson AW, Clay RP, Gloviczki P. Klippel-Trenaunay syndrome: spectrum and management. *Mayo Clin Proc*. 1998;73:28-36.
10. Servelle M. Klippel and Trenaunay's syndrome.768 operated cases. *Ann Surg*. 1985;201(3):365-73.
11. Capraro PA, Fisher J, Hammond DC, Grossman JA. Klippel-Trenaunay syndrome. Plastic Reconstr Surg. 2002;109:2052-62.
12. Gloviczki P, Driscoll DJ. Klippel-Trenaunay syndrome: current management. *Phlebology*. 2007; 22:291-8.
13. Weber FP. Hemangiectatic Hypertrophy of Limbs-Congenital Phlebacteriectasis and So-called Congenital Varicose Veins. Brit J Child Dis. 1918;15:13-7.
14. Lindenauer SM. The Klippel Trenaunay syndrome: varicosity, hypertrophy and haemangioma with no arteriovenous fistula. Ann Surg. 1965;162:303-14.
15. Baskerville PA, Ackroyd JS, Lea Thomas M, Browse NL. The Klippel-Trenaunay syndrome: clinical, radiological and haemodynamic features and management. Br J Surg. 1985;72: 232-6.
16. Baskerville PA, Ackroyd JS, Browse NL. The etiology of the Klippel-Trenaunay syndrome. Ann Surg. 1985;202:624-7.
17. Browse NL, Burnand KG, Thomas ML. The Klippel-Trenaunay syndrome.In: Browse NL, Burnand KG, Thomas ML, editors. Diseases of the veins: pathology, diagnosis and treatment. London:Edward Arnold; 1988. p. 609-25.
18. Samuel M, Spitz L. Klippel-Trenaunay syndrome: clinical features, complications and management in children. Br J Surg. 1995;82:757-61.
19. Gloviczki P, Stanson AW, Stickler GB, Johnson CM, Toomey BJ, Meland NB et al. Klippel Trenaunay syndrome: the risks and benefits of vascular interventions. Surgery. 1991;110:469-79.
20. Gorenstein A, Katz S, Schiller M. Congenital angiodysplasia of the superficial venous system of the lower extremities in children. Ann Surg. 1988;207:312-8.
21. Mattassi R, Vaghi M. Management of the marginal vein: current issues. Phlebology. 2007;22:283-6.
22. Harrison CC, Holdstock JM, Price BA, Whiteley MS. Endovenous radiofrequency ablation and combined foam sclerotherapy treatment of multiple refluxing perforator veins in a Klippel-Trenaunay syndrome patient. Phlebology. 2014 Dec;29(10):698-700.
23. McGrory BJ, Amadio PC. Klippel-Trenaunay syndrome: orthopaedic considerations. Orthop Rev. 1993;22:41-50.

J Surg Med. 2018;2(3):359-360.
DOI: 10.28982/josam.419440

Journal of Surgery and Medicine
e-ISSN: 2602-2079

The rupture of the diaphragm: Case report

Diyafram rüptürü: Olgu sunumu

Eddy Oleko Ekuke [1], Jamal Zhar [1], Hicham El Bouhaddouti [1]

[1] Department of Visceral Surgery, Hassan II University Hospital, Fez, Morocco

ORCID ID of the authors
EOE: 0000-0003-0381-4870
JZ: 0000-0002-5587-9329
HEB: 0000-0001-8881-0101

Abstract

Diaphragmatic ruptures represent a rare but potentially serious clinical entity that is often integrated into polytrauma. We report a case of left diaphragmatic rupture, discovered twenty days after an accident on the public highway. For the diagnosis, it is necessary to insist on the body scan, whose sensitivity is undoubtedly less than that of other more specific examinations, but which is easily interpretable and accessible in most emergency centers. The order of surgical management is taken at clinical examination, and before the existence of an abdominal emergency.

Keywords: Diaphragmatic rupture, Body scans

Öz

Diyafragma rüptürleri, sıklıkla politravmaya entegre olan nadir fakat potansiyel olarak ciddi bir klinik durumu temsil eder. Karayolu üzerinde meydana gelen bir kazadan yirmi gün sonra ortaya çıkan bir sol diyafragma rüptürü vakasını sunduk. Teşhis için, vücudun taramasında ısrar etmek gerekir; hassasiyeti diğer özel muayene tekniklerinden daha azdır, ancak çoğu acil merkezde kolayca yorumlanabilir ve erişilebilirdir. Cerrahi tedavi sırası, klinik muayenede ve bir abdominal acil durum varlığına göre önceye alınır.

Anahtar kelimeler: Diyafragma rüptürü, Vücut taraması

Introduction

Diaphragmatic ruptures represent a classic entity in thoracoabdominal trauma. Traumatic ruptures of the diaphragm are rare and represent 6% of the injuries observed during a public road accident. They are the witness of violent trauma and most often occur on the left dome (85 to 90%) [1]. They are potentially severe with a high incidence of associated life-threatening injuries. They pose a diagnostic problem which is carried out in more than half of the cases intraoperatively. We report one case of left diaphragmatic rupture, diagnosed twenty days after a highway accident.

Case presentation

Patient aged 68 years asthmatic under ventoline on request admitted to emergency for dyspnea twenty days after road accident with thoracoabdominal impact point. A radiothorax shows a hydro-aeric level on the left with the mediastinum on the right. An abdominal thoraco-scan objectively performed a post-traumatic left diaphragmatic hernia with hernia of the stomach, left colic angle, proximal part of the descending colon ,part of the transverse colon, some Greek coves and mesentery (Figure 1 and 2). Patient operated in urgency by conventional way with exploration allowing to confirm the diagnosis of the left diaphagmatic rupture. The reintegration of the handles with a stomach was very adherent to the posterior thoracic wall. Its release puts in evidence a perforation with fibrous banks (Figure 3 and 4). We performed the closing of diaphragmatic breche by separate stitches to silk 2 as well as the sutures of the gastric wound by separate stitches that vicryl 3/0 after revival of the banks. A thoracic drain and an abdominal drain were left in place. The postoperative was uneventful.

Corresponding author / Sorumlu yazar:
Eddy Oleko Ekuke
Address / Adres: Department of Visceral Surgery, Hassan II University Hospital, Fez, Morocco
e-Mail: olekoekuke20121982@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 28.04.2018
Accepted / Kabul tarihi: 25.05.2018
Published / Yayın tarihi: 25.05.2018

How to cite / Atıf için: Ekuke EO, Zhar J, Bouhaddouti HE. The rupture of the diaphragm: Case report. J Surg Med. 2018;2(3):359-360.

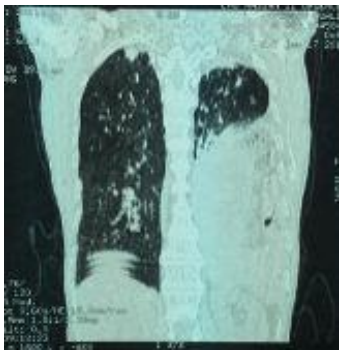


Figure 1: Thorax scan of the patient

Figure 2: Computed tomography scan of the patient

Figure 3: Intraoperative view

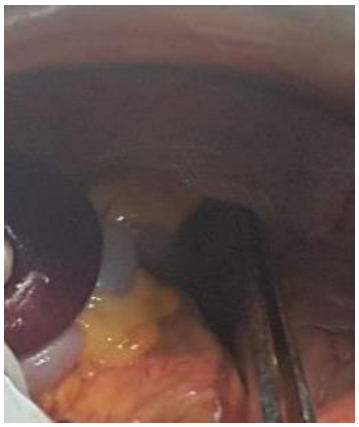


Figure 4: Intraoperative view

Discussion

Diaphragmatic ruptures represent a rare but potentially serious clinical entity that is often integrated into polytrauma. They are present in 0.2 to 7% of patients admitted for chest and/or abdominal contusion [2]. The rupture concerns the left dome in 60 to 75% of cases, and the right dome in 23 to 40% of cases as in our case. Despite liver protection, straight lesions are not exceptional. They are probably undervalued. Straight fractures are often associated with serious injuries resulting in the death of the injured before admission.

Isolated ruptures of the diaphragm are rare and often diagnosed late, especially if the lesion sits to the right. Bilateral ruptures are exceptional and occur in less than 2% of cases [3-4]. The dimensions of these ruptures are variable but in most cases greater than 10 cm 90% of the ruptures are secondary to highway accidents. Clinical diagnosis of diaphragmatic rupture is difficult due to the lack of symptomatology. Only 30 to 50% of the injured are diagnosed preoperatively. 20% to 40% of diaphragm ruptures are discovered during a laparotomy performed for another lesion.

For Lenriot et al. shock and respiratory distress dominate the clinical picture . However, these signs are non-specific and the diaphragmatic rupture may go completely unnoticed in the initial stage. The means of diagnosis are multiple: Chest X-rays, systematic in all polytraumatised patients, can reveal an elevation of the dome with mediastinum reflux, can affirm diagnosis by showing digestive elements or the path of the nasogastric tube in the thorax, but its sensitivity is low. This examination also has the advantage of suspecting a lesion of the aortic isthmus in front of an enlargement of the mediastinum. Transthoracic ultrasound can confirm the diagnosis by visualizing the intrathoracic herniated organs [5].

The thoracoabdominal CT scan made it possible to suspect this diagnosis in our observations. This examination, available as an emergency in most centres, allows a complete lesion examination.

The MRI allows a good evaluation of the thoracoabdominal region and represents an excellent means of diagnosis which makes it possible to visualize more clearly both the diaphragmatic defect and the herniated organs in the thorax. The diaphragm appears as a hypo-intense band, between on the one hand the hyperintense mediastinal fat and on the other hand the relatively hyperintense abdominal viscera [6,7].

Thoracoscopy is proposed by some authors but requires anesthesia and may ignore a peripheral rupture[1]. It can only be conceived on a stable injured person, having a priori an isolated lesion. It would reduce late diagnosis. Indeed, despite these imaging methods, early diagnosis is not always made, and rupture is sometimes recognized only after the 7th day (50% of cases). 10% to 20% of ruptures are undiagnosed in the acute phase. An unknown rupture may occur very late, up to 50 years after the trauma, either during imaging for another reason, or during epigastric or non-specific chest pain [6]. Any diagnosed diaphragmatic rupture must be surgically repaired as soon as possible to avoid strangulation of the ascended viscera in the thorax whose prognosis is pejorative [8]. Treatment as soon as possible is desirable to avoid complications. The emergency approach is the medial laparotomy allowing a complete lesional assessment and the treatment of associated visceral lesions. Diaphragmatic repair is easy outside peripheral desinsertions.

Diaphragmatic rupture may be addressed by laparotomy or thoracotomy, depending on the surgeon's experience and the presence or absence of associated chest and/or abdominal lesions. Laparoscopy and thoracoscopy are now frequently used, both for diagnostic and therapeutic purposes.

In conclusion, diaphragmatic rupture is a rare complication of thoracoabdominal trauma, whose diagnosis remains difficult despite the various means of investigation available. Surgical repair should be undertaken as soon as possible to avoid progression to life-threatening complications.

References

1. Shah R, Sabanathan S, Mearns AJ, Choudhury AK. Traumatic rupture of the diaphragm. Ann Thorac Surg. 1995;60:1444-9.
2. Scharff JR, Naunheim KS. Traumatic diaphragmatic injuries. Thorac Surg Clin. 2007;17:81–5.
3. Mihos P, Potaris K, Gakidis J, et al. Traumatic rupture of the diaphragm: experience with 65 patients. Injury. 2003;34:169–72.
4. Asensio JA, Petrone P. Diaphragmatic injury. In: Cameron JL (ed) Current surgical therapy. 2004 8th ed. Elsevier Mosby Co, Philadelphia, pp 946–55.
5. Somers JM, Gleeson FV, Flower CDR. Rupture of the right hemidiaphragm following blunt trauma: the use of ultrasound in diagnosis. Clin Radiolol. 1990;42:97-101.
6. Eren S, Kantarc M, Okur A. Imaging of diaphragmatic rupture after trauma. Clin Radiol. 2006;61:467–77.
7. Sacco R, Quitadamo S, Rotolo N, et al. Traumatic diaphragmatic rupture: personal experience. Acta Bio Medica. 2003;74 (Suppl. 2):71–3.
8. Turhan K, Makay O, Cakan A, et al. Traumatic diaphragmatic rupture: look to see. Eur J Cardio Thor Surg. 2008;33:1082–5.

J Surg Med. 2018;2(3):361-363.
DOI: 10.28982/josam.403513

Case report
Olgu sunumu

Journal of Surgery and Medicine
e-ISSN: 2602-2079

A case of langerhans cell histiocytosis associated with mantle cell lymphoma

Mantle hücreli lenfoma ile birliktelik gösteren bir langerhans hücreli histiyositozis olgusu

Gülen Gül [1], Mehmet Ali Özcan [2], Fatih Demirkan [2], Sermin Özkal [3]

[1] Department of Pathology, Tepecik Education and Research Hospital, Izmir, Turkey
[2] Department of Hematology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey
[3] Department of Pathology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey

ORCID ID of the authors
GG: 0000-0001-5750-0098
MAÖ: 0000-0001-7842-9702
FD: 0000-0002-1172-8668
SÖ: 0000-0002-8167-0238

Corresponding author / Sorumlu yazar:
Gülen Gül
Address / Adres: Tepecik Eğitim ve Araştırma Hastanesi, Patoloji Bölümü, İzmir, Türkiye
e-Mail: drguleng@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 08.03.2018
Accepted / Kabul tarihi: 29.05.2018
Published / Yayın tarihi: 29.05.2018

Abstract

Langerhans Cell Histiocytosis (LCH), which is caused by neoplastic clonal proliferation of Langerhans cells, may be associated with various malignant neoplasms, especially lymphomas, in rare cases. In literature some studies observed an unexpected number of second malignancies, both prior to and after the diagnosis of MCL. Here, we report a case with concurrent LCH and mantle cell lymphoma (MCL) in a same lymph node. To the best of our knowledge, this is the second reported case of LCH associated with mantle cell lymphoma in a lymph node.

Keywords: Langerhans cell histiocytosis, Mantle cell lymphoma, Lymphoma

Öz

Langerhans hücrelerinin neoplastik klonal proliferasyonundan oluşan Langerhans Hücreli Histiyositozis (LHH) nadir durumlarda, özellikle lenfomalar olmak üzere çeşitli malign neoplaziler ile ilişkili olabilir. Literatürdeki bazı çalışmalarda MHL tanısı öncesi ve sonrasında, beklenmeyen sayıda ikincil malignite olduğu görülmüştür. Burada aynı lenf nodunda LHH ve mantle hücreli lenfoma (MHL) birlikteliği olan bir olgu sunulmaktadır. Bildiğimiz kadarıyla, bu olgu MHL ve LHH birlikteliği olan ikinci vakadır.

Anahtar kelimeler: Langerhans hücreli histiyositozis, Mantle hücreli lenfoma, Lenfoma

Introduction

Langerhans Cell Histiocytosis (LCH) is a rare disease of unknown etiology a neoplasm of the clonal neoplastic proliferation of Langerhans cells. The clinical spectrum ranges from indolent isolated lesions to a life-threatening systemic disease [1,2]. In rare occasions, LCH can be associated with a variety of malignant neoplasms, especially lymphomas [1, 4-12]. While classic Hodgkin's lymphoma is the most common associated lymphoma, other non-Hodgkin's lymphoma cases associated with Langerhans cell histiocytosis have been reported only sporadically in the literature [11]. However, due to the uncommon nature of this association, biological effects and prognostic significance have not been thoroughly investigated [4]. Here, we report a case with concurrent LCH and mantle cell lymphoma in a same lymph node.

Case presentation

A 70-year-old man diagnosed with 17p del Chronic lymphocytic leukemia (CLL) at the external center came to our Hematology Clinic. A month after first application he had pleural effusion and pleural biopsy was performed. Microscopically pleural tissue was infiltrated by polymorphonuclear cells and lymphoid cells. Most of the lymphoid cells show positive staining with CD20 and CD5 (pale). CD23 and cyclin D1 were negative. Pleura biopsy diagnosed as “Small lymphoid neoplasm”. During this time, the patient continued to receive CLL therapy because of his first diagnosis. Due to his progression under the treatment, a right inguinal lymph node biopsy was done. In the sections of the lymph node, the normal structure was distorted in most areas and CD3 and CD5 positive T lymphocytes with diffuse patern were observed. Residual lymphoid follicles with few germinal centers (CD21 and CD23 positive) were seen.

How to cite / Atıf için: Gül G, Özcan MA, Demirkan F, Özkal S. A case of langerhans cell histiocytosis associated with mantle cell lymphoma. J Surg Med. 2018;2(3):361-363.

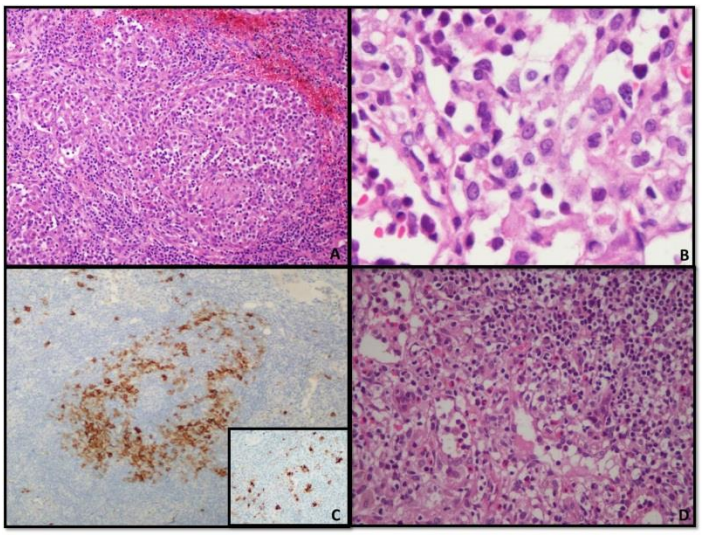


Figure 1: A, B: Plump histiocytes within the sinuses, hematoxylin and eosin staining [H&E]], magnification= 200x and 1000x, C: Immunhistochemically CD1a and langerin (inlet) positive histiyocytes, magnification=100x and 400x (inlet), D: Eosinophils admixed with lymphoctes and histiocytocyte, H&E staining, magnification=400x

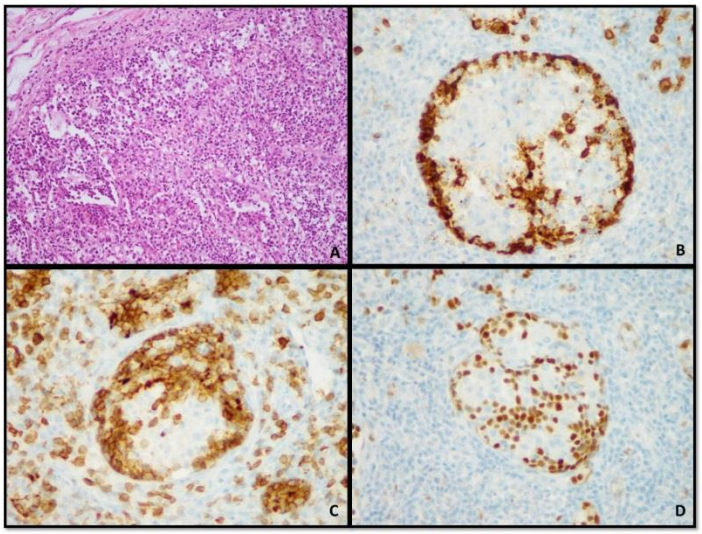


Figure 2: A: Neoplastic lymphocytes in the sinuses, H&E staining, magnification=200x, B: CD20 positivity of lymphocytes in the sinuses, magnification=400x, C: CD5 positivity of lymphocytes in the sinuses, magnification=400x, D: Cyclin D1 positivity of B lymphocytes, magnification=400x

Within the sinuses; plump histiocytes with oval to slightly irregular grooved nuclei, inconspicuous nucleoli, and abundant eosinophilic cytoplasm were observed (Figure 1A, 1B). These histiyocytes were CD68, CD11c, S100, CD1a and Langerin (Figure 1C). Also there were CD20 and PAX5 positive B lymphocytes in the sinuses that were associated with histiocytes and thought to be neoplastic (Figure 2A, 2B). Most of these B cells were cyclin D1 and CD5 (Figure 2C, 2D), and some were BCL-2 positives, but CD23, LEF1 and CD38 were negative. These were variably admixed with eosinophils in most areas (Figure 1D). CISH staining for EBV-encoded RNA (EBER) was negative and there were no V600E mutation of the BRAF gene. The histopathological diagnosis was Mantle cell Lymphoma and LCH.

Patient died because of aspiration pneumonia one year after the initial application.

Discussion

The Langerhans cell histiocytosis (LCH) is currently defined as a clonal proliferation of antigen-presenting dendritic type Langerhans cells (LCs) that express CD1a, Langerin (CD207) and S100 protein, and demonstrate Birbeck granules by ultrastructural examination [1,2]. Despite the advances in molecular biology and genetics, etiology is still uncertain. Current literature suggest that LCH is a myeloid neoplasia with inflammatory properties [10]. Chromosomal instability and gene mutations play an important role in the development of this disease [2,10]. Recurrent BRAF V600E mutation has been reported in more than half of LCH patients [12,13]. However, we have not observed BRAF mutation in our case.

Mantle cell lymphoma (MCL) was termed a lymphocytic lymphoma of intermediate differentiation and characterized by atypical small lymphoid cells with wide mantles around benign germinal centers [14]. In literature some studies observed an unexpected number of second malignancies, both prior to and after the diagnosis of MCL. Reasons for this observation are unclear, but it suggests either a genetic predisposition or some other common cause for both tumor groups [15].

LCH is defined concurrently with other tumor types, before, after, or synchronous with other tumor types, especially malignant lymphomas [1,3-9]. Egeler et al. [5] reviewed 91 LCH cases associated with other malignant tumors, the most common being malignant lymphoma (39 cases). A total of 40 cases with association of LCH and Hodgkin Lymphoma (HL) were reported in literature [11]. Proliferation of Langerhans cells in association with HL does not appear to portend a worse prognosis in most reports [9]. West et al. [8] showed a clonal relationship between the FL and Langerhans cell neoplasm with using a combination of immunoglobulin gene rearrangement and fluorescence in situ hybridization studies. Pina-Oviedo et al. [10] reported seven cases of LCH associated with lymphomas included five classical HL, one MCL and one angioimmunoblastic T-cell lymphoma and this is the first report of LCH associated with MCL. In their study all cases were negative for BRAF V600E and MAP2K1 mutations. Therefore they suggested that lymphoma-related LCH is a clinically benign process.

LCH is a rare neoplasm of the clonal neoplastic proliferation of Langerhans cells. Even more rare, LCH can be associated with a variety of malignant neoplasms. To the best of our knowledge, this is the second reported case of LCH associated with mantle cell lymphoma in a lymph node.

References

1. Christie LJ, Evans AT, Bray SE, Smith ME, Kernohan NM, Levison DA, et al. Lesions resembling Langerhans cell histiocytosis in association with other lymphoproliferative disorders: a reactive or neoplastic phenomenon?. Hum Pathol. 2006 Jan;37(1):32-9.
2. Lian C, Lu Y, Shen S. Langerhans cell histiocytosis in adults: a case report and review of the literature. Oncotarget. 2016 Apr 5;7(14):18678-83.
3. Benharroch D, Guterman G, Levy I, Shaco-Levy R. High content of Langerhans cells in malignant lymphoma-incidence and significance. Virchows Arch. 2010 Jul;457(1):63-7.
4. Roufosse C, Lespagnard L, Salés F, Bron D, Dargent JL. Langerhans' cell histiocytosis associated with simultaneous

lymphocyte predominance Hodgkin's disease and malignant melanoma. Hum Pathol. 1998 Feb;29(2):200-1.
5. Egeler RM, Neglia JP, Puccetti DM, Brennan CA, Nesbit ME. Association of Langerhans cell histiocytosis with malignant neoplasms. Cancer. 1993 Feb 1;71(3):865-73.
6. Feldman AL, Berthold F, Arceci RJ, Abramowsky C, Shehata BM, Mann KP, et al. Clonal relationship between precursor T-lymphoblastic leukaemia/lymphoma and Langerhans-cell histiocytosis. Lancet Oncol. 2005 Jun;6(6):435-7.
7. Moraveji S, Tonk V, Gaur S, Torabi A. Langerhans cell histiocytosis and diffuse large B-cell lymphoma with tetrasomy of PBX1 gene and t[14;19]: two entities in one lymph node. Pathology. 2016 Dec;48(7):728-31.
8. West DS, Dogan A, Quint PS, Tricker-Klar ML, Porcher JC, Ketterling RP, et al. Clonally related follicular lymphomas and Langerhans cell neoplasms: expanding the spectrum of transdifferentiation. Am J Surg Pathol. 2013 Jul;37(7):978-86.
9. Greaves WO, Bueso-Ramos C, Fayad L. Classical Hodgkin's lymphoma associated with Langerhans cell histiocytosis: multiagent chemotherapy resulted in histologic resolution of both the classical Hodgkin's lymphoma and Langerhans cell proliferation components. J Clin Oncol. 2011 Feb 1;29(4):e76-8.
10. Pina-Oviedo S, Medeiros LJ, Li S, Khoury JD, Patel KP, Alayed K, et al. Langerhans cell histiocytosis associated with lymphoma: an incidental finding that is not associated with BRAF or MAP2K1 mutations. Mod Pathol. 2017 May;30(5):734-44.
11. Das DK, Sheikh ZA, Alansary TA, Amir T, Al-Rabiy FN, Junaid TA. A case of Langerhans' cell histiocytosis associated with Hodgkin's lymphoma: Fine-needle aspiration cytologic and histopathological features. Diagn Cytopathol. 2016 Feb;44(2):128-32.
12. Zeng K, Wang Z, Ohshima K, Liu Y, Zhang W, Wang L, et al. BRAF V600E mutation correlates with suppressive tumor immune microenvironment and reduced disease-free survival in Langerhans cell histiocytosis. Oncoimmunology. 2016 Jun 14;5(7):e1185582.
13. Nakamine H, Yamakawa M, Yoshino T, Fukumoto T, Enomoto Y, Matsumura I. Langerhans Cell Histiocytosis and Langerhans Cell Sarcoma: Current Understanding and Differential Diagnosis. J Clin Exp Hematop. 2016;56(2):109-18.
14. Vose JM. Mantle cell lymphoma: 2015 update on diagnosis, risk-stratification, and clinical management. Am J Hematol. 2015 Aug;90(8):739-45.
15. Barista I, Cabanillas F, Romaguera JE, Khouri IF, Yang Y, Smith TL, et al. Is there an increased rate of additional malignancies in patients with mantle cell lymphoma? Ann Oncol. 2002 Feb;13(2):318-22.

J Surg Med. 2018;2(3):364-366.
DOI: 10.28982/josam.417557

Case report
Olgu sunumu

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Tuba-ovarian abscess in a sexually inactive teenager with Down syndrome: Case report and brief review of literature

Down sendromlu cinsel olarak aktif olmayan bir gençte tubo-ovaryan apse: Olgu sunumu ve literatürün kısa bir gözden geçirilmesi

Ramazan Cahit Temizkan [1], Muhammet Mesut Nezir Engin [2], Harun Güneş [3], Önder Kılıçaslan [2], Emine Dağdelen [2], Merve Aslantaş [2], Murat Kaya [4], Kenan Kocabay [2]

[1] Duzce University, Faculty of Medicine, Department of Pediatric Emergency Medicine, Duzce, Turkey
[2] Duzce University, Faculty of Medicine, Department of Pediatrics, Duzce, Turkey
[3] Duzce University, Faculty of Medicine, Department of Emergency Medicine, Duzce, Turkey
[4] Duzce University, Faculty of Medicine Department of Pediatric Surgery, Duzce, Turkey

ORCID ID of the authors
RCT: 0000-0001-8821-6292
MMNE: 0000-0002-0874-6857
HG: 0000-0003-4899-828x
ÖK: 0000-0002-9311-006X
ED: 0000-0002-3954-1184
MA: 0000-0001-6490-2984
MK: 0000-0002-7569-6618
KK: 0000-0002-4030-1145

Corresponding author / Sorumlu yazar:
Muhammet Mesut Nezir Engin
Address / Adres: Düzce Üniversitesi, Tıp Fakütesi, Çocuk Hastalıkları Kliniği, Düzce, Türkiye
e-Mail: doktormesut@hotmail.com

Informed Consent: The author stated that the written consent was obtained from the parent of the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastanın yakınından yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 21.04.2018
Accepted / Kabul tarihi: 31.05.2018
Published / Yayın tarihi: 31.05.2018

Abstract

Tuba-ovarian abscess, a complication of pelvic inflammatory disease commonly seen in sexually active women, is very rarely encountered in sexually inactive ones. It commonly presents with non-specific symptoms like abdominal pain and fever and/or less commonly with vaginal discharge so it may be challenging for the emergency physician to make the diagnosis promptly. Point-of-care ultrasound may help physician to rapidly diagnose or exclude tuba-ovarian abscess. It can be treated medically (with broad-spectrum antibiotic therapy) or surgically (by drainage or removal of the lesion). If pelvic inflammatory disease and tuba-ovarian abscess are not included in the differential diagnosis of patients admitted to emergency department due to abdominal pain because the patient is not sexually active, the patient may suffer from some serious complications due to delayed diagnosis. Emergency physicians should be vigilant due to the possibility of sexual abuse while treating a sexually inactive patient with tuba-ovarian abscess. The first case of tuba-ovarian abscess, thought to be related to poor personal hygiene, in a child with Down syndrome was presented together with a short review of the literature.
Keywords: Down syndrome, Point-of-care ultrasound, Poor personal hygiene, Tubo-ovarian abscess

Öz

Tubo-ovaryan apse, cinsel olarak aktif olan kadınlarda pelvik inflamatuar hastalık komplikasyonu olarak sık görülürken, cinsel olarak aktif olmayanlarda çok nadir görülür. Hastalık genellikle karın ağrısı ve ateş gibi spesifik olmayan semptomlarla ve / veya daha az sıklıkla vajinal akıntı ile kendini gösterir, bu nedenle acil hekiminin erken tanı koyması zor olabilir. Hekimin tubo-ovaryan apseyi hızlı bir şekilde teşhis etmesine veya dışlamasına ‘’point-of-care ultrasound’’ sistemi yani taşınabilir ultrason cihazı ile yatak başında hastanın ultrasonografisini yapması yardımcı olur. Tıbbi olarak (geniş spektrumlu antibiyotik tedavisi ile) veya cerrahi olarak (lezyonun drenaj veya çıkarılmasıyla) tedavi edilir. Karın ağrısı nedeniyle acil servise başvuran hastaların ayırıcı tanısında cinsel olarak aktif olmadıkları için pelvik inflamatuvar hastalık ve tubo-ovaryan apse yer almıyorsa, gecikmeli tanıya bağlı ciddi komplikasyonlar görülebilir. Acil hekimleri cinsel olarak aktif olmayan hastada tubo-ovaryan apse tanısını koyup tedavi ederken cinsel istismar yönünden uyanık olmalıdırlar. Down sendromu olan bir çocukta, zayıf kişisel hijyen ile ilişkili olduğu düşünülen ilk tubo-ovaryan apse literatürün kısa bir gözden geçirmesiyle birlikte sunuldu.
Anahtar kelimeler: Down sendromu, Point-of-care ultrasound, Kötü kişisel hijyen, Tubo-ovaryan apse

Introduction

Tuba-ovarian abscess (TOA) as a complication of pelvic inflammatory disease is commonly seen in sexually active women, and is very rarely encountered in sexually inactive ones. It commonly presents with non-specific symptoms like abdominal pain and fever and/or less commonly with vaginal discharge so it may be challenging for the emergency physician to make the diagnosis promptly [1-3]. The first case of tuba-ovarian abscess, thought to be related to poor personal hygiene, in a child with Down syndrome was presented together with a short review of the literature.

How to cite / Atıf için: Temizkan RC, Engin MMN, Güneş H, Kılıçaslan Ö, Dağdelen E, Aslantaş M, Kaya M, Kocabay K. Tuba-ovarian abscess in a sexually inactive teenager with Down syndrome: Case report and brief review of literature. J Surg Med. 2018;2(3):364-366.

Case presentation

A 17-year-old female with Down syndrome was admitted to the emergency department due to recurrent abdominal pain lasting for more than one month. On physical examination, a mass lesion was felt on palpation in the left lower quadrant. Point-of-care ultrasonography performed by the emergency physician revealed the mass was a cystic lesion. Results of the patient's laboratory tests were as follows: White blood cell count (WBC), 21000/mm3; neutrophil percent, 82.6% and C-reactive protein (CRP) level, 26.76 mg/dL. Intravenous contrast-enhanced abdominal computed tomography scan (CT), performed for differential diagnosis of the lesion, showed the cystic lesion with the dimensions of ~7x6x5 cm, filled with dense material, including multiple septations within in the left ovarian region (Figure 1). The lesion was excised surgically. Histological examination of the lesion confirmed the diagnosis of TOA. No complications developed later, and the patient was discharged after 6 days of inpatient follow-up. Written consent was received from the parent of the patient.

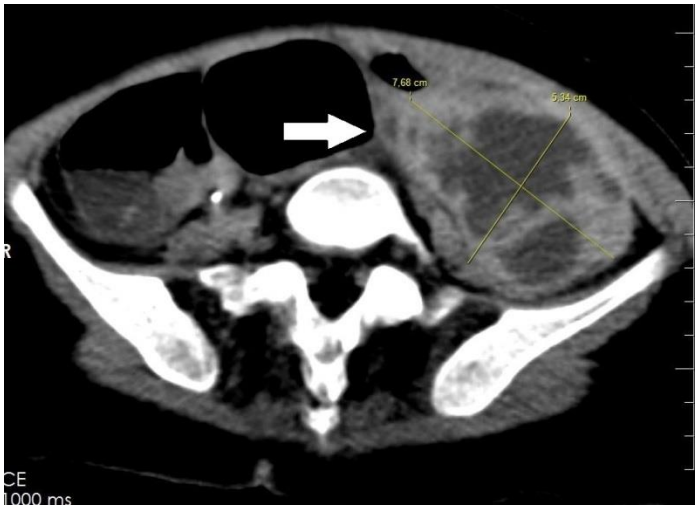


Figure 1: Intravenous contrast-enhanced abdominal computed tomography showing a cystic lesion with the dimensions of ~7x6x5 cm filled with a dense material, including multiple septations within in the left ovarian region (arrow).

Discussion

TOA is generally seen as a complication of pelvic inflammatory disease (PID) [1]. PID occurs when infectious agents spread upwards from the lower genitourinary tract and reach adjacent structures such as endometrium, fallopian tubes, ovaries and pelvic peritoneum. TOA is commonly encountered in sexually active women with PID; it is very rarely seen in sexually inactive ones [2,3]. Its clinical presentation is usually non-specific [4]. Typical signs and symptoms include abdominal pain, fever and less commonly vaginal discharge. It is a real emergency due to risk of development of serious complications including tubal occlusion, infertility, ectopic pregnancy and pelvic adhesions leading to chronic pelvic pain [2,4]. It can be treated either medically (with antimicrobial therapy) or surgically (by drainage or excision of the lesion) [4]. A teenager with Down Syndrome diagnosed with TOA was presented.

TOA occurs in 3% of patients with PID as a result of progression of the disease, and 71% of TOA cases are seen during the 3rd and 4th decades [5]. Although TOA is not common in sexually inactive girls it may rarely occur related to poor personal hygiene or dissemination of infectious agents through systemic blood circulation in patients with intra-abdominal disorders (e.g. intestinal injury, obstruction of the visceral organs, blood flow abnormalities, peritonitis secondary to systemic diseases, intra-abdominal operations) [3,4,6-16]. Ascending regurgitation of urine into the vagina increases the risk of PID and TOA [14].

TOA has been rarely reported in sexually inactive patients. One of the reported cases was a 15-year-old girl with mental retardation [16]. The present case resembles that patient since she has mental retardation, too, due to having Down syndrome. Mental retardation and Down syndrome may increase the predisposition to PID and TOA by impairing personal hygiene. Besides, patients with Down syndrome have relatively higher predisposition to infections because cellular and humoral immunity are generally defective in these patients. TOA may be the primary manifestation of Crohn's disease. It may occur related to obesity, constipation, recurrent urinary tract infections or poor personal hygiene or a combination of these factors [5]. It was also reported in a patient with Henoch-Schonlein vasculitis [6].

The diagnosis of TOA in sexually inactive patients especially in those in the pediatric age group may be challenging because the physician cannot think of -due to extremely lower prevalence in these groups and non-specific presentation of the disease- the patient may have the disease [4]. Delayed diagnosis of the disease and development of complications due to misconception the disease is seen only in sexually active women negatively affect the patient's prognosis and increase the burden on social security systems. PID and TOA should be considered every time a female patient with abdominal pain is encountered in the emergency department regardless of the patient's sexual activity status especially if the patient has one or more of the predisposing factors mentioned above [3,4,6-15]. Sexual abuse should also be considered and questioned in the case of the diagnosis of a child with TOA. No suspicious findings were detected in the present case.

Ultrasound evaluation of the patient by emergency physician is useful in rapid diagnosis of TOA. Because the present case had recurrent abdominal pain in the left lower quadrant, and a mass lesion was found in the same region the diagnosis of acute appendicitis was virtually excluded. Emergency physicians should act rapidly while dealing with TOA or other intra-pelvic disorders which may be needed to be treated surgically, otherwise life-threatening complications may develop, or the patient may lose fertility as a result of complications.

In conclusion, PID and TOA should be included in the differential diagnosis in patients admitting with abdominal pain even if the patient is not sexually active. Evaluation of the patient with point-of-care ultrasound by the emergency physician will decrease the elapsed time till the diagnosis is confirmed. Finally, child abuse should not be missed when a patient in the pediatric age group was diagnosed with TOA.

References

1. Soper DF. Genitourinary infections and sexually transmitted diseases. In: Berek JS, ed, Novak's Gynecology. 14th Ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007: 549–52.

2. Krivak TC, Cooksey C, Propst AM. Tubo-ovarian abscess: diagnosis, medical and surgical management. Compr Ther. 2004;30(2):93-100.
3. Cho HW, Koo YJ, Min KJ, et al. Pelvic Inflammatory Disease in Virgin Women With Tubo-ovarian Abscess: a Single-Center Experience and Literature Review. J Pediatr Adolesc Gynecol. 2017;30(2):203-8.
4. Ashrafganjooei T, Harirchi I, Iravanlo G. Tubo-ovarian abscess in a virgin girl. Iran J Reprod Med. 2011;9(3):247–50.
5. Clark JF, Moore-Hines S. A study of tubo-ovarian abscess at Howard University Hospital (1965 through 1975). J Natl Med Assoc. 1979;71(11):1109-11.
6. Hartmann KA, Lerand SJ, Jay MS. Tubo-ovarian abscess in virginal adolescents: exposure of the underlying etiology. J Pediatr Adolesc Gynecol. 2009;22:13-6.
7. Pomeranz A, Korzets Z, Eliakim A, et al. Relapsing Henoch-Schönlein purpura associated with a tubo-ovarian abscess due to Morganella morganii. Am J Nephrol. 1997;17(5):471-3.
8. Kim MH, Shin YK, Eun BL, et al. A Case of Bilateral Tubo-Ovarian Abscesses in a One-and-Half Year-Old Girl. Korean J Pediatr. 2000;43(3):432-7.
9. Sirotnak AP, Eppes SC, Klein JD. Tuboovarian Abscess and Peritonitis Caused by Streptococcus pneumoniae Serotype 1 in Young Girls. Clin Infect Dis. 1996;22(6):993-6.
10. Arda IS, Ergeneli M, Coskun M, et al. Tubo-ovarian abscess in a sexually inactive adolescent patient. Eur J Pediatr Surg. 2004;14(1):70-2.
11. Goodwin K, Fleming N, Dumont T. Tubo-ovarian abscess in virginal adolescent females: a case report and review of the literature. J Pediatr Adolesc Gynecol. 2013;26(4):99-102.
12. Cheong LHA, Emil S. Non-sexually transmitted tubo-ovarian abscess in an adolescent. J Ped Surg Case Reports. 2013;1:378-80.
13. Sacks DA, Niswander KR, Easton TH. Tubo-ovarian abscess at puberty. West J Med. 1977;127(6):513-15.
14. Moore MM, Cardosi RJ, Barrionuevo MJ. Tubo-ovarian Abscess in an Adolescent Virgin Female. Arch Pediatr Adolesc Med. 1999;153(1):91-2.
15. Simpson-Camp L, Richardson EJ, Alaish SM. Streptococcus viridans tubo-ovarian abscess in an adolescent virgin. Pediatr Int. 2012;54(5):706-9.
16. Sakar MN, Gul T, Atay AE. Tubo-ovarian abscess presenting as an ovarian tumor in a virginal adolescent: A case report. Clin Exp Obstet Gynecol. 2012;39(3):388-9.

J Surg Med. 2018;2(3):367-369.
DOI: 10.28982/josam.420716

Case report
Olgu sunumu

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Long term extracorporeal membrane oxygenation therapy for H1N1 influenza related acute respiratory distress syndrome and several complications

H1N1 influenza ilişkili akut respiratuar distres sendromunda uzun dönem ekstrakorporeal membran oksijenatör tedavisi ve birçok komplikasyon

Behiye Deniz Kosovalı [1], Fatma İrem Yeşiler [1], Tülay Tunçer Peker [1], Mustafa Kemal Bayar [1]

[1] Ankara University, Faculty of Medicine, Department of Anesthesiyology and Reanimation, Division of Intensive Care Unit, Ankara, Turkey

ORCID ID of the authors
BDK: 0000-0001-9385-6542
FİY: 0000-0002-0612-8481
TTP: 0000-0001-6467-407X
MKB: 0000-0002-0506-4869

Corresponding author / Sorumlu yazar:
Behiye Deniz Kosovalı
Address / Adres: Ankara Üniversitesi Tıp Fakültesi, İbn-i Sina Hastanesi, Anesteziyoloji ve Reanimasyon Kliniği, Altındağ, Ankara, Türkiye
e-Mail: kosovalideniz@yahoo.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 05.03.2018
Accepted / Kabul tarihi: 15.06.2018
Published / Yayın tarihi: 22.06.2018

Abstract

Extracorporeal membrane oxygenation (ECMO) has significantly advanced in recent years. During the 2009 H1N1 influenza a pandemic, the use of venovenous (VV) ECMO represented a successful rescue treatment for acute respiratory distress syndrome (ARDS) in patients failing conventional ventilation techniques. The patient was thirty nine year-old and 38 weeks pregnant who had a seizure and then aspiration pneumonia occurred. Due to respiratory failure and hemodynamic instability she was intubated and vasopressor agent was initiated. Her chest X ray showed bilateral nonhomogeneous opacity; hence she was diagnosed with severe ARDS and septic shock. VVECMO was applied by a cardiovascular surgery team and the patient was transferred with the ECMO from hospital to our institution. During her hospitalization, multiple complications occurred, such as pneumothorax, critical illness polyneuropathy, clinical illness myopathy, oxygenator clotting and she was treated successfully.

Keywords: Acute respiratory distress syndrome, Respiratory failure, Intensive care unit, Extracorporal membrane oxygenator

Öz

Ekstrakorporeal membrane oksijenatörü (ECMO) son yıllarda oldukça gelişmiştir. 2009'daki H1N1 influenza pandemisi sırasında konvansiyonel ventilasyon tekniklerinin başarısız olduğu akut respiratuar distress sendromlu (ARDS) hastalarda venovenöz (VV) ECMO'nun başarılı bir tedavi olduğu gösterildi. Yirmi dokuz yaşında, 38 hafta gebe hastada sezaryen ile doğum sonrası aspirasyon pnömonisi gelişti. Solunum yetmezliği ve hemodinamik instabilite nedeniyle entübe edildi ve vazopresör ajan başlandı. Akciğer grafisinde bilateral nonhomojenöz opasite artışı gözlendi; bu sebeple ARDS ve septik şok tanısı aldı. VVECMO kardiyovasküler cerrahi ekibi tarafından kuruldu ve hasta ECMO ile hastanemize transfer edildi. Hastanede yatışı süresince pnömotoraks, kritik hastalık polinöropatisi, kritik hastalık myopatisi, oksijenatörün pıhtılaşması gibi birçok komplikasyon ortaya çıktı ve hasta başarı ile tedavi edildi.

Anahtar kelimeler: Akut respiratuar distress sendromu, Solunum yetmezliği, Yoğun bakım ünitesi, Ekstrakorporal membran oksijenatörü

Introduction

In 2009, human infection with the novel influenza A/H1N1 virus was first introduced [1]. Novel influenza usually affects patients with comorbidities such as, asthma, chronic bronchitis, malignancy, transplants, obese, elderly patient and especially pregnant women [2]. H1N1 influenza also can cause severe ARDS. In 2009, during H1N1 influenza pandemia, ECMO was used for the rescue and support therapy on patients with ARDS or severe hypoxemia. 1972, an adult patient with post-traumatic respiratory failure, long-term ECMO as support for severe respiratory failure was first successfully used [3]. The usage of ECMO was abstained until the conventional ventilator support vs ECMO for severe adult respiratory failure (CESAR) trial [4]. After the CESAR trial many centers have started and continued to use ECMO.

This case report presentation is about H1N1 influenza related ARDS, and the patient was treated successfully in spite of multiple complications by using several treatment modalities.

How to cite / Atıf için: Kosovalı BD, Yeşiler Fİ, Peker TT, Bayar MK. Long term extracorporeal membrane oxygenation therapy for H1N1 influenza related acute respiratory distress syndrome and several complications. J Surg Med. 2018;2(3):367-369.

Case presentation

Thirty nine year-old and 38 weeks pregnant patient was admitted to a hospital due to upper respiratory tract infection symptoms. In her postpartum period, she had a seizure attack and then aspiration pneumonia occurred and owing to respiratory failure and hemodynamic instability; she was intubated with an orotracheal intubation tube and connected to invasive mechanical ventilation (MV) and vasopressor agent was initiated. On her chest X ray showed bilateral multiple nonhomogenous opacity, the ratio of arterial partial pressure oxygen to fractional of inspired oxygen (PaO_2/FiO_2) lower than 100% hence she was diagnosed with severe ARDS, septic shock and aspiration pneumonia (Figure 1).

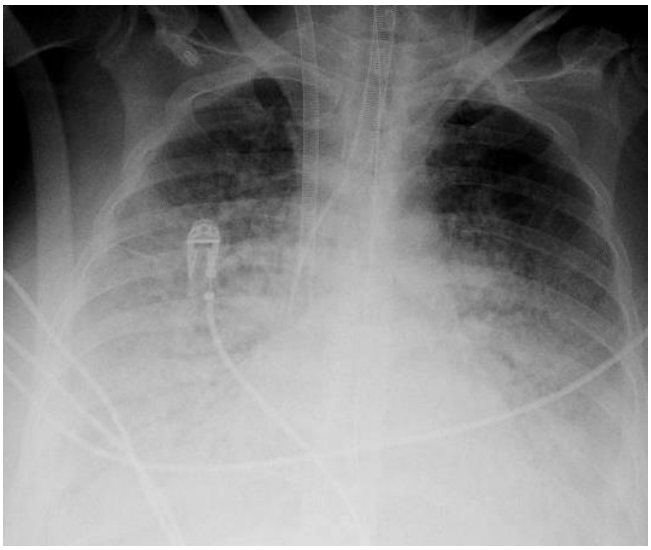


Figure 1: Bilateral nonhomogenous opacity

Broad spectrum antibiotics and antiviral therapy were initiated. Tracheal aspiration culture, blood culture, urine sample culture, a viral and bacterial panel were taken. After three days, her medical situation was getting worse and in spite of lung protective ventilation strategy arterial blood gas analysis (ABGA) showed hypoxemia, PaO_2/FiO_2 ratio 40%, therefore she was referred to our hospital. When the patient was evaluated we decided to install a VVECMO. First, VVECMO was applied by a cardiovascular surgery team and then the patient was transferred with the VVECMO from hospital to our institution. Initial ECMO parameters were blood flow (BF) 4.5 L/min, sweep gas flow 3-5 L/min, ECMOFiO_2 (FmO_2) 100%. At the same time, MV mode was synchronized intermittent mechanical ventilation-pressure control (SIMV-P). MV parameters were tidal volume 6 ml/kg, respiratory rate 8-10 breath/minute, positive end expiratory pressure (PEEP) 10 cmH_2O, FiO_2 30-60%, plateau pressure 20-25 cmH_2O. We applied sedative, neuromuscular blocking drugs (NMBDs) and unfractionated heparin infusion during the period of ECMO. Activated clotting time (ACT) level was measure and unfractionated heparin dose was regulated as to target ACT level which was 160-220 sn. The viral bacterial panel detected H1N1 influenza virus and oseltamivir was maintained. On the twentieth day, hypoxemia deepened, ABGA had pH: 7.23, pCO_2:55.2 mmHg, pO_2: 69.5 mmHg, HCO_3: 20.3mmol/L, SO_2: 91%, according to ABGA, ECMO parameters rearranged. Consequently the membrane of ECMO was checked by ABGA and according to results, oxygenator clotting was thought and the membrane of the ECMO was changed. During fourteen days 2mg/kg/day methylprednisolone was applied. On the twenty second, she was lain in prone position over the course of 12 hours. After the position and changing the ECMO membrane, her ABGA and chest X ray was getting better. ABGA was pH: 7.53, pCO_2:34.6 mmHg, pO_2: 82.7 mmHg, HCO_3: 28.7 mmol/L, SO_2: 97% (FiO_2:70%). After twenty five days, in spite of lung protective MV strategies pneumothorax occurred in her left hemithorax and a chest tube was placed. Five days later, pneumothorax regressed and the chest tube was removed. After thirty one days, the ECMO BF 1L/min, sweep gas flow was 1 L/min, too and MV support was maintained. ECMO was weaned on the thirty first day. Percutaneous tracheostomy was applied cause of prolonged duration of MV support and no complication occurs. After that, the sedation was discontinued. On neurologic examination she was conscious, could orient herself, and was cooperative. On the other side, bilaterally, her upper and lower extremities had loss of strength, deep tendon reflexes were not determined and she had paralysis of all her extremities. Critical illness polyneuropathy (CIP) and critical illness myopathy (CIM) were diagnosed and she was treated with physiotherapy. After the physiotherapy rehabilitation, she could move autonomously. In addition, MV support was decreased and MV mode was changed to continue positive airway pressure mode and positive end expiratory pressure 10cmH2O, pressure support 8 cmH_2O, FiO_2:40%. After the changing mode, T tube was connected (3-4 L/min oxygen) and her chest X ray was regressed (Figure 2).

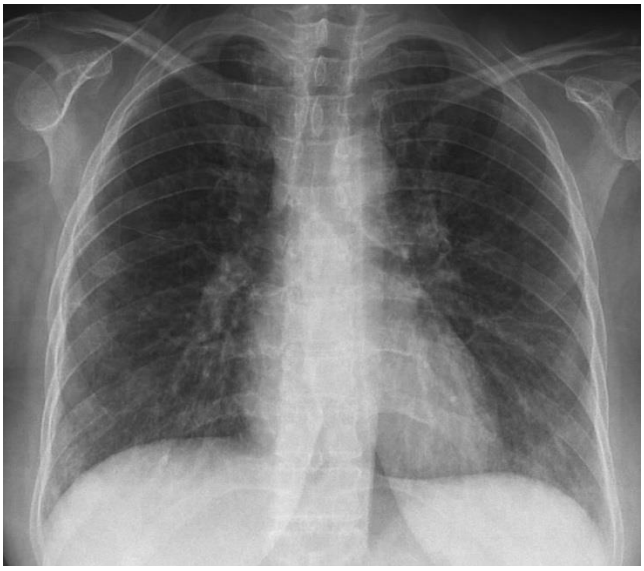


Figure 2: Bilateral opacity in regression

When PaO_2/FiO_2 ratio was 350%, tracheotomy was decided to decannulate on sixty third days on stay of ICU. After the decannulation neither dyspnea nor hypoxemia occurred, hence the patient was transferred to the general ward and then was discharged from hospital to home. She was healthy in follow-up.

Discussion

ARDS is characterized by hypoxemia and bilateral radiographic opacities, associated with increased venous admixture, increased physiological dead space, and decreased lung compliance. The mortality range of ARDS is very high. According to Berlin Definition, mortality rate was more than 50% in the severe ARDS group patients [5]. There are countless

reasons to become ARDS. One of them is H1N1 influenza virus that plays a role in the ethology of ARDS. In this presented case, severe ARDS occurred due to H1N1 influenza infection in her postpartum term. In this case our first aim recovered hypoxemia, ensured the oxygen delivery to tissues and to buy time until her clinical situation was getting better. ELSO guidelines suggest that during VVECMO for ARDS the achievement of SaO_2>80% and SvO_2>70% indicates adequate support [6,7]. In the presented case, although lung protective strategies and hemodynamically support had been supplied, ABGA showed severe hypoxemia PaO_2/FiO_2 ratio <100% hence we decided to implement VVECMO. During acute respiratory failure VVECMO can be used as a rescue therapy to buy time until improvement of the underlying disease. VVECMO is used to supply oxygenation and CO_2 removal, or both while the lungs recover, or as a bridge to transplant in case of end stage lung disease [8]. During H1N1 pandemic of 2009 and 2010 the German ARDS Network reported their research. 116 patients were identified who had H1N1 disease and 61 of them received ECMO. The overall mortality was 38%; among patients receiving ECMO, the mortality was 54% [9]. The patient was accepted with VVECMO installed in another hospital and she was transported by ECMO team. The patient's safety is dependent on the adherence to transport's team and protocols. Our ECMO team consisted of two cardiovascular surgeons, two anesthetists, a nurse and a perfusionist. In the literature a retrospective case series is about mobile ECMO team has consisted of two intensivists, an ICU nurse and a perfusionist, too [10]. Prone position is another treatment modality well-known procedure to increase oxygenation in patients with ARDS under MV. Guervilly et al. [11] informed during VVECMO therapy, fifteen patients with ARDS turned to prone positioning and didn't occur any major complications. In this presented case, prone positioning was performed three times during 12 hours while VVECMO was being applied. We detected that ABGA and radiological imagination were better than supine positioning. Undergoing with VVECMO, the movement can become very difficult and health risk for the patients. When the patient moves unstrained, the cannula can remove or kink. The bleeding complication or oxygenator clotting or blocking ECMO system can occur. Hence sedative or NMBDs can be administered which have several beneficial influences on ARDS patients with ECMO. Especially in the early period of VVECMO, sedation helps during the secure transfer of the patient On the other hand NMBDs, immobilization and malnutrition can cause muscle weakness, atrophy CIP and CIM. In our case NMBDs were administered during VVECMO. After ECMO removed, we detected NMBDs related to CIP and CIM. There are many factors for CIP/CIM such as hypotension, hypoxia, hyperpyrexia, aminoglycosides, renal failure, renal replacement therapy, duration of ICU stay, vasopressor and inotropes support, NMBDs and corticosteroids [12]. In the literature a pediatric patient with ARDS who has CIP and CIM to perform active rehabilitation while on VVECMO and successfully recover [13]. In this case she possessed lots of risk factors. As distinct from our patient couldn't perform active or passive rehabilitation during VVECMO that's cause of NMBDs administration. For the treatment to CIP and CIM, drugs therapy was stopped at first and then the passive physical therapy and then active physical therapy were performed. After the rehabilitation she could move by herself.

In the literature, there are many of case reports which have H1N1 influenza virus related ARDS and ECMO was used. The most important difference between these cases and this case is one of the prolonged stay with VVECMO cases and the other important situation is administration of patient with ECMO to ICU. Movement with ECMO is very hard and has a health risk. During the ECMO period, anticoagulant therapy was administered so tracheostomy was not applied earlier and the prolonged intubation and MV duration were the other problems. Another impressive point is a lot of complications which were CIP and CIM, pneumothorax but despite all of this difficultness, she was treated successfully.

References

1. Jain S, Kamimoto L, Bramley AM, Schmitz AM, Benoit SR, Louie J, et al. Pandemic Influenza A (H1N1) Virus Hospitalizations Investigation Team. Hospitalized patients with 2009 H1N1 influenza in the United States, April-June 2009. N Engl J Med. 2009;361(20):1935–44.
2. Jaber S, Conseil M, Coisel Y, Jung B, Chanques G. ARDS and influenza A (H1N1): patients' characteristics and management in intensive care unit. Ann Fr Anesth Reanim. 2010;29(2):117–25.
3. Hill JD, O'Brien TG, Murray JJ, et al. Prolonged extracorporeal oxygenation for acute post-traumatic respiratory failure (shock-lung syndrome). Use of the Bramson membrane lung. N Engl J Med. 1972;286:629-34.
4. Peek GJ, Clemens F, Elbourne D, Firmin R, Hardy P, Hibbert C, et al. CESAR: conventional ventilatory support vs extracorporeal membrane oxygenation for severe adult respiratory failure. BMC Health Services Resarch. 2006;6:163.
5. ARDS Definition Task Force. Acute respiratory distress syndrome: the Berlin Definitio. JAMA. 2012 Jun 20;307(23):2526-33.
6. Extracorporeal Life Support Organization: ELSO Guidelines for Cardiopulmonary Extracorporeal Life Support. Version 1.1. Ann Arbor, MI, April 2009.
7. Zwischenberger JB, Bartlett RH. Management of blood flow and gas exchange during ECLS, in ECMO Extracorporeal Cardiopulmonary Support in Critical Care. 4th ed. Ann Arbor, MI: ELSO, 2012;149–56.
8. Makdisi G, Wang I. Extra corporeal membrane oxygenation (ECMO) review of a lifesaving technology. J Thorac Dis. 2015;7(7):E166-E76.
9. Huh JW. Update on the extracorporeal life support. Tuberc Respir Dis. 2015;78:149-55.
10. Lucchini A, De Felippis C, Elli S, Gariboldi R, Vimercati S, Tundo P, et al. Mobile ECMO team for inter-hospital transportation of patients with ARDS: a retrospective case series. Heart Lung and Vessels. 2014;6(4):262-73.
11. Guervilly C, Hraiech S, Gariboldi V, et al. Prone during veno-venous extracorporeal membrane oxygenation for severe acute respiratory distress syndrome in adults. Minerve Anestesiol. 2014;80:307-12.
12. Herman G, Jonghe B, Brunyninckx F, Van den Berghe G. Clinical review: Critical illness polyneuropathy and myopathy. Critical Care. 2008;12:238.
13. Zebuhr C, Sinha A, Skilman H, Buckvold S. Active rehabilitation in pediatric extracorporeal membrane oxygenation patient. PMR. 2014;6;456-60.

J Surg Med. 2018;2(3):370-373.
DOI: 10.28982/josam.421505

Case report
Olgu sunumu

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Life-threatening isosulfan blue induced anaphylaxis during laparoscopic hysterectomy

Laparoskopik histerektomi ameliyatı sırasında gelişen izosulfan mavisi ilişkili hayatı tehdit eden anafilaksi

Melike Korkmaz Toker [1], Başak Altıparmak [1], Mustafa Turan [1], Bakiye Uğur [1], Semra Gümüş Demirbilek [1]

[1] Mugla Sıtkı Kocman University Training and Research Hospital, Anesthesiology and Reanimation Department, Mugla, Turkey

ORCID ID of the authors
MKT: 0000-0003-1916-4454
BA: 0000-0002-8165-3438
MT: 0000-0001-5038-6691
BU: 0000-0002-4998-427X
SGD: 0000-0001-7721-4582

Corresponding author / Sorumlu yazar:
Melike Korkmaz Toker
Address / Adres: Muğla Sıtkı Kocman Üniversitesi Eğitim ve Araştırma Hastanesi, Anestezi ve Reanimasyon Kliniği, Muğla, Türkiye
e-Mail: meltoker@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 07.05.2018
Accepted / Kabul tarihi: 16.06.2018
Published / Yayın tarihi: 22.06.2018

Abstract

The use of blue dye alone is the first described technique for sentinel lymph node (SLN) identification in patients with cervical carcinoma. In this procedure, Isosulfan Blue (IB), Methylene Blue or Patent Blue is injected into each quadrant of the cervix. We present an anaphylactic reaction to IB in a patient who underwent a laparoscopic hysterectomy. Approximately 15 min after the dye injection, the patient developed hypotension (55/35 mmHg) with an increase in heart rate (120 beats/minute) and a decrease of pulse oximetry to 85%. She was treated successfully with ephedrine, adrenaline, and fluid administration. When sterile drapes were removed, blue urticarial rashes all over the body were detected. The operation was halted, and the patient was transferred to the intensive care unit (ICU). Almost 4 hours after injection of IB, she experienced a second attack of bronchospasm under mechanical ventilation. She recovered uneventfully and was discharged from the ICU. The patient was referred to a skin prick test which was positive for IB. SLN biopsy for cervical cancers may have an increased risk of anaphylaxis probability due to administered blue dyes. It is crucial that the medical staff involved in these procedures be aware of anaphylactic reactions. This case report highlights the necessity of close monitoring of these patients in both the intraoperative and postoperative periods.
Keywords: Anaphylaxis, Sentinel lymph node, Hysterectomy, Isosulfan blue

Öz

Tek başına mavi boya kullanımı servikal karsinomlu hastalarda sentinel lenf nodu (SLN) tanımlaması için ilk tarif edilen tekniktir. Bu prosedürde, serviksin her çeyreğine İzosulfan Mavisi (İM), Metilen Mavisi veya Patent Mavisi enjekte edilir. Biz bu olguda laparoskopik histerektomi uygulanan bir hastada İM'ye karşı gelişen anafilaktik bir reaksiyonu sunduk. Boya enjeksiyonundan yaklaşık 15 dakika sonra hastada kalp atım hızında artış (120 atım / dakika) ve nabız oksimetresinde %85'e varan bir azalma ile hipotansiyon (55/35 mmHg) gelişti. Hasta, efedrin, adrenalin ve sıvı uygulaması ile başarılı bir şekilde tedavi edildi. Steril örtüler açıldığında, vücudun her yerinde mavi ürtiker döküntüleri tespit edildi. Operasyon durduruldu ve hasta yoğun bakım ünitesine (YBÜ) transfer edildi. Hasta İM'nin enjeksiyonundan yaklaşık 4 saat sonra, mekanik ventilasyon altında ikinci bir bronkospazm atağı yaşadı. Hasta sorunsuz bir şekilde iyileşti ve yoğun bakımdan taburcu edildi. Hasta, İM için pozitif olan bir deri testine yönlendirildi. Servikal kanserler için SLN biyopsisi, uygulanan mavi boyalara bağlı olarak artmış anafilaksi riski taşıyabilir. Bu prosedürlere dahil olan tıbbi personelin anafilaktik reaksiyonlara karşı dikkatli çok önemlidir. Bu olgu sunumu, bu hastaların hem intraoperatif hem de postoperatif dönemde yakından izlenmesinin gerekliliğini vurgulamaktadır.
Anahtar kelimeler: Anafilaksi, Sentinel lenf nodu, Histerektomi, İzosulfan mavisi

Introduction

Intraoperative identification of sentinel lymph node (SLN) status is both a major prognostic factor for patients with cervical carcinoma and a decision benchmark for adjuvant therapy. If the node is positive for tumor metastasis, a radical hysterectomy should be omitted, and adjuvant chemo-radiation is commonly administered [1,2]. The use of blue dye alone is the first described technique for SLN identification in patients with cervical carcinoma [3]. In this procedure, Isosulfan Blue (IB), Methylene Blue, or Patent Blue is injected into each quadrant of the cervix [4].

Anaphylaxis resulting from IB (CAS number: 68238-36-8) is well described in the literature. Multiple studies report rates of anaphylaxis to IB ranging from 0.1% to 1.1% [5]. A literature search for case reports available on PubMed (https://www.ncbi.nlm.nih.gov/pubmed) from 2000 to 2017 using the search terms, anaphylaxis, isosulfan blue, sentinel lymph node and hysterectomy identified 35 results, of which the majority of cases were about breast or skin cancers, but none of them was about cervical cancer.

How to cite / Atıf için: Toker MK, Altıparmak B, Turan M, Uğur B, Demirbilek SG. Life-threatening isosulfan blue induced anaphylaxis during laparoscopic hysterectomy. J Surg Med. 2018;2(3):370-373.

We believe that this is the first case of intraoperative anaphylaxis after injection of IB during cervical cancer staging. This case report describes an episode of severe anaphylaxis, characterized by bronchospasm, which occurred after intracervical injection of IB. The literature on management of severe reactions is subsequently reviewed. Using this case report of intraoperative anaphylaxis to IB and an overview of the literature, we attempt to draw attention to this important group of dyes and their potential to cause intraoperative anaphylaxis.

Case presentation

TA 38-year-old woman (weight: 68 kg; height: 170cm) was scheduled for a laparoscopic abdominal hysterectomy because of atypical endometrial cells on biopsy. Her only co-morbidity was asthma, and she reported using salbutamol (Vent-O-Sal®) as a rescue inhaler during an asthma attack. She did not have drug, food, or other allergies. Past surgical and anesthetic history included endometrial biopsy under moderate sedation (with propofol, midazolam, and fentanyl citrate), which was uneventful. Her preoperative laboratory workup and chest radiogram, as well as her electrocardiogram (ECG), were normal.

Before the operation, she was premedicated with 80 mg prednisolone for asthma. In the operating room, standard American Society of Anesthesiologists monitors were applied. Her arms were positioned at her sides, and soft gel pads were applied around her hips, elbows, and shoulders. General anaesthesia was induced by propofol, fentanyl, and rocuronium. After endotracheal intubation, anesthesia was maintained with a 50%/50% oxygen/air mixture and sevoflurane with an end-tidal concentration of 2%. Mechanical ventilation was delivered by volume-controlled ventilation with a tidal volume of 500 mL, respiratory rate of 12 breaths/min, and positive end-expiratory pressure of 5 cm H_20. The surgical procedure began with SLN mapping, and 3 ml of IB was injected into the cervix while the patient was in the lithotomy position. Approximately 15 minutes later, the patient experienced acute hypotension and desaturation during the incisions for laparoscopy trocars. Her blood pressure suddenly dropped to 55/35 mmHg and pulse oximetry decreased to 85%, while her heart rate increased to 120 beats/minute. In the meantime, peak inspiratory pressure increased to 42 mmHg, suggesting severe bronchospasm. The operation was halted, the inspired O_2 concentration was increased to 100%, and sevoflurane was discontinued. A total of 30 mg ephedrine and 0.2 mg adrenaline (1:10000) were applied intravenously in a few minutes. As her mean arterial pressure (MAP) continued to decrease to 30 mmHg, 1000 ml of colloid and 500 ml of crystalloid solutions were administered. Additionally, a 0.01 $mcgr.kg^{-1}.min^{-1}$noradrenaline infusion was started in peripheral veins. A few minutes later, MAP increased to 55-60 mmHg and the pulse oximetry reading reached 100%. After observing periorbital edema and blue urticarial rashes all over the face, sterile drapes were removed, and similar blue urticarial rashes were detected all over the body. An arterial line was placed in the right radial artery, and a central venous catheter was inserted into the right jugular vein. The patient was then transferred to the intensive care unit (ICU) for close hemodynamic monitoring and mechanical ventilation support. A thorax computed tomography was performed to rule out pulmonary embolism, but no pulmonary pathology was detected. During ICU follow-up, antineurotic edema on the eyelids (Figure 1), persistent blue urticarial rashes on the auricle (Figure 2), and blue urine discoloration (Figure 3) were considered to be an anaphylactic reaction to IB dye.

Figure 1: Presence of blue urticarial rashes all over the face and periorbital edema

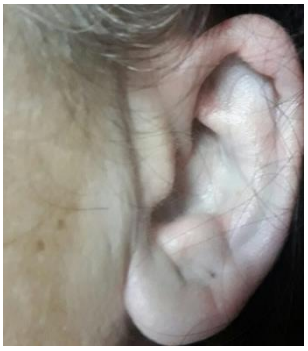


Figure 2: Blue urticarial rashes on the auricle

Figure 3: Blue urine discoloration

Almost 4 hours after injection of IB, she experienced a second attack of bronchospasm under mechanical ventilation. She received intravenous 4 mg prednisolone every 6 hours for the next 48 hours and 40 mg intravenous pheniramine maleate every 12 hours for the next 24 hours. Her blue urticarial rashes resolved, and she was extubated uneventfully on the second day of ICU admission. She was discharged from the hospital after several days without a residual effect. She was referred to a skin prick test (SPT), and a positive SPT was obtained for IB dye. SPT for propofol and egg was negative. She underwent laparoscopic hysterectomy without SLN mapping six weeks later. The second procedure was completed uneventfully. The authors obtained written permission from the patient to publish this report.

Discussion

The combination of laparoscopic intraoperative SLN mapping and radical laparoscopic surgery is a feasible modality for the management of patients with early cervical carcinoma [6]. IB, otherwise known as lymphazurin blue, binds to albumin and other local proteins and is absorbed by the lymphatic system, which makes it suitable for SLN biopsies [7]. Anaphylactic reactions induced with IB have been previously reported with an incidence ranging from 0.1% to 1.1 [5,8]. Its incidence has presumably increased because of the growing use of the dye to delineate lymphatic spread of cancerous tissues [9]. Smurfish blue urticaria, biphasic cardiovascular collapse, hypoxia, and

bronchospasm have been interpreted as related to anaphylactic reactions [10,12].

IB dye-induced anaphylaxis is an IgE-mediated type I hypersensitivity reaction involving basophils and mast cells [13]. During the IgE-mediated anaphylaxis, released mediators produce a symptom complex of bronchospasm and upper airway edema in the respiratory system, and vasodilation and increased capillary permeability in the cardiovascular system [14].Treatment should be directed to blood pressure and airway management. Primarily, our patient had experienced a sudden drop in blood pressure and pulse oximetry mimicking a massive pulmonary embolism. Ephedrine is suggested as the first-line treatment of intraoperative hypotension during general anesthesia and a better choice to maintain cardiac output, so we administered intravenous ephedrine to our patient [15]. As her blood pressure continued to fall, we applied intravenous adrenaline to provide a more prominent α-1 effect. Although we did not consider anaphylaxis as a differential diagnosis in the first step, intravenous adrenalin administration probably prevented the exacerbation of bronchospasm.

In the current case, accompanying asthma disease might have exacerbated bronchospasm. The Association of Anesthetists of Great Britain and Ireland has warned that individuals with a history of asthma appear to be at increased risk of anaphylaxis [16]. Also, the IB product inserts states that reactions are more likely to occur in people with a family story of bronchial asthma, significant allergies, and previous reactions to triphenylmethanes. Biphasic bronchospasm in the ICU follow-up might be related to pre-existing asthma [12].

Raut et al. [17] studied whether prophylactic intravenous glucocorticoid, diphenhydramine, and famotidine administration just before or at induction of anaesthesia could prevent anaphylaxis. They reported that no episodes of hypotension were observed and none of the patients required vasopressors, ventilator support, or intensive care. Although our patient had received prednisolone prophylaxis, an anaphylactic reaction developed with severe hypotension contrary to the previous report. We believe that, although anaphylaxis could not be avoided, the severity of reactions had been reduced by the pre-treatment with a glucocorticoid regimen.

The sudden drop of the pulse oximetry might not be associated with bronchospasm and airway obstruction. Vokach-Brodsky et al. [18] demonstrated that IB alters the absorbency properties of blood and interferes with pulse oximetry that may be interpreted as arterial desaturation. Thus, the decreased pulse oximetry reading of 85% in our case can be explained by not only the hypoperfusion state of the patient's hypotension but also the interference of measuring the absorption of IB and oxyhemoglobin.

Liang et al. [11] suggested that patients who exhibit any hemodynamic instability should not have further surgery in the same setting. Due to their recommendation, we decided to postpone the operation to investigate the certain cause of anaphylaxis.

In the previous reports, preoperative testing, using minimum dye volume, using an alternative dye or no dye have been proposed to reduce the risk of life-threatening IB-induced anaphylaxis [19]. In the current case, we decided not to administer IB during the second operation in consensus with the surgeons.

Positive skin test for allergies to patent blue and increased serum histamine levels, IgE, and tryptase (due to mast cell degranulation) are usually present in these patients. Serum tryptase has a peak plasma level within an hour and remains high for 6 h [20]. Two samples of tryptase with 60 and 120 min are recommended. Normal tryptase levels do not exclude a hypersensitivity reaction, as some allergic reactions are mediated by basophils and complement activation, which does not increase the serum levels of tryptase [21]. Unfortunately, in our institution and in our city tryptase levels cannot be measured in laboratories. Hence, we could not report any tryptase level for this patient.

SLN biopsies for cervical cancer operations have an increased risk of anaphylaxis due to administered blue dyes. It is crucial that the medical staff involved in these procedures be aware of the signs and symptoms of anaphylactic reactions. This case report highlights the necessity of close monitoring of these patients in both the intraoperative and postoperative periods.

References

1. Lambaudie E, Collinet P, Narducci F, Sonoda Y, Papageorgiou T, Carpentier P, et al. Laparoscopic identification of sentinel lymph nodes in early stage cervical cancer: Prospective study using a combination of patent blue dye injection and technetium radiocolloid injection. Gynecol Oncol. 2003;89(1):84–7. doi: 10.1016/S0090-8258(03)00059-3
2. Plante M, Renaud M-C, Têtu B, Harel F, Roy M. Laparoscopic sentinel node mapping in early-stage cervical cancer. Gynecol Oncol. 2003 Dec;91(3):494–503. doi: 10.1016/j.ygyno.2003.08.024
3. Cabanas RM. An approach for the treatment of penile carcinoma. Cancer. 1977; Feb,39(2):456-66. doi: 10.1245/s10434-011-2036-1
4. Dargent D, Enria R. Laparoscopic assessment of the sentinel lymph nodes in early cervical cancer. Technique--preliminary results and future developments. Crit Rev Oncol Hematol. 2003;48(3):305–10. doi: 10.1016/S1040-8428(03)00129-X
5. Bézu C, Coutant C, Salengro A, Daraï E, Rouzier R, Uzan S. Anaphylactic response to blue dye during sentinel lymph node biopsy. Vol. 20, Surgical Oncology. 2011. doi: 10.1016/j.suronc.2010.10.002
6. Gil-Moreno A, Díaz-Feijoo B, Roca I, Puig O, Pérez-Benavente MA, Aguilar I, et al. Total laparoscopic radical hysterectomy with intraoperative sentinel node identification in patients with early invasive cervical cancer. Gynecol Oncol. 2005;96(1):187–93. doi: 10.1016/j.ygyno.2004.09.055
7. Albo D, Wayne JD, Hunt KK, Rahlfs TF, Singletary SE, Ames FC, et al. Anaphylactic reactions to isosulfan blue dye during sentinel lymph node biopsy for breast cancer. Am J Surg. 2001;182(4):393–8. doi: 10.1016/S0002-9610(01)00734-6
8. Leong SP, Donegan E, Heffernon W, Dean S, Katz JA. Adverse reactions to isosulfan blue during selective sentinel lymph node dissection in melanoma. Ann Surg Oncol. 2000;7(5):361–6. doi: 10.1007/s10434-000-0361-x
9. Sandhu S, Farag E, Argalious M. Anaphylaxis to isosulfan blue dye during sentinel lymph node biopsy. J Clin Anesth. 2005;17(8):633–5. doi: 10.1016/j.jclinane.2005.03.006
10. Beenen E, de Roy van Zuidewijn DBW. Patients blue on patent blue: An adverse reaction during four sentinel node procedures. Surg Oncol. 2005;14(4):151–4. doi: 10.1016/j.suronc.2005.12.001
11. Liang MI, Carson WE. Biphasic anaphylactic reaction to blue dye during sentinel lymph node biopsy. World J Surg Oncol. 2008;6. doi: 10.1186/1477-7819-6-79
12. Reed H, Shaw C, Rice M, Le HT. Isosulfan blue dye anaphylaxis presenting as impaired ability to ventilate via a laryngeal. Case Reports. 2014;3(1):1–2. doi: 10.1213/XAA.0000000000000036
13. Hepner DL, Castells MC. Anaphylaxis During the Perioperative Period. Anesth Analg. 2003;1381–95. doi: 10.1213/01.ANE.0000082993.84883.7D
14. Levy JH. Anaphylactic reactions. In: Barash PG, editor. Clinical Anesthesia. 7th ed. Philadelphia: LIPPINCOTT WILLIAMS & WILKINS; 2013. p. 287–302.

15. Lonjaret L, Lairez O, Minville V, Geeraerts T. Optimal perioperative management of arterial blood pressure. Integr Blood Press Control. 2014;7:49–59.
16. Harper NJN, Dixon T, Dugué, Edgar DM, Fay A, Gooi HC, et al. Guidelines suspected anaphylactic reactions associated with anaesthesia. Anaesthesia. 2009;64(2):199–211.
17. Raut CP, Hunt KK, Akins JS, Daley MD, Ross MI, Singletary SE, et al. Incidence of anaphylactoid reactions to isosulfan blue dye during breast carcinoma lymphatic mapping in patients treated with preoperative prophylaxis: Results of a surgical prospective clinical practice protocol. Cancer. 2005;104(4):692–9. doi: 10.1002/cncr.21226
18. Vokach-Brodsky L, Jeffrey SS, Lemmens HJM, Brock-Utne JG. Isosulfan blue affects pulse oximetry. Anesthesiology. 2000;93(4):1002–3. PMID: 11020754
19. Ortiz D, Alvikas J, Riker AI. A Case of Severe Anaphylactic Reaction Secondary to Isosulfan Blue Dye Injection. Ochsner J. 2015;15(2):183–6.
20. Howard JD, Moo V, Sivalingam P. Anaphylaxis and other adversereactions to blue dyes: a case series. Anesth Intensive Care.2011;39:287-92.
21. Brenet O, Lalourcey L, Queinnec M, et al. Hypersensitivity reac-tions to Patent Blue V in breast cancer surgery: a prospectivemulticentre study. Acta Anesthesiol Scand. 2013; 57:106-11.

J Surg Med. 2018;2(3):374-376.
DOI: 10.28982/josam.424326

Journal of Surgery and Medicine
e-ISSN: 2602-2079

A case of postmenopausal ovarian hyperandrogenemia diagnosed only by selective catheterization of ovarian vein

Ovaryen venlerin selektif kateterizasyonu ile tanı alan bir postmenapozal ovaryen hiperandrojenemi vakası

Vedat Uğurel [1], Mehmet Musa Aslan [2], Koray Elter [1]

[1] Trakya University, Faculty of Medicine, Department of Gynecology and Obstetrics, Edirne, Turkey
[2] Muş State Hospital, Department of Gynecology and Obstetrics, Muş, Turkey

ORCID ID of the authors
VU: 0000-0002-1307-4688
MMA: 0000-0002-7830-5002
KE: 0000-0001-7143-6037

Corresponding author / Sorumlu yazar:
Mehmet Musa Aslan
Address / Adres: Muş Devlet Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, Muş, Türkiye
e-Mail: jinopdrmma@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

06 – 09 Mart 2016 tarihleri arasında Grand Yazıcı Otel Uludağ'da gerçekleştirilen 1.Üreme Endokrinolojisi ve İntertilite Akedemisi 6. Jinekolojik Endoskopi Sempozyum ve Çalıştayında bildiriri olarak sunulmuştur

Received / Geliş tarihi: 17.05.2018
Accepted / Kabul tarihi: 25.06.2018
Published / Yayın tarihi: 25.06.2018

Abstract

Hyperandrogenemia in a postmenopausal woman is usually related to a tumor in either ovaries or adrenal glands. To differentiate between these two endocrine organs is a diagnostic challenge when the tumor size is too small to be detected with the aid of usual imaging modalities. 54 years-old postmenopausal woman with signs of virilization was referred to our institution with serum total testosterone levels of 294 ng/dl. Contrast-enhanced computed tomography (CT) revealed a lesion consistent with the tumor 1 cm in diameter in the adrenal gland and magnetic resonance imaging (MRI) could not confirm this finding. The location of androgen hypersecretion could only be determined after selective venous catheterization and hormonal sampling of both adrenal and ovarian veins. The right ovarian venous total testosterone level was found as > 1009.40 ng / dl. A right-sided ovarian Leydig cell tumor was diagnosed in the specimen of laparoscopic hysterectomy and bilateral salpingo-oopherectomy. This case report underlines the importance to carry on the search with the selective venous catheterization and hormonal sampling from both the ovarian and the adrenal veins when there is difficulty to demonstrate the true source of androgen hypersecretion in a postmenopausal woman.

Keywords: Postmenopause, Hyperandrogenism, Ovarian Neoplasms, Leydig cell tumor, Selective venous catheterization

Öz

Postmenapozal dönemde hiperandrojenemi genellikle over veya adrenal bezlerdeki tümörlerle ilişkilidir. Her iki endokrin organdaki tümörlerin çapları çok küçük olduğunda görüntüleme yöntemleri tanıda yetersiz kalmaktadır. 54 yaşında postmenapozal hasta, klitoromegali ve artış gösteren hirsutizm bulguları olan hasta serum total testosteron seviyesi 294 ng/dl ile bölümümüze başvurdu. Kontrastlı bilgisayarlı tomografide (BT) adrenal bezde 1 cm çapında tümör ile uyumlu lezyon saptandı ancak manyetik rezonans (MR) ile bu bulgu teyit edilemedi. Androjen hipersekresyonunun orijininin tespit edilememesi üzerine bilateral ovaryen ve adrenal venlerin selektif venöz kateterizasyonu ve hormonal örneklemesi yapıldı. Sağ ovaryan ven total testosteron düzeyi >1009,40 ng/dl olarak bulundu. Laparoskopik histerektomi ve bilateral salpingooferektomi yapılan hastanın patoloji sonucu sağ over kaynaklı Leydin Hücreli Tümör olarak geldi.

Bu olgu sunumunda, postmenopozal bir kadında androjen hipersekresyonu kaynağını bulunamadığında , hem ovaryen venden hem de adrenal venlerden selektif venöz kateterizasyon ve hormonal örnekleme yapmanın önemi vurgulanmaktadır.

Anahtar kelimeler: Postmenopoz, Hiperandrojenizm, Yumurtalık Neoplazmaları, Leydig hücreli tümör, Selektif venöz kateterizasyon

Introduction

Androgens in premenopausal women are synthesized in the ovaries, adrenal glands and from the peripheral conversion of dehydroepiandrosterone sulfate (DHEA-S), dehydroepiandrosterone (DHEA) and androstenedione (A). Serum concentrations of potent androgens, namely testosterone (T) and dihydrotestosterone (DHT) are low compared to the precursor hormones of DHEA-S, DHEA and A [1]. A half of serum T is produced from the peripheral conversion of A. The remaining 50% is split between the ovaries and the adrenal glands with equal contribution [2]. Although adrenal androgen production declines after the third decade of life to a nadir between 70 to 80 years of age, ovarian T production remains constant after natural menopause.

Hyperandrogenism is the most common endocrinopathy during the reproductive period with a prevalence of 5-10%. Polycystic ovary syndrome comprises 82% of cases as the most common cause whereas androgen-secreting neoplasms make up only 0.2% of cases [3].

How to cite / Atıf için: Uğurel V, Aslan MM, Elter K. A case of postmenopausal ovarian hyperandrogenemia diagnosed only by selective catheterization of ovarian vein. J Surg Med. 2018;2(3):374-376.

However in postmenopausal women, hyperandrogenism with recently developed and rapidly progressing clinical signs might indicate the presence of a tumor more than so in the reproductive age women.

After the exogenous causes of androgen excess are ruled out the attention is directed to find out the exact location of endogenous androgen hypersecretion to determine the type of surgical operation. Although transvaginal ultrasound, computed tomography or magnetic resonance imaging (MRI) might sometimes demonstrate a tumor, a small lesion of less than 2 cm is usually difficult to be detected [4]. Selective venous catheterization and hormonal sampling (SVCHS) of at least four venous vessels (bilateral ovarian-adrenal veins) might help to confirm the presence of an androgen producing tumor either in the ovary or adrenal gland and its laterality [5]. We report a case of postmenopausal virilizing 1.5 cm Leydig cell tumor on the right ovary which could only be diagnosed after the selective catheterization of the adrenal and ovarian veins.

Case presentation

A 54-year-old, postmenopausal woman (gravida:2) was referred to our department with symptoms of worsening hirsutism and clitoromegaly for 1 year. She was in menopause for 17 years. On admission, Ferriman–Gallwey score of hirsutism was 18 (Figure 1). She had a bitemporal alopecia and a cliteromegaly of 3.5 cm in length (Figure 2).

Figure 1: Ferriman–Gallwey score of hirsutism was 18

Figure 2: Cliteromegaly of 3.5 cm in length

She reported that she was aggressive and had mood swings but did not disclose her sexual history. The patient was class II obese (body mass index 37 kg/m2) and hypertensive (arterial blood pressure 140/90). She had a history of diabetes mellitus and hypothyroidism and was on metformin 1000 mg and levothyroxin 50 µg treatment for 3 years. Family history was negative for hirsutism or other hyperandrogenism signs.

Laboratory evaluation revealed substantially elevated levels of serum total testosterone (Total T 294 ng/dl [normal values 13-108 ng/dl]) and elevated postmenopausal-range follicle-stimulating hormone (FSH 85.1 mlU/ml) and luteinizing hormone (LH 31.9 mlU/ml) values. Serum estradiol level was undetectable. Androstenedion, Cortisol, Sex Hormone Binding Globulin, Adrenocorticotropic Hormone, DHEA-S, 17α-hydroxyprogesterone levels were in normal ranges. Serum cortisol was suppressed after the 1-mg overnight dexamethasone suppression test.

Because the transvaginal ultrasonography of both ovaries failed to demonstrate any tumor, we proceeded to other imaging modalities. The contrast-enhanced CT scan of the abdomen and pelvis demonstrated a nodule of low density approximately 1 cm in diameter with no distinct borders at the lateral crus of the left adrenal gland. The radiology department suggested ordering an MRI scan to further investigate the suspected adrenal tumor but the upper and lower abdominal MRI was negative for any lesion including both the ovaries and adrenal glands. PET/CT of the patient was reported to show no FDG uptake in any body parts but as expected, low FDG affinity malignant disorders could not be excluded.

A decision to perform SVCHS (Figure 3) was taken upon the inability to find the location of androgen hypersecretion and the rapid rise of total testosterone level up to 518 ng/dl until the aforementioned imaging studies were completed. The venous sampling results of five vessels are shown in Table 1. Total laparoscopic hysterectomy and bilateral salpingo-oophorectomy was performed and the uterus and ovaries were sent for pathologic diagnosis (Figure 4).

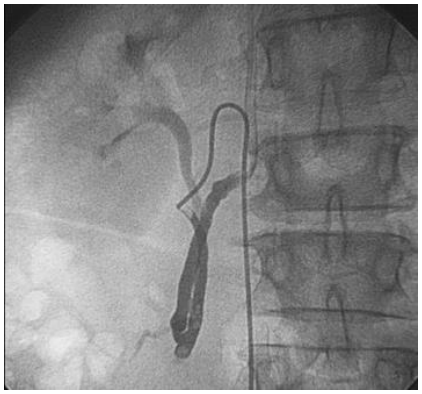


Figure 3: Selective venous catheterization and hormonal sampling

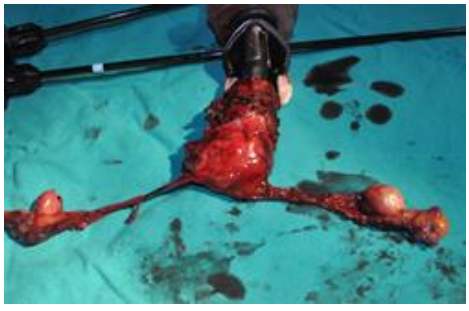


Figure 4: Total laparoscopic hysterectomy and bilateral salpingo-oophorectomy specimen

Table 1: Serum TT and DHEA-S levels of the samples 5 catheterized veins.

	ROV	LOV	IVC	RRV	LRV
TT (ng/dl)	>1009.40	334.39	390.31	284	402.57
DHEA-S (µg/dl)	40.2	38.1	41.2	39.9	41.2

TT: Total testosterone, DHEA-S: Dehydroepiandrosterone sulfate, ROV: Right ovarian vein, LOV: Left ovarian vein, IVC: Inferior vena cava, RRV: Right renal vein, LRV: Left renal vein

The dimension of the right ovary on pathologic examination was 3x2x2 cm and it was noted that there was a 1.5 cm brown-yellow solid tumor on cross-section. The left ovary was 2x1.5x1.5 cm with nonspecific findings.

Immunohistochemical evaluation of the right ovarian tumor was positive for inhibin, calretinin, vimentin and 1-3 % positive for Kİ-67 but negative for CK7, CEA and AFP.

Microscopic examination revealed the eosinophilic cytoplasm and the low mitotic index of 1-2% of the tumor. The final diagnosis was an ovarian Leydig cell tumor less than 1 mm close but not reaching to the ovarian cortex.

Discussion

Virilization in a postmenopausal woman almost always indicates a serious endocrinopathy related to a tumor. The diagnostic work-up is directed to discern the source of hypersecretion between two paired endocrine organs, the ovaries and the adrenal glands.

Ovarian sex cord-stromal tumors are a rare group of neoplasms comprising only 1.2 % of all primary ovarian cancers [6]. They arise from the cells surrounding oocytes. They may secrete ovarian hormones and lead to signs of estrogen or androgen excess [7,8]. These neoplasms are classified as malignant but they generally demonstrate low-grade cytological abnormalities. Sertoli-Leydig cell type of sex cord-stromal tumors constitutes only 0.5 % of all ovarian tumors [9]. There is a predilection to be found in younger patients (the average age at diagnosis 25 years) than their epithelial counterparts which are the most common histologic type of ovarian cancer [10].

Tubular structures that produce androgens are the main histologic figures; hence they may lead to rapidly progressing virilization [11]. Because sex cord-stromal tumors are diagnosed at an early stage and rarely metastasize to lymph nodes, total abdominal hysterectomy and bilateral salpingo-oopherectomy is the preferred surgical intervention in postmenopausal patients. The diameter of these tumors range from 1 to 50 cm with an average size of 13 cm. Small sized tumors may escape detection with transvaginal ultrasound. As in our case, CT or MRI findings may indicate the suspected presence of an adrenal lesion which is not the source of androgen hypersecretion and may fail to demonstrate the ovarian tumor. In this case the final management may differ and the patient might even be operated for a ghost adrenal tumor. Due to the low grade nature of these neoplasms, PET/CT may not demonstrate the presence of an active FDG (Floro 2 Deoksi Glukoz) uptake by the tumor [10,11].

More sophisticated diagnostic methods are required to sample the venous blood to differentiate the origin. Some researchers favor the use of SVCHS, but also point out its low feasibility, the need for expertise and the high failure rate of catheterization as drawbacks. SVCHS is not recommended to be performed routinely for the investigation of hyperandrogenic women but in the presence of a small ovarian tumor when all endocrinologic studies and imaging results fail, it should be kept in mind as a last resort for definitive diagnosis [4].

Hyperandrogenemia with signs of virilization in a postmenopausal woman might be due to an androgen secreting ovarian tumor which might be too small to be detected by imaging techniques including high resolution transvaginal ultrasound, contrast-enhanced CT or MRI. Moreover, the presence of an adrenal tumor might be over-reported by the radiologist under the pressure to find a focus [8-11].

This case report underlines the importance to carry on the search with selective venous catheterization and hormonal sampling from both the ovarian and the adrenal veins to demonstrate the true source of androgen hypersecretion.

References

1. Burger HG. Androgen production in women. Fertility and Sterility. 2002;77 Suppl 4:S3-5.
2. Longcope C. Adrenal and gonadal androgen secretion in normal females. Clinics in endocrinology and metabolism. 1986;15:213-28.
3. Azziz R, Sanchez LA, Knochenhauer ES, Moran C, Lazenby J, Stephens KC *et al.* Androgen excess in women: experience with over 1000 consecutive patients. The Journal of clinical endocrinology and metabolism. 2004;89:453-62.
4. Kaltsas GA, Mukherjee JJ, Kola B, Isidori AM, Hanson JA, Dacie JE *et al.* Is ovarian and adrenal venous catheterization and sampling helpful in the investigation of hyperandrogenic women? Clinical endocrinology. 2003;59:34-43.
5. Nishiyama S, Hirota Y, Udagawa Y, Kato R, Hayakawa N, Tukada K. Efficacy of selective venous catheterization in localizing a small androgen-producing tumor in ovary. Medical science monitor : international medical journal of experimental and clinical research. 2008;14:Cs9-12.
6. Quirk JT, Natarajan N. Ovarian cancer incidence in the United States, 1992-1999. Gynecologic oncology. 2005;97:519-23.
7. Varras M, Vasilakaki T, Skafida E, Akrivis C. Clinical, ultrasonographic, computed tomography and histopathological manifestations of ovarian steroid cell tumour, not otherwise specified: our experience of a rare case with female virilisation and review of the literature. Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology. 2011;27:412-8.
8. Busquets M, Gonzalez-Bosquet E, Muchart J, Rovira C, Lailla JM. Granulosa cell tumor and endometrial cancer: a case report and review of the literature. European journal of gynaecological oncology. 2010;31:575-8.
9. DiSaia PJ CW. Germ cell, stromal and other ovarian tumors. In: Clinical Gynecologic Oncology, Mosby-Yearbook, 1997: p.351
10. Schneider DT, Calaminus G, Harms D, Gobel U. Ovarian sex cord-stromal tumors in children and adolescents. The Journal of reproductive medicine. 2005;50:439-46.
11. Young RH, Scully RE. Ovarian Sertoli-Leydig cell tumors. A clinicopathological analysis of 207 cases. The American journal of surgical pathology. 1985;9:543-69.

J Surg Med. 2018;2(3):377-379.
DOI: 10.28982/josam.426196

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Cystic intestinal pneumatosis revealed by peritonitis in perforated peptic ulcer: A case report

Perfore peptik ülserde peritonit ile ortaya çıkan kistik intestinal pnömatozis: Olgu sunumu

Ismaël Dandakoye Soumana [1], Anas Belhaj [1], Moussa Sylla [1], Somuah Tenkorang [2], Mouaqit Ouadii [1], Ibn Majdoub Hassani [1], Imane Toughrai [1], Hassan Moulay Farih [1], Khalid Mazaz [1], Ait Taleb Khalid [1]

[1] Visceral and Endocrinological Surgery Service II, Chu Hassan II, Fes, Morocco

ORCID ID of the authors
IDS: 0000-0003-2451-4199
AB: 0000-0002-1118-1594
MS: 0000-0002-5739-7382
ST: 0000-0001-5657-7253
MO: 0000-0003-3286-7568
IMH: 0000-0002-0421-7296
IT: 0000-0003-0401-3012
HMF: 0000-0001-8997-5717
KM: 0000-0001-7779-7802
ATK: 0000-0002-0920-796X

Abstract

Cystic intestinal pneumatosis is a rare condition characterized by the presence of cyst-like formations in the walls of the digestive tract. Cystic intestinal pneumatosis can affect any part of the digestive tract. However, the small and large bowels are the most affected. This pathology is more common in men and after the age of 50 years. Cystic pneumatosis of the intestines may be idiopathic or most often secondary to various diseases. The primitive forms preferentially affect the left colon with essentially submucous gaseous cysts, whereas the secondary intestinal cystic pneumatosis tend to affect the small intestines especially in the subserosa. The origin of this pathology is multifactorial but the main cause is not definitively proven. The long list of pathological associations has led to the development of various etiopathogenic theories that are not antinomic since some mechanisms may be associated.

Cystic intestinal pneumatosis is most often asymptomatic and therefore fortuitously discovered. This pathology could have clinical signs like bloody and glairy stools, abdominal pain, and diarrhea. Endoscopic and radiological examinations are easy to diagnose and avoid unnecessary laparotomy explorations in benign pneumoperitoneum. Treatment varies according to its etiology. For primary forms, antibiotic therapy to reduce the hydrogen-producing colonic flora is indicated as first-line treatment. If unsuccessful, oxygen mask or hyperbaric, which will promote the replacement of hydrogen with oxygen, must be attempted. For secondary forms, the treatment is that of the causal affection. In most cases, cystic intestinal pneumatosis is asymptomatic and no treatment is needed. Surgery remains reserved for serious forms of this disease.

Keywords: Cystic intestinal pneumatosis, Cysts, Pneumoperitoneum, Perforated peptic ulcer

Öz

Kistik bağırsak pneumatosisis sindirim sistemi duvarlarında kist benzeri oluşumların varlığı ile karakterize nadir bir durumdur. Kistik bağırsak pnömotozu sindirim sisteminin herhangi bir bölümünü etkileyebilir. Bununla birlikte, küçük ve büyük bağırsaklar en çok etkilenenlerdir. Bu patoloji erkeklerde ve 50 yaşından sonra daha yaygındır. Bağırsakların kistik pnömatozu, idiopatik veya çoğu zaman çeşitli hastalıklara ikincil olabilir. İlkel formlar, esas olarak submukozlu gazlı kistler ile sol kolonunu tercih ederler, oysa sekonder intestinal kistik pnömatozlar, özellikle ince bağırsakların subserozasını etkileme eğilimindedir. Bu patolojinin kökeni çok faktörlüdür, ancak ana sebep kesin olarak kanıtlanmamıştır. Patolojik ilişkilerin uzun listesi, çeşitli etiyopatojenik teorilerin gelişmesine yol açmıştır.

Kistik bağırsak pnömotozu en sık asemptomatiktir ve bu nedenle tesadüfi bir şekilde saptanır. Bu patoloji kanlı dışkılama, karın ağrısı ve diyare gibi klinik belirtilere sahip olabilir. Endoskopik ve radyolojik incelemeler benign pnömoperitoneumda gereksiz laparotomi eksplorasyonlarını tespit etmek ve önlemek için faydalıdır. Tedavi etiyolojisine göre değişir. Birincil formlar için, hidrojen üreten kolonik florayı azaltmak için antibiyotik tedavisi, birinci basamak tedavi olarak belirtilmektedir. Başarısız ise, oksijen ile oksijen değiştirilmesini teşvik edecek oksijen maskesi veya hiperbarik tedavi denenmelidir. Sekonder formlar için tedavi, nedensel olarak değişkendir. Çoğu durumda, kistik bağırsak pnömatozu asemptomatiktir ve tedaviye gerek yoktur. Cerrahi, bu hastalığın ciddi formları için ayrılmıştır.

Anahtar kelimeler: Kistik bağırsak pnömatozu, Kist, Pnömoperiton, Peptik ülser perforasyonu

Corresponding author / Sorumlu yazar:
Ismaël Dandakoye Soumana
Address / Adres: Visceral and Endocrinological Surgery Service II, Chu Hassan II, Fes, Morocco
e-Mail: sairaisma14@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 23.05.2018
Accepted / Kabul tarihi: 27.06.2018
Published / Yayın tarihi: 29.06.2018

How to cite / Atıf için: Soumana ID, Belhaj A, Sylla M, Tenkorang S, Ouadii M, Hassani IM, Toughrai I, Farih HM, Mazaz K, Khalid AT. Cystic intestinal pneumatosis revealed by peritonitis in perforated peptic ulcer: A case report. J Surg Med. 2018;2(3):377-379.

Introduction

Cystic intestinal pneumatosis (CIP), which is characterized by the presence of pseudocysts or air bubbles in the subserosa or submucosa of the digestive wall, is a rare benign condition [1]. It can be localized in the various segments of the digestive tract, from the esophagus to the rectum [2,3]. The small intestine appears to be more affected than the colon. Both small intestine and colon can be affected in 20% of cases [4,5].

This pathology is often asymptomatic and therefore discovered fortuitously. Endoscopic and radiological examinations are easy tools to diagnose this pathology. These diagnostic tools help to avoid unnecessary laparotomy in benign pneumoperitoneum. In most cases, CIP is asymptomatic and no treatment is needed. Surgery is reserved for particularly serious forms [4-7]. We report the case of a 37-year-old chronic smoker admitted to the emergency department for management of diffuse abdominal pain with incidental discovery of CIP.

Case presentation

A 37-year-old patient, with a 20 year history of cigarette smoking, presented with epigastric pain associated with a subocclussive syndrome, fever and a few episodes of vomiting. These symptoms had begun two days prior to his admission to the emergency department. Clinical examination found a feverish, conscious patient with a body temperature of 38 °C. Abdominal examination revealed a diffuse abdominal sensitivity more accentuated at the epigastric level. Laboratory test were within normal limits except C-reactive protein at 32mg/l and renal insufficiency. Plain abdominal X-ray objectified multiple air fluid levels without pneumoperitoneum. Abdominal non contrast computed tomography (CT) scan performed objectified pneumoperitoneum with suspicion of intestinal pneumatosis (Figure 1).

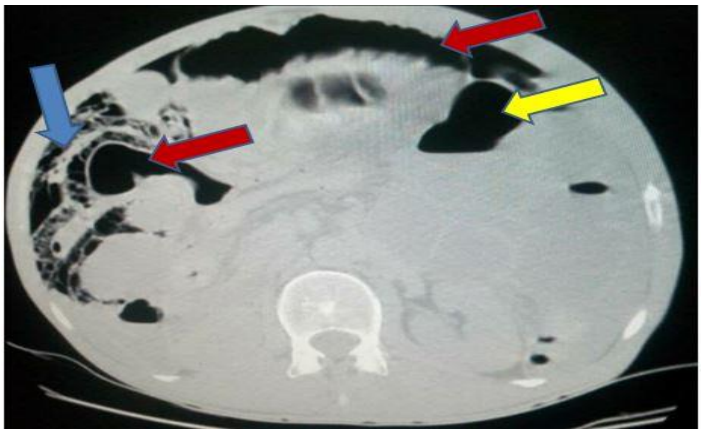


Figure 1: Abdominal computed tomography of the patient. Blue arrow: Suspicion of parietal pneumatosis, red arrow: gas in the small intestine, yellow arrow: hydro-aeric level colic type

Surgical exploration revealed a 1 cm perforation on the anterior surface of the duodenal bulb (Figure 2). We also found a cystic pneumatosis affecting 1.3m of the small bowel. The perforated zone was repaired with abundant rinsing and drainage of the peritoneal cavity. No action was taken for the CIP.

Figure 2: View in operation. Blue arrow: normal small intestine, black arrow: pathological small intestine

The postoperative course was marked with no incident. The patient was discharged on the 3rd day after surgery.

Discussion

CIP is characterized by the presence of cysts-like formations localized in the submucosa or subserosa of the digestive tract. These formations measure from a few millimeters to several centimeters. The cysts may concern a segment of the intestine or be diffused in the intestine extending to several meters, sometimes unrelated to the site of the causal lesion. The small bowel are the most frequent affected (42%) followed by the colon (32%); It is relatively less frequent to have both small and large bowels affected. When the large bowel is involved, sigmoid colon is the most frequent affected (70% of cases), followed by the descending colon in 40% of cases, and other segments in 15 to 25% of cases, including 10% for the caecum [6].

CIP are generally submucous in the colon, appearing as sessile polypoid nodules. They are more often subserosal in the small intestine, taking the form of air bubbles in grape-like clusters and are mostly localized on the mesenteric edge [6]. The wall of cysts is sometimes very thin and can be broken, either spontaneously or after an endoscopic biopsy causing pneumoperitoneum [8-10].

In 85% of cases, CIP secondary or associated with other gastrointestinal pathologies (inflammatory bowel disease, peptic ulcer, pyloric stenosis, abdominal trauma) or extra gastrointestinal (chronic obstructive pulmonary disease, heart disease, cystic fibrosis, lupus, periarteritis nodosa); primitive forms account for only 15% of cases reported [8-9]. In our patient, we found cystic pneumatosis linked to a peptic ulcer.

Many theories have been proposed to explain how CIP occur. Currently the most likely pathogenesis combines mechanical and bacterial theories: association of mucosal lesions, an increase in digestive intraluminal pressure allowing anaerobic bacteria (producing hydrogen) to enter the intestinal wall. The principal mechanism of this pathology is the mucous breach which seems indispensable [11-13]. For others, pneumatosis is explained by a deficit in hydrogen reducing bacteria: methanogenic bacteria [13].

CIP is usually pauci-symptomatic. Most authors report nonspecific signs in 30% of cases: diarrhea, bloody or glairy stools, meteorism, vomiting, constipation, tenesmus [6]. Abdominal meteorism is found in 38% of cases in the Jamart

series [6]; luminal occlusion associated with cysts may be responsible for transit disorders. Some rare complications related to cystic volume have been described (3%): volvulus, intussusception, perforation, hemorrhage. These complications may require segmental intestinal resections [14].

Plain X-rays of the abdomen often show pneumoperitoneum due to rupture of subserosal cysts in the peritoneal cavity. Cystic pneumatosis is the first cause of pneumoperitoneum without digestive perforation. It is present in 15% of the cystic pneumatosis in the small bowel and in 2% of the affected colon [11,12]. Cysts are best seen on the colon wall. They are effected by the presence of air formations contiguous to each other having the appearance of 'grape-like clusters' in the wall of the colon [11,15].

Computed tomography with intestinal opacification has a good diagnostic accuracy [16]. It reveals gaseous density images in the digestive wall, well detectable in a cross-sectional and lung window view [17,18]. The presence of these images associated with an asymptomatic pneumoperitoneum is almost pathognomonic of CIP [6]. An ultrasound appearance has been described associating a thinning of the intestinal wall and echogenic gas bubbles often seen as a circle [19]. There is an important diagnostic criterion, which is the gas in the portal vein (unlike intestinal gangrene) on the CT scan or ultrasound [20]. In endoscopy, cysts correspond to large hemispherical sessile polyps, covered with pale and transparent mucosa, which is sometimes ulcerated. Typically, the cyst is collapsed by puncture or biopsy with a burst sound effect [21].

The treatment of CIP is most often medical. Its purpose is to reduce or eliminate cysts by reducing the anaerobic bacteria that cause them. Anti-anaerobic antibiotherapy with metronidazole is often effective [12,15], but other antibiotics such as ampicillin or fluoroquinolones have been successful [11]. Hyperbaric oxygen therapy is used for its anti-anaerobic power and for its ability to collapse cysts by promoting exchanges with blood [12,22]. Other therapeutic options such as octreotide or endoscopic fenestrations have been used with varying results [12]. Surgical treatment is indicated in case of complications and in case of symptoms that are resistant to medical treatment [12,22]. It involves resecting the intestinal segment through laparotomy or via laparoscopy. The latter is preferred because of the benignity of the pathology and the favorable local conditions (absence of inflammation, absence of adhesion attributable to this pathology) [22,23].

In conclusion, cystic pneumatosis of the small intestine is a rare benign affection that is diagnosed with the means of radiological techniques. It should not be confused with a simple pneumoperitoneum or pneumatosis by intestinal gangrene. For this, the multidetector CT scan is extremely efficient to detect air of air in the digestive serosa, the different peritoneal and extra spaces. The CT scan also guides the surgeon to treat a possible complication such as peritonitis by perforation of the digestive tract.

References

1. Boerner RM, Fried DB, Warshauer DM, Isaacs K. Pneumatosis intestinalis. Two case reports and a retrospective review of the literature from 1985 to 1995. Dig Dis Sci. 1996;41:2272-85.
2. Danse EM, Vanbeers BE, Gilles A, Jacquet I. Sonographic detection of intestinal pneumatosis. Eur J ultrasound 2000;11:201-03.
3. Rybacj LD, Shopiro RS, Carano K, Halton KP. Massive pneumatosisintestinalis: CT diagnosis. Comput Med Imaging Graph. 1999;23:165-8.
4. Xavier JL, Boscangi G, Claudel N, et al. La pneumatose kystique intestinale. Ann Radiol. 1991;34:401-6.
5. Kaassis M, Ben bouali A, Arnaud JP. Pneumatose kystique occlusive du côlon gauche (quelle attitude thérapeutique faut-il adopter?). J Chir. 1995;132:183-5.
6. Vernoi JG Du. AnatomischeBeobachtung under der Æussen und innern Haut der Gedaermeeingeschlossenen. Luft Phys Med Abhandl Acad Wisseusch Petersb. 1783;2:182.
7. Jamart J. Pneumatosiscystoides intestinalis-A statistical study of 919 cases. ActaHepatogastroenterol (Stuttg). 1979;26(5):419–22.
8. Holt S, Stewart IC, Heading RC, Macpherson AI. Resolution of primary pneumatosis coli. J R Coll Surg Edinb. 1978;23(5):297–9.
9. Heng Y, Schuffler MD, Haggitt RC, Rohrmann CA. Pneumatosis intestinalis: a review. Am J Gastroenterol. 1995;90(10):1747–58.
10. Grasland A, Pouchot J, Leport J, Barge J, Vinceneux P. Pneumatosiscystoidesintestinalis. Presse Med. 1998;27(35):1804–12.
11. Guillem P. Radiologic pneumoperitoneum without perforation of a hollow viscus. J Chir (Paris). 2002;139(1):5–15.
12. Quintart C, Choghari C, Michez D, Lefebvre P, Ramdani B. Pneumatosiscystoides intestinalis - Diagnostic elements and therapeutic approach. Ann Chir. 1997;15(9):1032–5.
13. Boland C, De Ronde T, Lacrosse M, Trigaux JP, Delaunois L, Melange M. Pneumatosiscystoides intestinalis associated with Steinert disease. Gastroenterol Clin Biol. 1995;19(3):305–8.
14. Levitt MD, Olsson S. Pneumatosiscystoides intestinalis and high breath H2 excretion: insights into the role of H2 in this condition. Gastroenterology. 1995;108(5):1560–5.
15. Meikle G. A case of pneumatosis coli: pneumatosiscystoides intestinalis of the sigmoid colon causing intestinal obstruction, stercoral ulcer and perforation. J R Coll Surg Edinb. 1965;11(1):65–7.
16. Estermann F, Denis B, Gaucher P, Regent D, Sondag D. Pneumatosiscystoides of the colon: knowing how to recognize it -Apropos of 8 cases. Ann Gastroenterol Hepatol (Paris). 1994;30(4):151–5.
17. Pun YL, Russell DM, Taggart GJ, Barraclough DR. Pneumatosis intestinalis and pneumoperitoneum complicating mixed connective tissue disease. Br J Rheumatol. 1991;30(2):146–9.
18. Scheidler J, Stabler A, Kleber G, Neidhardt D. Computed tomography in pneumatosis intestinalis: differential diagnosis and therapeutic consequences. Abdom Imaging. 1995;20(6):523–8.
19. Brientini F, Debilly M, Litzler JF, Raclot G, Le Mouel A. Colonic cystic pneumatosis -A specific x-ray computed tomographic diagnosis: apropos of 2 cases. J Radiol. 1995;76(2-3):135–40.
20. Kohzaki S, Hayashi K, Fukuda T, Uetani M, Kawano Y, Iriarte WL. Case report: the "aurora sign"--a new sonographic sign of pneumatosiscystoides intestinalis. Br J Radiol. 1994;67(804):1275–7.
21. Feczko PJ, Mezwa DG, White BD. Clinical significance of pneumatosis of the bowel wall. Radiographics. 1992;12(6):1069–78.
22. Rogy MA, Mirza DF, Kovats E, Rauhs R. Pneumatosiscystoidesintestinalis (PCI). Int J Colorectal Dis. 1990;5(2):120–4.
23. Boerner RM, Fried DB, Warshauer DM, Isaacs K. Pneumatosis intestinalis -Two case reports and a retrospective review of the literature from 1985 to 1995. Dig Dis Sci. 1996;41(11):2272–85.

J Surg Med. 2018;2(3):380-382.
DOI: 10.28982/josam.426924

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Kidney clear cell sarcoma: About one case

Böbrek berrak hücreli sarkom: Bir olgu hakkında

Allouche Fadwa [1], Asmae Mazti [2], Fatima Zahra Terrab [1], Sanae Ghammad [1], Touria Bouhafa [1], Abderrahmane El Mazghi [1], Khalid Hassouni [1]

[1] Radiotherapy Service, Chu Hassan II, Fez, Morocco
[2] Department of Pathology, Chu Hassan II, Fez, Morocco

ORCID ID of the authors
AF: 0000-0002-6793-4911
AM: 0000-0002-9075-2825
FZT: 0000-0002-9257-1964
SG: 0000-0002-7940-8396
TB: 0000-0002-9857-1594
AEM: 0000-0003-2079-0815
KH: 0000-0002-1442-255X

Corresponding author / Sorumlu yazar:
Allouche Fadwa
Address / Adres: Radiotherapy Service, Chu Hassan II, Fez, Morocco
e-Mail: dr.allouch.fadwa@gmail.com

Informed Consent: The author stated that the written consent was obtained from the parents of the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastanın ebeveynlerinden yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 24.05.2018
Accepted / Kabul tarihi: 27.06.2018
Published / Yayın tarihi: 29.06.2018

Abstract

Kidney Clear Cell Sarcoma (SRCC) is a rare malignant tumor of the child, recognized for its aggressiveness, its high bone metastatic potential and its tendency to recur. We report a case diagnosed SRCC in a 22-month-old infant with a large right lumbar mass. An observation of Kidney tumor type clear-cell sarcoma, whose diagnosis was placed on a piece of anatomo-pathology, insofar as the imaging remained uncertain as to the Kidney origin of this mass. Apart from the histological aspect, there is currently no criterion for its diagnosis. Its prognosis has been markedly improved by the introduction of new treatment regimens.

Keywords: Tumor, Kidney, Child, Sarcoma, Clear cells

Öz

Böbrek Berrak Hücreli Sarkom (SRCC), saldırganlığı, yüksek kemik metastatik potansiyeli ve tekrarlama eğilimi nedeniyle tanınan, çocuğun nadir görülen malign tümörüdür. Büyük bir sağ lomber kitle olan 22 aylık bir bebekte SRCC tanısı alan bir olgu sunuyoruz. Bu kitlenin tanısı bir anatomi-patoloji üzerine yerleştirilmiş şeffaf hücreli sarkomu olup, böbrek kitlesinin tanısı böbrek kanseri ile ilgili belirsiz kalmıştır. Histolojik özellik dışında, şu anda tanısı için bir kriter bulunmamaktadır. Yeni tedavi rejimlerinin uygulamaya konması ile prognozu belirgin bir şekilde artmıştır.

Anahtar kelimeler: Tümör, Böbrek, Çocuk, Sarkoma, Berrak hücreler

Introduction

Kidney clear cell sarcoma is a rare tumor (4% of Kidney tumors) in children [1]. It is one of the most frequent aggressive Kidney tumors, said to have adverse histology, belonging to the group of non-Wilms kidney tumors [1,2].

Case presentation

We report a case of SRCC diagnosed in a 22-month-old infant with a large right lumbar spine. Computed tomography (CT) showed one of a large right mediastinal mass, well limited, hypodense, heterogeneously enhanced after contrast laminating the renal parenchyma, measuring 11x8.5x12 cm. This mass represses and compresses the ipsilateral renal pedicle, the inferior vena cava (IVC) and comes into contact with the abdominal aorta on a <90 ° surface. It also displaces the digestive structure, the diaphragmatic pillar and the visceral face of the right liver with loss of greasy edema of separation, with no sign of invasion. It comes into contact with the lateral abdominal wall without evidence of invasion (Figure 1).

How to cite / Atıf için: Fadwa A, Mazti A, Terrab FZ, Ghammad S, Bouhafa T, El Mazghi A1, Hassouni K. Kidney clear cell sarcoma: About one case. J Surg Med. 2018;2(3):380-382.

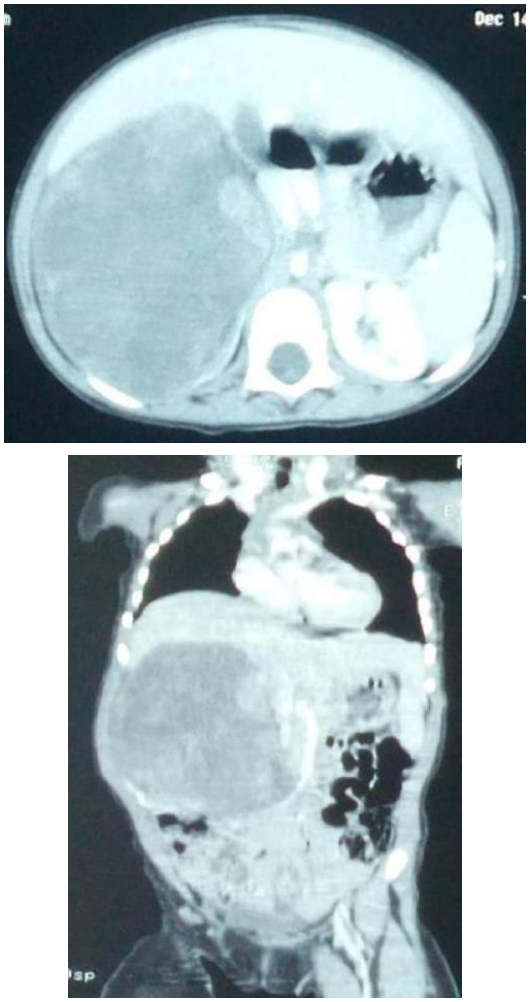


Figure 1: Computed tomography appearance of a bulky abdominal mass, un-encapsulated, heterogeneous density and whose relationships with the kidney are imprecise

Pulmonary, cerebral and bone extension assessment did not indicate secondary localization. Preoperative chemotherapy was administered according to GFA-Nephro 2005, with no toxicity 0. At the end of preoperative chemotherapy, abdominopelvic CT showed no reduction in tumor volume. Surgery consisted of an extended right anterior trans-peritoneal nephro-uretectomy with lymph node dissection was performed. The operative piece measured 15x10x 9cm. The ureter measures 3x0.5 cm. At the opening, the entire kidney is occupied by a beige tumor, homogeneous, massively infiltrating the kidney and having cystic areas. Histologically, there was tumor proliferation arranged in layers. It is made of cells sometimes rounded, sometimes oval or fusiform. The nuclei are small, with fine chromatin. These cells are located on an abundant myxoid background with formation of cystic foci bordered by tumor cells. The tumor stroma has vessels and fine-walled capillaries, absence of anaplasia, heterologous component or nephrogenic residue with negative cleansing (latero-cellar + inter-aortic-cellar). Tumor cells diffuse vimentin and cyclin D1 and do not express BCL2 or desmin (Figure 2). Histological and immune-histochemical appearance compatible with a clear cell sarcoma, classified according to the SIOP (International Society of Pediatric Oncology) 2001 high risk, stage II.

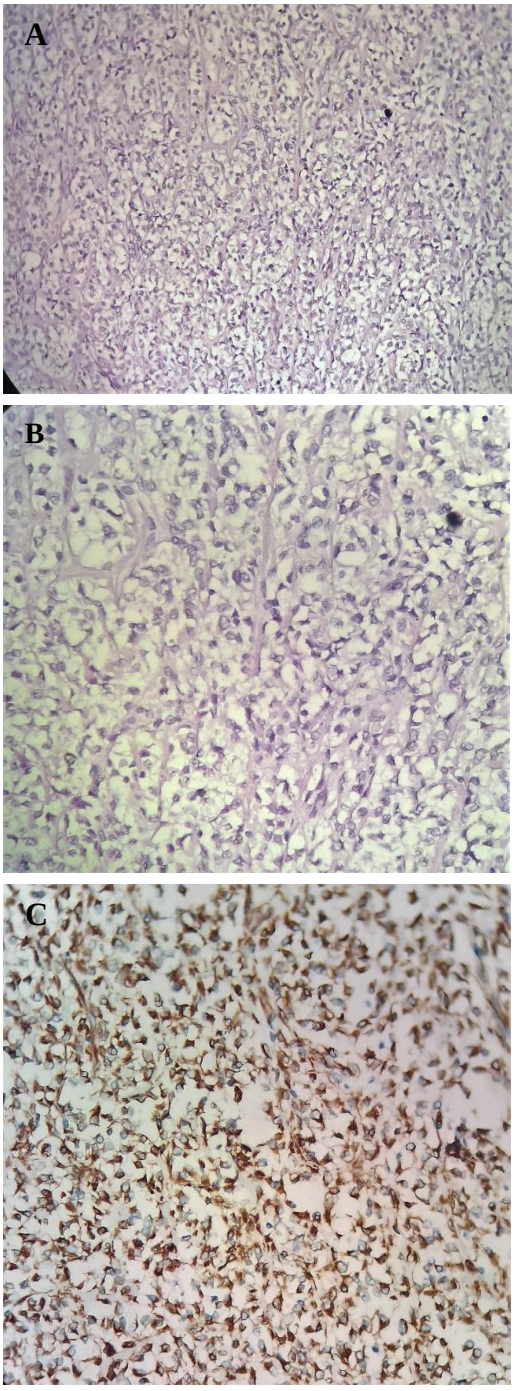


Figure 2: A: HES X 10: Tumor proliferation arranged in diffuse layer, made of clear cells, B: HESX400: tumor cells are round or oval, with clarified nuclei and clear cytoplasm; Note the presence of a fine vascularization connected, C: tumor cells strongly express vimentin

In accordance with the therapeutic recommendations developed by the SIOP 2001 Committee, prolonged postoperative chemotherapy according to GFA-nephro 2005 post op. The tumor was classified as high-risk stage II R0, so the action to be taken was the irradiation of the right flank of 10.8 Gy in 6 fractions of 1.8Gy / Fraction, without boost, at the end of the radiotherapy, we do not have toxicity. Currently, the child is in complete remission more than 8 months from the diagnosis.

Discussion

Kidney clear cell sarcoma accounts for about 4% of childhood kidney tumors and usually occurs in children aged 18 months to five years (average 30 months). Because of the age of their occurrence, the absence of specific imaging and the histological similarity of certain variants, these tumors can pose

diagnostic difficulties. Indeed, the Kidney clear cell sarcoma is a rare tumor of the child and exceptional in the adult [3]. The abdominal mass sums up the whole clinical history and is the essential reason for consultation. Associated abdominal ultrasonography and / or abdominal CT scan alone usually provide the diagnosis of renal tumor [4].

Histologically, it is a tumor with an in fi ltering tendency, unlike nephroblastoma, which is encapsulated. In the classical form, it is a homogeneous tumor and in 90% of cases, it is a richly vascularized proliferation, arranged in nests or cords. The cells are fusiform or oval, with a clear cytoplasm and nucleus. A small fibro-vascular stroma typically lobulates this tumor. The presence of tubes and glomeruli enclosed within the tumor is frequently observed [5,6]. Our case is consistent with the literature data.

Immunohistochemistry is not specific. Only vimentin is positive. The expression of Bcl-2 is not constant, that of epithelial markers is only objectified at the renal tubes engulfed in proliferation. In our observation, cyclin D1 was also expressed [7]. The differential diagnosis of Kidney clear cell sarcoma can in children discuss a nephroblastoma in its sarcomatous or pure blastematous variety, a mesoblastic nephrome in its cellular form, a rhabdoid tumor and an embryonic rhabdomyosarcoma, some histological, immunohistochemical and molecular elements allow their distinction [5,7].

Rare cases of reported SRCC have t (10; 17) translocation and / or 14q deletion. No specific genetic criterion for Kidney clear cell sarcoma is currently known. However, the study of Huang et al [8]. Demonstrates that these four tumors have different genetic profiles.

To date, few studies have focused on therapeutic management. The current treatment, according to the SIOP 2001 protocol, recommends extensive nephrectomy, radiotherapy and intensive and prolonged multidrug therapy based on alkylants, anthracyclines, epipodophyllotoxins and platinum derivatives. National Wilms' Tumour Study 1, 2, 3 and 4 studies [9,10] show that the addition of doxorubicin (D) improves prognosis with a six-year relapse-free survival of 63.4% versus 25% without (D). In the same way, a multidrug therapy prolonged for 15 months offers a better survival at eight years, namely 87% versus 60.6% for a period of six months.

The utility of radiotherapy in intermediate-risk tumors is more debated, with Europeans generally favoring a chemotherapeutic approach, while North Americans are more inclined to associate a radio-therapeutic approach. High-risk tumors, including clear-cell sarcomas, are treated by the combination of radiotherapy and additional cytostatics such as carboplatin, etoposide and cyclophosphamide. The total duration of treatment, administered mostly outpatient, varies according to stages and classification of the tumor between one and eight months. Close monitoring is necessary given the tendency to recur and metastases, mainly bone [9,10].

In conclusion, kidney clear cell sarcoma is a rare, highly aggressive and often histologically discovered pediatric tumor that is considered to be a high-risk tumor. Such progress has been made over the years through improved combined management, medical-surgical, and better stratification of less-risk tumors, leading to better selection of required treatment intensity.

References

1. Brockert B. Non-Wilms' renal tumors in children. Urol Clin North Am. 2000;27:463–9.
2. Kidd JM. Exclusion of certain renal neoplasms from the category of Wilms' tumor. Am J Pathol. 1970;59:16a.
3. Benchekroun A, Ghadouane M, Zannoud M, Alami M, Amhaji R, Faik M. Clear cell sarcoma of the kidney in an adult. A case reports. Ann Urol (Paris). 2002;36:33–5.
4. Glass RBJ, Davidson AJ, Fernbach SK. Clear cell sarcoma of the kidney: CT, Sonographic, and Pathologic correlation. Radiology. 1991;180:715.
5. Argani P, Perlman EJ, Breslow NE, Browning NG, Green DM, D'Angio GJ, et al. Clear cell sarcoma of the kidney. A review of 351 cases from the national Wilms tumor study group pathology center.Am J Surg Pathol. 2000;24:4–18.
6. Bienvenu L, (de) Pinieux G, Dupin P, Choudat L, Vieillefond A. Sarcome à cellules claires du rein chez un jeune adulte. Ann Pathol. 1997;17:396–9.
7. Looi LM, Cheah PL. An immunohistochemical study comparing clear cell sarcoma of the kidney and. Pathology. 1993;25:106–9.
8. Huang CC, Cutcliffe C, Coffin C, Sorensen PH, Beckwith JB, Perlman EJ. Classification of malignant pediatric renal tumors by gene expression. Pediatr Blood Cancer. 2006;46(7):728-38.
9. Green DM, Breslow NE, Beckwith JB, Moksness J, Finklestein JZ, D'Angio GJ. The treatment of children with clear-cell sarcoma of the kidney: A report from the National Wilms' Tumor Study Group. J Clin Oncol. 1994;12:2132-7.
10. Seibel NL, Li S, Breslow NE, Beckwith JB, Green DM, Haase GM, et al. Effect of duration of treatment on treatment outcome for patients with clear-cell sarcoma of the kidney: a report from the National Wilms' Tumor Study Group. J Clin Oncol. 2004;22:468-73.

J Surg Med. 2018;2(3):383-384.
DOI: 10.28982/josam.428003

Journal of Surgery and Medicine
e-ISSN: 2602-2079

A case report of gastrointestinal stromal tumor located in the jejunum

Jejunumda bulunan gastrointestinal stromal tümör olgusu

Anas Belhaj [1], Fatima Zahrae Terrab [2], Somuah Tenkorang [3], Karim Ibn Majdoub [1], Imane Toughrai [1], Moulay Hassan Farih [3], Khalid Hassouni [2], Khalid Mazaz [1]

[1] Visceral Surgery Department, Hassan II University Hospital, Fez, Morocco
[2] Radiotherapy Department, Hassan II University Hospital, Fez, Morocco
[3] Urology Department, Hassan II University Hospital, Fez, Morocco

ORCID ID of the authors
AB: 0000-0002-1118-1594
FZT: 0000-0001-6508-5066
ST: 0000-0001-5657-7253
KIM: 0000-0002-0421-7296
IT: 0000-0003-0401-3012
MHF: 0000-0001-8997-5717
KH: 0000-0002-1442-255X
KM: 0000-0001-7779-7802

Abstract

Among rare primary mesenchymal tumors in the digestive tract are gastrointestinal stromal tumors which are often located in the stomach. This tumor is rarely found in the jejunum with an incidence of 20 to 30% of cases. We report the case of a gastrointestinal stromal tumor of the jejunum in a 67-year-old diabetic patient undergoing treatment.

Keywords: Stromal tumors, Jejunum, Surgery, Chemotherapy

Öz

Sindirim sistemindeki nadir görülen primer mezenkimal tümörler genellikle midede bulunan gastrointestinal stromal tümörlerdir. Bu tümör, jejunumda nadiren %20 ila %30 oranında görülür. Bu çalışmada tedaviye dirençli 67 yaşında diyabetik bir hastada jejunumun gastrointestinal stromal tümörü olgusunu sunuyoruz.

Anahtar kelimeler: Stromal tümörler, Jejunum, Cerrahi, Kemoterapi

Introduction

Gastrointestinal Stromal Tumors (GIST) are rare primitive mesenchymal tumors of the gastrointestinal tract [1], characterized by the cell surface expression of a specific gene c-kit (CD117). They can be localized in any segment of the digestive tract, with a predilection for the stomach (60%). The jejunal location of stromal tumors is rare. Its incidence is 20 to 30% of cases [2]. We report a case of a jejunal stromal tumor diagnosed during an abdominal pain syndrome with melena and confirmed by pathological examination in a 67-year-old diabetic patient undergoing treatment.

Case presentation

A 67-year-old diabetic patient under Oral anti diabetic drug presented with diffuse abdominal pain with melena with no other associated symptoms. She complained that these symptoms had begun 10 days prior to her consultation in our department. Oesogastroduodenal fibroscopy was normal. The patient received an abdominal angio-scanner that objectified a tumor process of the first jejunal loop intensely enhanced during the arterial phase suggestive of a stromal tumor. The patient was surgically treated during which an exophytic tumor of about 3 cm was observed at the level of the jejunum precisely about 6 cm from the angle of Treitz (Figure 1). The segment of the jejunum containing this tumor was resected after which we performed a termino-terminal anastomosis.

Corresponding author / Sorumlu yazar:
Anas Blehaj
Address / Adres: Visceral Surgery Department, Hassan II University Hospital, Fez, Morocco
e-Mail: dr.anasbelhaj@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 29.05.2018
Accepted / Kabul tarihi: 27.06.2018
Published / Yayın tarihi: 03.07.2018

How to cite / Atıf için: Belhaj A, Terrab FZ, Tenkorang S, Majdoub KI, Toughrai I, Farih MH, Hassouni K, Mazaz K. A case report of gastrointestinal stromal tumor located in the jejunum. J Surg Med. 2018;2(3):383-384.

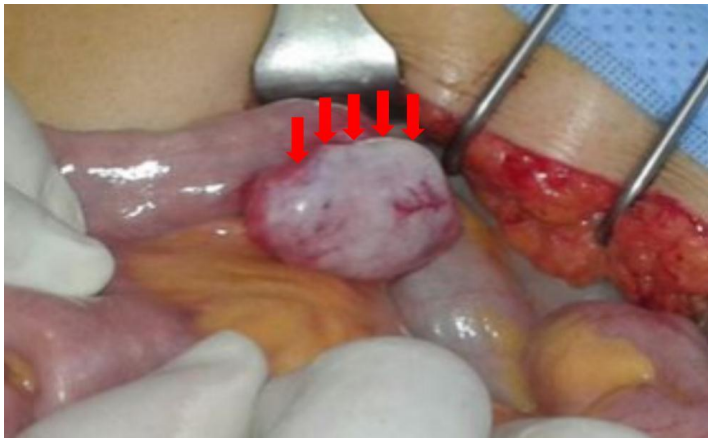


Figure 1: Image showing the tumor

The postoperative course was unremarkable. Pathological examination of the resected specimen confirmed the diagnosis of a high-grade gastrointestinal stromal tumor according to the Miettinen classification. Adjuvant chemotherapy was indicated after the patient's case was discussed in our multidisciplinary staff meeting. The patient was however referred to our oncology department for follow-up care.

Discussion

Gastrointestinal stromal tumors are rare primary mesenchymal tumors of the digestive tract [1]. They can occur at any age, usually between the ages of 50 and 60 years. They are most often localized in the stomach and small intestine but rarely localized in the mesentery and omentum [3]. Jejunal localization of this tumor occurs in 20 to 30% of cases [1].

GIST in the small intestine may be asymptomatic. Diagnosis is established fortuitously during physical examination or surgery. Clinical signs usually occur when they become voluminous or during a complication: digestive hemorrhage, abdominal pain, palpation of a mass [4].

Abdominal computed tomography and magnetic resonance imaging are considered the most appropriate imaging methods for the preoperative diagnosis of GIST [5].

Pathological diagnosis of GIST is based on its typical histological features and on the immuno-histochemical evidence of the two most characteristic markers, CD34 and c-kit protein.

Surgery is the only curative treatment [4]. Complete monoblock surgical resection of the tumor (R0 resection) is the only potentially curative treatment [6,7]. It is essential to avoid per-operative perforation which results in peritoneal dissemination. This places the patient's survival similar to that of patients with incomplete excision in some studies. In case of incomplete excision (R2 resection) or excision of associated peritoneal metastatic nodules, the spontaneous prognosis is poor. The case of R1 resections remains the subject of discussion, as R1 resection has not been shown to be associated with a worse prognosis [6].

The efficacy of chemotherapy in GIST is very low, with 0 to 10% response. Radiotherapy was used only occasionally, with symptomatic aim, for fixed tumors that are responsible for pain or hemorrhage. It is based on Imatinib. There are two situations:

- As neo-adjuvant: indicated

o In the forms that are difficult to resect due to their anatomical localization

o In the forms compromising functional prognosis

o In the forms where surgery poses a significant risk of morbidity

- As adjuvant: indicated in the forms with intermediate and high risk or in case of tumoral rupture

- o It is based on Imatinib. The optimal duration of Imatinib treatment is still being evaluated.
- o For intermediate and high risk forms, the recommended treatment time is at least 3 years.
- o In case of tumor rupture, long-term treatment is recommended [8].

Imatinib may also be used to try to reduce the size of the tumor and thus allow it to be removed through surgery.

After excision, late recurrences of tumors with reduced malignancy potential are possible.

Conclusion

Gastrointestinal stromal tumors of the jejunum are rare. They have various clinical manifestations. Surgery remains the only curative treatment for this disease.

References

1. Gupta P, Tewari M, Shukla HS. Gastrointestinal Stromal Tumor Journal of Surgical Oncology. 2008;17:129-38.
2. Miettinen M, Monihan JM, Sariomo RM, Kovavitch AJ, Carr NJ, Emory TS, et al. Gastrointestinal Stromal Tumors/Smooth muscle Tumors (GISTs) Primary in the omentum and mesentery: clinicopathologic and immunohistochemical study of 26 cases The American Journal of Surgical Pathology. 1999;23:1109-18.
3. Landi B. Endoscopicapproach to GIST. Journal of surgery. 2008;145:6S4-6S7.
4. Zhao X, Yue C. Gastrointestinal stromal tumor. Journal of grastrointestinal oncology. 2012;3:189–208.
5. Tervahartiala P, Halavaara J. Radiology of GIST Annales chirurgiae et gynaecologiae. 1998;87:291-2.
6. The ESMO/European Sarcoma Network Working Group. Gastrointestinal stromal tumors: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2014;25:iii21-iii26.
7. Demetri GD, von Mehren M, Antonescu CR, DeMatteo RP, Ganjoo KN, Maki RG, et al. NCCN Task Force report: update on the management of patients with gastrointestinal stromal tumors. Journal of the National Comprehensive Cancer Network. 2010;8:S1-41.
8. DeMatteo RP, Ballman KV, Antonescu CR, Maki RG, et al. Adjuvant imatinib mesylate after resection of localised, primary gastrointestinal stromal tumour: a randomised, double blind, placebo-controlled trial. Lancet. 2009;373:1097–104.

J Surg Med. 2018;2(3):385-386.
DOI: 10.28982/josam.428348

Case report
Olgu sunumu

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Ileal lipoma: A rare cause of ileo-colic intussusception in adult

İleal lipom: Erişkinlerde nadir bir ileokolik intususepsiyon nedeni

Ahmed Zerhouni [1], Mourad Badri [1], Anas Belhaj [1], Karim Ibn Majdoub [1], Imane Toughrai [1], Khalid Mazaz [1]

[1] Visceral and Endocrinological Surgery Service II, Chu Hassan II, Fes, Morocco

ORCID ID of the authors
AZ: 0000-0001-8441-016X
MB: 0000-0001-5085-0941
AB: 0000-0002-1118-1594
KIM: 0000-0001-7646-685X
IT: 0000-0003-0401-3012
KM: 0000-0001-7779-7802

Abstract

We report in this publication a case of acute intestinal intussusception on ileal lipoma in a 40-year-old patient that has been diagnosed on an emergency abdominopelvic CT scan for an occlusive syndrome. The treatment consisted of manual disinvagination with resection of the thin portion of the small bowel containing the lipoma and a mechanical anastomosis.

Keywords: Lipoma, Intussusceptions, Adult

Öz

Bu yayında, oklüzif bir sendrom için acil abdominopelvik BT taraması tanısı konan 40 yaşında bir hastada ileal lipomda akut intestinal intususepsiyon olgusunu sunduk. Tedavi, lipomayı ve mekanik bir anastomozu içeren ince bağırsağın ince kısmının rezeksiyonu ile manuel definvagasyondan oluşuyordu.

Anahtar kelimeler: Lipom, Intussusceptions, Yetişkin

Introduction

Acute intussusception in adults is rare; it represents 1 to 5% of obstruction causes in adults and its diagnosis is difficult and usually late. In the adult, an organic cause of intussusceptions is often found and the treatment is always surgical [1-3]. A case of bowel obstruction admitted to the emergency room, generated a lot of interest from the guard team; it is the case of an adult who had an intussusception of the small intestine on the colon, due to the presence of a lipoma. The surgery was minimalist and the evolution was towards healing. The rarity of the case has led us to want to share it with the scientific community.

Case presentation

A 40 years old patient, who has been smoking for 20 years, was admitted to the emergency room for peri-umbilical and right iliac fossa abdominal pain of sudden onset, rebellious to symptomatic treatment, associated with a bowel obstruction. The patient was in good general condition stable with a blood pressure at 140/80 mmHg, the heart rate was 89 beats / min, and apyrexic. On the other hand, abdomen was distended, tympanic and painful requiring the administration of the morphine derivative. However, no abdominal mass was noted, water-air noises were present, and hernia areas were free. The usual laboratory tests did not show leukocytosis (whites at 9000 / mm), anemia (Hemoglobin at 14.5g / dl), correct kidney function and the rest of the biological parameters were also correct. An abdominal x-ray did not find any pneumoperitoneum, but it revealed the presence of diffuse hydroaeric levels. Abdominal CT was urgently indicated and referred to the diagnosis by showing the presence of an invaginated intestinal loop over a 30mm oval lump, of a lipoma-like fat nature.

In this case of small bowel – large bowel invagination on a lipoma, the surgical intervention was carried out urgently, and the operative exploration showed the presence of a distended intestinal upstream over an invagination of about 80 cm of the colonic ileum (Figure 1).

Corresponding author / Sorumlu yazar:
Mourad Badri
Address / Adres: Visceral and Endocrinological Surgery Service II, Chu Hassan II, Fes, Morocco
e-Mail: mouradbadri79@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 29.05.2018
Accepted / Kabul tarihi: 29.06.2018
Published / Yayın tarihi: 03.07.2018

How to cite / Atıf için: Zerhouni A, Badri M, Belhaj A, Majdoub KI, Toughrai I, Mazaz K. Ileal lipoma: A rare cause of ileo-colic intussusception in adult. J Surg Med. 2018;2(3):385-386.

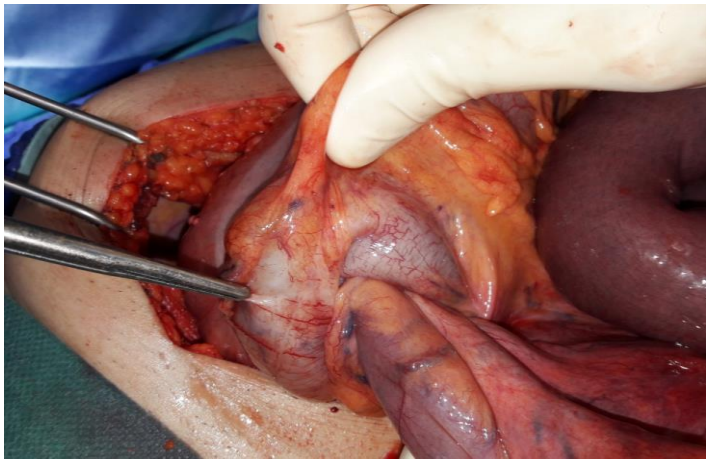


Figure 1: Image showing the intussusception

The gesture consisted in a manual extroversion with discovery of a 30 mm lipoma located 70 cm from the ileocecal angle (Figure 2).

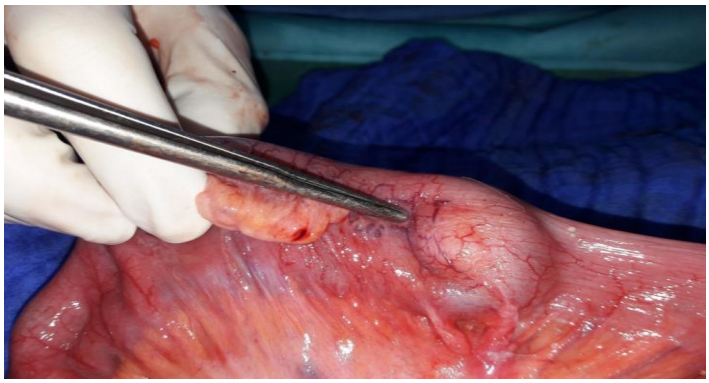


Figure 2: The lipoma in the small bowel after extroversion

Then, we proceeded to the resection of the portion of the intestine containing the lipoma, and the making of a latero-lateral mechanical anastomosis. The follow-ups were ordinary, with a hospital stay of 4 days. Anatomopathological examination of the operative specimen confirmed the fatty nature of the resected mass (Figure 3).

Figure 3: Lipoma after extraction

Discussion

Intestinal intussusception is defined by a smashing intestinal portion into the underlying potion. It is much more common in children but rare in adults, since only 5% of them occur in adults [1,2]. In adults, it is often secondary to an organic cause in 90% of cases, either a benign or malignant tumor (50 to 90% of cases), or inflammatory lesions (appendicitis, Meckel diverticulitis), or cicatricial adherences. In the small intestine, there are most frequently benign tumors, unlike the colon where most often there are malignant causes. Lipoma can be found at all levels of the digestive tract, but it is often seated in the colon in 70% of cases [3] and only in 20 to 25% of cases the lipoma is in the small bowel. It is often unique and develops in the submucosal layer of the intestinal wall. Primary malignant tumors (adenocarcinoma, lymphoma, carcinoid, leiomyosarcoma) or metastatic (melanoma) represent 6 to 30% of cases.

Intussusception is rarely idiopathic in adults (less than 10% of cases) [4], mostly ileoileale. The diagnosis is difficult and most of the time is intraoperative. It is frequently manifested by nonspecific and variable signs of episodic occurrence, favoring delayed diagnosis; more rarely, it is manifested by an acute syndrome related to occlusion or perforation with acute peritonitis. CT scan is the better suited [5] to distinguish intussusception from other causes of intestinal obstruction. It shows a tissue density corresponding to the edematous wall of the invaginated loop, accompanied by an eccentric crescent image of greasy density corresponding to the mesentery. Sometimes, it identifies the causal lesion (fat density of a lipoma). The surgical procedure must be systematic in the adult, which makes it possible to carry out an intestinal resection taking away the cause. It is reasonable not to make any attempts at withering and to consider from the start a resection of the affected small bowel in the case where the presence of a malignant tumor is suspected. In this case, the resection should be wide and oncologic. In the late stage of irreversible necrosis, it is better to perform a resection without intestinal extroversion. In case the diagnosis is made early, at a stage without ischemia or intestinal necrosis, the first reduction is justified. The laparoscopic approach of a small intussusception could be performed immediately if the preoperative imaging evokes the existence of a benign cause and if the patient is seen early [6]. In the case of colonic intussusception, laparoscopy does not seem appropriate because of the frequency of malignant tumors.

Conclusion

Intestinal intussusception can occur on any segment of the digestive tract. It is rare in adults and the diagnosis is difficult. The CT scan is the ideal test to make the diagnosis and highlight the etiology. The treatment is always surgical in the adult. The ileocolic invagination is most often of benign cause. Invagination can be reduced by laparoscopy.

References

1. Ahn JH, Choi SC, Lee KJ, Jung YS. A clinical overview of a retrospective study about adult intussusceptions: focusing on discrepancies among previous studies. Dig Dis Sci. 2009 Dec; 54(12):2643–9.
2. Balik AA, Ozturk G, Aydinli B, Alper F, Gumus H, Yildirgan MI, Basoglu M. Intussusception in adults. Acta Chir Belg. 2006;106:409–12.
3. Oyen TL, Wolthuis AM, Tollens T, Aelvoet C, Vanrijkel JP. Ileo-ileal intussusceptions secondary to a lipoma: a literature review Acta Chir Belg. 2007; 107:60-3.
4. Amoruso M, D'Abbicco D, Praino S, Conversano A, Margari A. Idiopathic adult colo-colonic intussusception: Case report and review of the literature. Int J Surg Case Rep. 2013; 4(4): 416–418.
5. Eisen LK, Cunningham JD, Aufses AH. Intussusception in adults: institutional review J Am Coll Surg. 1999;188:390-5.
6. Yamaguchi S, Fujii S, Ike H, Shimada H. Laparoscopic reduction of appendicocecal intussusception due to mucinous cystadenoma in an adult. JSLS. 2004;8(3):279–82.

J Surg Med. 2018;2(3):387-388.
DOI: 10.28982/josam.423536

Case report
Olgu sunumu

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Avascular necrosis of lunate bone: Kienbock disease

Lunat kemiğin avasküler nekrozu: Kienböck hastalığı

Cihan Bedel [1], Göker Coşkun [2], Sefa Türkoğlu [3]

[1] University of Health Sciences, Antalya Training and Research Hospital, Department of Emergency Medicine, Antalya, Turkey
[2] Süleyman Demirel University, Faculty of Medicine, Department of Emergency Medicine, Isparta, Turkey
[3] Denizli State Hospital, Department of Radiology, Denizli, Turkey

ORCID ID of the authors
CB: 0000-0002-3823-2929
GC: 0000-0002-6800-7511
ST: 0000-0002-9623-0083

Abstract
Kienbock disease is a rare disorder involving the lunate, one of the carpal bones, and is therefore not generally included in the differential diagnosis of patients presenting to the emergency department with wrist pain. In this case report, we would like to highlight a case of Kienbock disease in a 28-year-old female patient without any medical or traumatic history. Although it is a very rare disease of the lunate, emergency physicians should consider Kienbock disease in those patients with complaints of pain, swelling and limitation of motion of the wrist. An overlooked diagnosis or misdiagnosis may lead to bony ischemia, necrosis, and ultimately collapse of the bone.
Keywords: Kienbock disease, Avascular necrosis, Wrist pain

Öz
Kienböck hastalığı, el bileğindeki lunat kemiği ilgilendiren nadir bir hastalıktır, bu nedenle acil servise el bileği ağrısı ile başvuran hastaların ayırıcı tanısında yer almamaktadır. Bu olgu sunumunda, hastalık veya travma öyküsü olmayan 28 yaşındaki bir kadın hastada Kienböck hastalığını vurgulamak istiyoruz. Her ne kadar Kienbock hastalığı lunat kemiğin nadir bir hastalığı olmasına rağmen, acil doktorları el bileğinde ağrı, şişlik ve hareket kısıtlılığı olan hastalarda bu hastalığını akılda tutmalıdırlar. Göz ardı edilen teşhis veya yanlış tanı, kemik iskemisine, nekrozuna neden olabilir.
Anahtar kelimeler: Kienböck hastalığı, Avasküler nekroz, Bilek ağrısı

Introduction

Kienbock disease (KD) is a very uncommon condition of the lunate bone that is characterized by sclerosis, cystic changes, fragmentation and progressive osteonecrosis [1,2]. Diagnosis of the disease is usually delayed because of a lack of significant radiographic changes during the early stages of disease [1]. Patients usually have the history of recurrent trauma. Osteonecrosis of the lunate bone is most common between the second and fifth decades of life [3]. In this case, we would like to highlight a case of KD in a 28-year-old female patient without any medical or traumatic history.

Case presentation

A 28-year-old female patient was admitted to our emergency department (ED) with complaint of right wrist pain and difficulty to move her hand lasting 1 week in duration. She described the pain level of her wrist as moderate, rating it 6 of 10 on the pain scale. In her history she had never injured or sustained any minor or major trauma to the right wrist before presenting to the ED. The patient's pain was sharp, aggravated with extension of the wrist and relieved with immobilization. The patient had no past medical and surgical history. She was not taking any medications and had no known allergies. She denied current or past use of tobacco and demonstrated moderate alcohol consumption. She is right-hand dominant.

On examination of the wrist, the right wrist demonstrated no obvious asymmetry or deformity compared with the left wrist. There was no surface trauma, open wounds, bruising or deformity. There was also no overlying erythema or warmth to touch. There was moderate swelling and tenderness on palpation on the dorsum midwrist. There was no scaphoid fullness or tenderness on direct palpation or axial loading. She has limited active and passive range of motion of her right wrist. Other physical and neurological examination including sensation, deep tendon reflexes and motor strength was unremarkable. Radial and ulnar arterial pulses were palpable. Radiograph of the right wrists was obtained. It revealed mild sclerosis, cystic lesions and irregularity on the borders of lunate bone (Figure 1).

Corresponding author / Sorumlu yazar:
Cihan Bedel
Address / Adres: Antalya Eğitim ve Araştırma Hastanesi, Acil Tıp Anabilim Dalı, Antalya, Türkiye
e-Mail: cihanbedel@hotmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 14.05.2018
Accepted / Kabul tarihi: 05.07.2018
Published / Yayın tarihi: 09.07.2018

How to cite / Atıf için: Bedel C, Coşkun G, Türkoğlu S. Avascular necrosis of lunate bone: Kienbock disease. J Surg Med. 2018;2(3):387-388.

A Magnetic resonance imaging (MRI) study of the right wrist showed hypointense lesion and sclerosis in the lunate bone (Figure 2). These findings were consistent with osteonecrosis of the lunate bone and the final diagnosis was KD. The patient was referred to orthopedic surgeon and started to use forearm split for immobilization of wrist and analgesic therapy. After a 3-week follow-up period, the patient reported that her complaints regressed.

Figure 1: Cystic lesion and irregularity on lunate bone at radiography.

Figure 2: Hypointense lesion in the lunate bone on T1-weighted MRI

Table 1: Stahl-Lichtman classification system

Stages	Explanation
Stage I	Normal radiograph
Stage II	Lunate sclerosis without collapse
Stage III	Lunate fragmentation and collapse
IIIa	Without carpal collapse
IIIb	With carpal collapse
Stage IV	Degenerative changes around lunate

Discussion

Although the etiology is quite controversial in the literature, KD should be regarded in the differential diagnosis of the patients who were admitted to the ED with complaints of pain, swelling, and limitation of motion in the wrist [1,4].

KD is most common between the second and fifth decades of life and it affects men more than women [3]. KD is a very rare disease which is characterized by sclerosis, cystic changes, fragmentation and progressive osteonecrosis. Osteonecrosis is seen due to interrupted blood flow to the bone [1]. The disease commonly affects the dominant wrist, as in our case and generally related with the hyperextension of wrist. However, there are also 3 etiological mechanism of the disease: mechanical, vascular and traumatic. Other reasons are alcohol over intake, obesity, steroid intake, coagulation disorders, decreased blood flow and increased venous pressure [1,5,6].

The patients typically present with pain localized to the radiolunate facet, decreased motion, swelling and weakness in the affected hand. Pain is classically insidious in onset, often related to activity and can be present for extended periods before presentation [3]. In our case, the patient presented to ED with similar complaints.

Radiography is the initial imaging technique for assessing KD and also can be used to rule out other pathological conditions, such as fractures [7]. MRI is effective in the early stage diagnosis of KD [8]. It is generally diagnosed radiologically at late stages. The most commonly used staging system in the classification of KD is Stahl-Lichtman classification system. It is shown in the table 1 [9,10]. This classification is highly reliable and reproducible and has the most clinical relevance because it helps in determining the most appropriate treatment [7]. A lot of treatment methods which extend from conservative treatment to surgical have been described in the treatment of KD. However, none of the treatment methods was accepted as standard [11]. Immobilization and antiinflammatory drug therapy are recommended at the early stage [12]. For the conservative treatment of KD, immobilization with splinting or casting and activity modification can be used [4,13,14]. If this therapy is unsuccessful, joint leveling technique should be considered [15,16].

Although KD is a very rare disease of the lunate, one of the carpal bones, emergency physicians should consider KD in those patients who were admitted to the ED with complaints of pain, swelling and limitation of motion of the wrist. An overlooked diagnosis or misdiagnosis may lead to bony ischemia, necrosis and ultimately collapse of the bone.

References

1. Laframboise MA, Gringmuth R, Greenwood C. Kienbock's disease in a varsity football player: a case report and review of the literature. J Can Chiropr Assoc. 2012;56:275.
2. Kienböck R. Concerning traumatic malacia of the lunate and its consequences: degeneration and compression fractures. Clin Orthop. 1980;149:4-8.
3. Omor Y, Nassar I, Ajana A, Moatassimbillah N. Kienböck's disease: a case report. Pan Afr Med J. 2015;22:246.
4. Schuind F, Eslami S, Ledoux P. Kienböck's disease. Bone Joint J. 2008;90:133-9.
5. Keith PP, Nuttall D, Trail I. Long-term outcome of nonsurgically managed Kienböck's disease. J Hand Surg Am. 2004;29:63-7.
6. Dias JJ, Lunn P. Ten questions on Kienböck's disease of the lunate. J Hand Surg. 2010;35:538-43.
7. Arnaiz J, Piedra T, Cerezal L, et al. Imaging of Kienböck disease. Am J Roentgenol. 2014;203:131-9.
8. Rizzo M, Urbaniak J. Osteonecrosis, Kelley's textbook of rheumatology, Elsevier Saunders, Philadelphia; 2005. p.1812-28.
9. Özcanlı H, AB Y. Kienböck hastalığı. Acta Orthop. Traumatol. Turc. 2010;9:35-40.
10. Luo J, Diao E. Kienböck's disease: an approach to treatment. Hand Clin. 2006;22:465-73.
11. Karalezli N, Karalezli K, Iltar S, Uz A, Esmer AF, Demirtaş M, ve ark. Anchovy from Wrist Extansors in Resection Artroplasty for Kienböck's Disease Treatment. Gulhane Med J. 2004; 46(2):125-128.
12. Garcia-Elias M, Vidal A. Kienböck's disease. Curr Orthop Pract. 1997;11:28-35.
13. Freedman DM, Botte MJ, Gelberman RH. Vascularity of the Carpus. Clin Orthop Relat Res. 2001;383:47-59.
14. Van den Dungen S, Dury M, Foucher G, Braun FM, Lorea P. Conservative treatment versus scaphotrapeziotrapezoid arthrodesis for Kienbock's disease. Chir Main. 2006;25:141-5.
15. Innes L, Strauch RJ. Systematic review of the treatment of Kienböck's disease in its early and late stages. J Hand Surg. 2010;35:713-7.
16. Delaere O, Dury M, Molderez A, Foucher G. Conservative versus operative treatment for Kienböck's disease: a retrospective study. J Hand Surg. 1998;23:33-6.

J Surg Med. 2018;2(3):389-390.
DOI: 10.28982/josam.426336

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Bilateral giant styloid process: Case report

Bilateral dev styloid çıkıntı: Olgu sunumu

Burak Kersin [1], Ahmet Mahmut Tekin [2]

[1] Department of Otolaryngology, Head and Neck Surgery, Marmara University Istanbul, Turkey
[2] Department of Otolaryngology, Head and Neck Surgery, Bilecik State Hospital, Bilecik, Turkey

ORCID ID of the authors
BK: 0000-0002-9644-4583
AMT: 0000-0003-1604-3382

Abstract
Eagle's syndrome occurs when an elongated styloid process or calcified stylohyoid ligament causes recurrent foreign body sensation or sore throat, neck pain, swallowing difficulty or facial pain. Also, throat pain may radiate to the ipsilateral ear. The treatment of Eagle's syndrome is primarily surgical. The elongated styloid process can be excised via intraoral or external cervical approach. A 29-year-old male patient with bilateral, extremely elongated styloid processes, causing the symptoms of Eagle's syndrome reported with the relevant literature review.
Keywords: Giant styloid process, Bilateral, Eagle syndrome

Öz
Eagle sendromu uzamış bir styloid çıkıntı veya kalsifiye stylohyoid ligamanın tekrarlayan yabancı cisim hissi veya boğaz ağrısı, boyun ağrısı, yutma güçlüğü veya yüz ağrısına neden olduğu durumlarda ortaya çıkar. Ayrıca boğaz ağrısı aynı taraftaki kulağa yansıyabilir. Eagle sendromu'nun tedavisi öncelikle cerrahidir. Uzamış styloid proses intraoral veya eksternal servikal yaklaşımla eksize edilebilir. İki taraflı, aşırı uzamış styloid prosesleri olan ve Eagle sendromu'na neden olan 29 yaşında erkek hasta, ilgili literatür taraması ile bildirildi.
Anahtar kelimeler: Dev stiloid çıkıntı, Bilateral, Eagle sendromu

Introduction

Eagle's syndrome is defined as symptomatic prolongation of the styloid process (SP) or calcification of the stylohyoid and stylomandibular ligament [1]. Symptomatology, clinical, radiological diagnosis and treatment related to elongated styloid process were first described by WW Eagle in 1937 [2]. Eagle has reported that the styloid process is long in 4 out of every 100 patients as a result of various studies. However, only 4% of these cases are symptomatic [3].

The stylohyoid complex consists of the styloid process, the stylohyoid ligament, and the small horn of the hyoid bone. Embryologically, these structures, especially the styloid process, develop from the second branchial arch, Reichert cartilage [4]. Eagle's syndrome can be referred to us with non-specific complaints such as sore throat, earache, foreign body sensation in the throat. Symptoms that cause us to suspect Eagle's syndrome include persistant sore throat during swallowing, chewing, head rotation and tongue movements [5].

We aim to present our case, which is bilateral longest styloid process in the literature and long enough to be articulated with hyoid bone, due to this feature, we think it will contribute to the literature.

Case presentation

A twenty nine-year-old male patient was admitted to our hospital with a feeling of stinging on the right side of his neck for about 6 months and a constant need for swallowing. The patient had no symptoms of weight loss, hoarseness, breathing problems and reflux complaints. No characteristics were found in the personal and family history but he was a cage fighter as a hobby. There were no pathological findings in the nose, ear and oropharynx examination. Stiffness and sensitivity were determined in the right tonsil region by palpation. Endoscopic nasopharynx, tongue base, hypopharynx and laryngeal examination did not show pathological findings. Neck ultrasonography revealed no pathology. With these findings in order to support the diagnosis of possible Eagle syndrome, neck tomography and 3D reconstruction were requested. There was significant prolongation in both styloid processes (right 83 mm, left 80 mm) and extending to the hyoid bone (Figure 1, 2).

Corresponding author / Sorumlu yazar:
Burak Kersin
Address / Adres: Fevzi Çakmak Mahallesi, Muhsin Yazıcıoğlu Cd, No:10, 34899, Pendik, Istanbul, Türkiye
e-Mail: bkersin@hotmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 23.05.2018
Accepted / Kabul tarihi: 09.07.2018
Published / Yayın tarihi: 11.07.2018

How to cite / Atıf için: Kersin B, Tekin AM. Bilateral Giant Styloid Process: Case report. J Surg Med. 2018;2(3):389-390.

Figure 1: Lateral view of Eagle syndrome in 3D computerized tomography

Figure 2: Anterior view of Eagle syndrome in 3D computerized tomography

The operation was recommended the patient through the oral route, if necessary, also external approach from the neck. However, when the patient did not accept the operation, analgesic and anti-inflammatory treatment was given and it was suggested to avoid neck trauma.

Discussion

Eagle syndrome is defined as pain in the face, throat and neck because of the elongated styloid process. Swallowing difficulty, tinnitus and earache are also seen less frequently. Detected symptoms and findings are related to the anatomical relationship between the styloid process and surrounding tissues [5]. We have information about pathogenesis of the Eagle Syndrome that does not go beyond theories. Congenital ossification at the upper part of the stylohyoid ligament and/or lower junction is the suggested mechanism in pathogenesis [6]. In the emergence of pain; fracture in the stylohyoid ligament with a sudden movement, pressure of the elongated styloid process (ESP) on glossopharyngeal nerve, lower branch of the trigeminal nerve and chorda tympani, degeneration and inflammatory changes of the stylohyoid ligament junction, deterioration of circulation by compression of carotid artery with elongated styloid process are thought to be responsible. Syncope attacks or stroke due to carotid artery compression have also been reported [7].

Corell et al. [8] showed that the ESP frequency was determined as 18.2% and 93% of them are bilateral. Symptoms may not be seen despite the presence of ESP radiologically in some patients. Despite the presence of bilateral ESP in computerized tomography, the symptoms were only present on the right side in our case.

In differential diagnosis; cranial nerve neuralgia (glossopharyngeal, trigeminal, etc.), temporomandibular joint diseases, cervical myofascial pain syndrome, chronic tonsillopharyngitis, molar teeth or dental prosthesis problems, pharynx and tongue base tumors should be kept in mind. ESP can be overlooked in patients with these complaints [9].

Surgical excision is the only treatment modality for the relief of symptoms associated with ESP. Eagle described the method of tonsillostylodectomy through the mouth. Stylodectomy can also be performed with the incision of the neck from the mastoid to the hyoid level. The morbidity is higher and the cosmetic results are worse than the intraoral approach. Though ESP is excised in sufficient length, surgical failure is still possible. In 20% of patients, complaints have not been fully resolved and symptoms have been reported to recur [10]. Symptomatic anti-inflammatory drugs can also be used in patients who do not accept surgery as in our case.

Conclusion

Neck, throat, ear, tooth, temporomandibular joint pain; difficulty in swallowing, and feelings of a foreign body in the throat are problems that a physician frequently confronts in daily practice. Although there are other reasons, ESP can be a cause of these complaints. For this reason, palpation of the tonsil region and 3D reconstructed neck tomography should be used in patients with this type of complaints. As in our case, it should be noted that although ESP is usually bilateral, the complaints may be unilateral and very rarely too long to joint with hyoid bone.

References

1. Diamond LH, Cottrell DA, Hunter MJ, Papageorge M. J Oral Maxillofac Surg. 2001;59:1420-6.
2. Eagle WW. Elongated styloid process: Report of 2 cases. Arch Otolaryngol. 1937;25:584.
3. Beder E, Ozgursoy OB, Karatayli Ozgursoy S, Anado¬lu Y. Three dimensional computed tomography and sur¬gical treatment for Eagle's syndrome. Ear Nose Throat J. 2006;85(7):443-5.
4. Fini G, Gasparini G, Filippini F, Becelli R, Marcotullio D. The long styloid process syndrome or Eagle's syndrome. J Craniomaxillofac Surg. 2000;28:123-7.
5. Gözil R, Yener N, Calgüner E, Araç M, Tunç E, Bahcelioğlu M. Morphological characteristics of styloid process evaluated by computerized axial tomography. Ann Anat. 2001;183:527-35.
6. Strauss M, Zohar Y, Laurian N. Elongated styloid process syndrome: intraoral versus external aproach for styloid surgery. Laryngoscope. 1985; 976-9.
7. Chuang WC, Short JH, McKinney AM, Anker L, Knoll B, McKinney ZJ. Reversible left hemispheric ischemia secondary to carotid compression in Eagle syndrome: surgical and CT angiographic correlation. Am J Neuroradiology. 2007;28:143-5.
8. Correll RW, Jensen JL, Taylor JB, Rhyne RR. Mineralization of the stylohyoid–stylomandibular ligament complex. Oral Surg Oral Med Oral Pathology. 1979;48:286–91.
9. Kasapoğlu F, Erişen L. Eagle sendromu: Bir olgunun pre, per ve postoperatif görüntüleri. Turk Arch Otolaryngology. 2009;47(3):147-50.
10. Chase DC, Zarmen A, Bigelow WC, McCoy JM. Eagle's syndrome: a comparison of intraoral versus extraoral surgical approaches. Oral Surg Oral Med Oral Pathology. 1986;62(6):625-9.

J Surg Med. 2018;2(3):391-395.
DOI: 10.28982/josam.430299

Case report
Olgu sunumu

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Ocular retinoblastoma and neuroblastoma: A cytological impression

Oküler Retinoblastom ve neuroblastoma: Bir sitolojik izlenim

Kafil Akhtar [1], Binjul Juneja [1], Sadaf Haiyat [1], Abdul Waris [1]

[1] Department of Pathology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, India

ORCID ID of the authors
KA: 0000-0002-3482-1195
BJ: 0000-0002-7804-8800
SH: 0000-0002-7552-0110
AW: 0000-0002-9569-4468

Corresponding author / Sorumlu yazar:
Kafil Akhtar
Address / Adres: Department of Pathology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, India
e-Mail: kafil_akhtar@yahoo.com

Informed Consent: The author stated that the written consent was obtained from the patients presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastalardan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 04.06.2018
Accepted / Kabul tarihi: 27.06.2018
Published / Yayın tarihi: 14.07.2018

Abstract
Small-round-blue-cell tumor (SRBCT) or a small-round-cell tumor (SRCT) is a group of malignant neoplasms which are seen more often in children (0-20 years-old) than in adults. They generally include Ewing's sarcoma, peripheral neuroectodermal tumor (PNET), rhabdomyosarcoma, synovial sarcoma, non-Hodgkin's lymphoma, retinoblastoma, neuroblastoma, hepatoblastoma, and nephroblastoma or Wilms' tumor as differential diagnoses of small round cell tumors. They have a characteristic appearance consisting of small round cells that stain blue on Hematoxylin and Eosin stained sections. They typically represent undifferentiated cells which are composed of primitive cells with minimal or no differentiation. Accurate diagnosis of these cancers is essential because the treatment options, responses to therapy and prognoses vary widely depending on the diagnosis. A multimodal approach is employed with fine needle aspiration cytology (FNAC) as an important modality of diagnosis for these tumors. We will discuss ocular retinoblastoma and neuroblastoma in our case series which were diagnosed on fine needle aspiration itself and were later confirmed on histopathological examination. This study was also undertaken to determine the utility and safety of intraocular FNAC as a supportive diagnostic tool where clinical features and imaging were found to be inconclusive.
Keywords: Fine needle aspiration cytology, Immunohistochemistry, Malignant small round cell tumors, Neuroblastoma, Ocular, Retinoblastoma

Öz
Küçük-yuvarlak-mavi hücreli tümör (SRBCT) veya küçük-yuvarlak hücreli tümör (SRCT), çocuklarda (0-20 yaş) yetişkinlerden daha sık görülen bir malign neoplazm grubudur. Bunlar genellikle küçük yuvarlak hücreli tümörlerin ayırıcı tanısı olarak Ewing sarkoması, periferik nöroektodermal tümör (PNET), rabdomiyosarkom, sinovyal sarkom, non-Hodgkin lenfoma, retinoblastoma, nöroblastoma, hepatoblastoma ve nefroblastom veya Wilms tümörünü içerir. Haematoksilen ve Eosin ile boyanmış kesitler üzerinde mavi leke veren küçük yuvarlak hücrelerden oluşan karakteristik bir görünüme sahiptirler. Bunlar tipik olarak minimal veya hiç farklılaşma ile ilkel hücrelerden oluşan farklılaşmamış hücreleri temsil ederler. Bu kanserlerin doğru teşhisi önemlidir çünkü tedavi seçenekleri, tedaviye yanıtlar ve prognozlar tanıya bağlı olarak geniş çapta değişir. Bu tümörlerin önemli bir modalitesi olarak ince iğne aspirasyon sitolojisi (FNAC) ile multimodal bir yaklaşım uygulanmaktadır. Olgu serimizde ince iğne aspirasyonu tanısı konan ve daha sonra histopatolojik incelemede doğrulanan oküler retinoblastom ve nöroblastoma tartışılacaktır. Bu çalışma, klinik özelliklerin ve görüntülemenin sonuçsuz olduğu tespit edilen destekleyici bir tanı aracı olarak intraoküler FNAC'ın kullanımını ve güvenliğini belirlemek için yapılmıştır.
Anahtar kelimeler: İnce iğne aspirasyon sitolojisi, İmmünhistokimya, Malign küçük yuvarlak hücreli tümörler, Nöroblastoma, Oküler, Retinoblastom

Introduction

Small round blue cell tumors of childhood include neuroblastoma, Retinoblastoma, rhabdomyosarcoma, non-Hodgkin's lymphoma, Ewing's sarcoma and the closely related primitive neuroectodermal tumor (PNET) and the blastemic component of Wilms' tumor. The histologic overlap of small round cell tumors is a challenge to the surgical pathologist. These tumors are characterized both cytologically and histologically by a predominantly small round to oval and relatively undifferentiated cells. The disparity in treatment modalities and clinical outcome in the different subsets of SBRCTs makes the correct diagnosis crucial [1,2].

How to cite / Atıf için: Akhtar K, Juneja B, Haiyat S, Waris A. Ocular retinoblastoma and neuroblastoma: A cytological impression. J Surg Med. 2018;2(3):391-395.

Retinoblastoma is the most common primary malignant intraocular tumor in children that develops from the immature cells of the retina which are the light-detecting cells of the eye. Children with retinoblastoma have a hereditary genetic defect associated with retinoblastoma, in other cases it is caused by a congenital mutation in the chromosome 13 gene, 13q14 [1]. It is almost exclusively found in young children with mean age of 5 years. It equally affects both the sex and the tumor has no predilection for left or right eye. Most common presentation is leucocoria with typically white papillary reflex (amaurotic cat's eye reflex) or proptosis in late stages of the disease in some developing countries as classic manifestation [2]. Other clinical features are strabismus, uveitis, hyphema, red eye, secondary glaucoma, panophthalmitis and orbital cellulitis [3]. It is necessary to differentiate retinoblastoma from pseudoretinoblastomas presenting with similar ocular conditions. Although, in rare circumstances pseudoretinoblastoma and retinoblastoma can coexist in a patient [4]. There are very few studies on the safety and efficacy of diagnostic FNAC in RB cases due to the risk of tumor dissemination and extraoccular spread associated with the procedure [5]. As a less invasive procedure, fine needle aspiration (FNA) cytology has a definite advantage over surgical excision to arrive at a tissue diagnosis before initiation of therapy.

Neuroblastoma is an infrequent tumor of childhood, usually located at any site containing neural tissue specifically immature cells of sympathetic nervous system - retroperitoneum and adrenal gland are the most common locations followed by thoracopulmonary region, mediastinum, head and neck, and pelvis. The symptoms vary depending on the location of the tumor. More than 50% of the cases present with signs and symptoms of metastatic disease. Children with metastasis to retrobulbar region present with proptosis [6,7]. In neuroblastoma, the raccoon eye appearance is due to obstruction of the palpebral vessels that are branches of ophthalmic and facial vessels by the tumor tissue in and around the orbit [8].

Case presentation

Case 1

A 4-year-old boy presented to the Ophthalmic clinic with a history of leucocoria in the right eye. On ophthalmological examination, visual acuity was absence of light perception in the affected eye. Fundus details could not be visualized due to advanced disease. The left eye was within normal limits. Imaging features on B-scan ultrasonography, CT scan and MRI of the orbit was inconclusive, but retinoblastoma could not be ruled out. Possible differentials were Coats' disease, endogenous endophthalmitis and retinoblastoma. To establish the diagnosis, intraocular FNAC was planned after taking an informed consent under general anesthesia. A 26-G needle mounted on a 5 ml syringe was introduced through the conjunctiva and the sclera into the intraocular mass. Careful controlled aspiration was done and cryotherapy was applied at the site of entry after the needle was withdrawn. The puncture fluid was very thick with a significant amount of white floccular exudates, as shown by the slit-lamp examination. Smears were prepared from the aspirated material and stained by Hematoxylin and Eosin stain. Cytology revealed a malignant round cell tumor, with round to oval, small and uniform cells, with scanty cytoplasm; in closely packed clusters of variable sizes, compatible with retinoblastoma (Figure 1). Enucleation surgery was performed. Histopathologic findings in enucleated eyes were consistent with the diagnosis of retinoblastoma showing the tumor composed of undifferentiated cells along dilated blood vessels with a large ischemic necrosis around it. Homer-Wright rosettes were present. Immunohistochemical staining showed cytoplasmic positivity with synaptophysin in the tumor cells. The child was followed-up for ophthalmic and systemic evaluation for 6 months with no evidence of local recurrence or systemic metastasis.

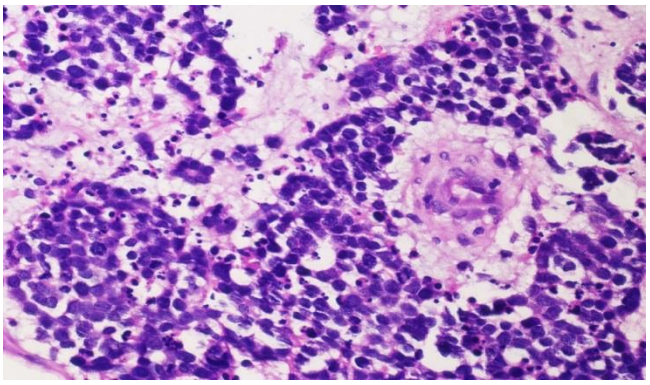


Figure 1: Retinoblastoma: Cytology revealed a malignant round cell tumor, with round to oval, small and uniform cells, with scanty cytoplasm, in closely packed clusters of variable sizes. Hematoxylin and Eosin x 40X.

Case 2

A 3-year-old female child presented to the Ophthalmic clinic with rapid onset of proptosis of the right eye. On ocular examination, she had proptosis of 29 mm with lid edema and ciliary congestion with total restriction of extraocular movements. There was a 1.5 cm × 1 cm firm nodule on the sclera with foci of hemorrhage. The anterior chamber was filled with exudate. The intraocular pressure was raised to 27.1 mm Hg in the right eye by schiotz tonometry. On general examination, the child was febrile. There was no palpable abdominal mass. The chest was clear and the cardiovascular system was normal. Computed tomography of orbit and brain revealed a 5 cm × 3.5 cm × 2.0 cm heterogenous mass filling the right orbit with areas of coarse calcification. The optic nerve was encased within the mass with perineural spread up to optic chiasma, with thinning of the floor of the orbit. Based on the tomography findings, retinoblastoma was suspected. Fine needle aspiration cytology of the mass showed varying numbers of small primitive cells with scanty cytoplasm, poorly to well-formed pseudorosettes, cell processes and a fibrillary matrix (Figure 2).

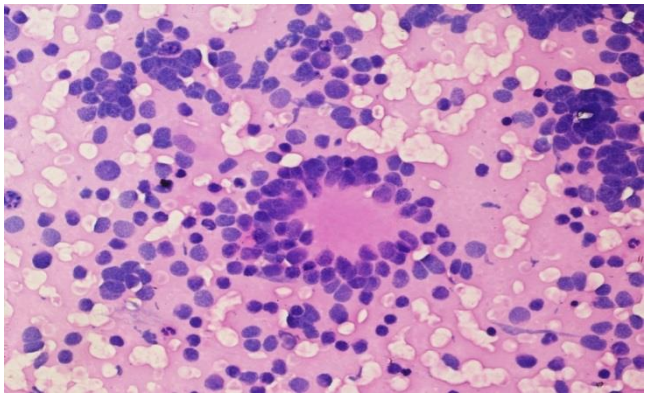


Figure 2: Neuroblastoma: Fine needle aspiration cytology of the mass showed varying numbers of small primitive cells with scanty cytoplasm, poorly to well-formed pseudorosettes, cell processes and a fibrillary matrix. Hematoxylin and Eosin x 40X.

Histopathological examination of incisional biopsy of orbital mass showed small round tumor cells in sheets separated by incomplete fibrous septa under low power. Examination at higher magnification revealed round to polygonal cells with high nucleocytoplasmic ratio, palisading of nuclei, and delicate cytoplasmic processes. Few foci with central fibrillary material with tumor cells around giving vague appearance of rosettes (Homer Wright) were seen. Immunohistochemistry was positive for neuron specific enolase and chromogranin and negative for both epithelial membrane antigen (EMA) and cytokeratin AE1/AE3, suggestive of neuroblastoma.

Discussion

Irrespective of the age and site, four common types of round cell tumors are Hematopoietic: lymphoma and leukemia, Neuroblastoma, Rhabdomyosarcoma and Ewing's sarcoma. Types of small cell tumors occurring primarily in bone are poorly differentiated chordoma, melanotic neuroectodermal tumor, mesenchymal chondrosarcoma and small cell osteosarcoma. Those occurring mostly in specific sites include desmoplastic small round cell tumor, germ cell tumors, NUT translocation carcinoma. Some of the organ-specific blastomas are Wilm's tumor (nephroblastoma), Hepatoblastoma, Sialoblastoma, pancreatoblastoma, pleuropulmonary blastoma.

Several genetic factors have also been proposed such as constitutional mutations, deletions, single nucleotide substitutions (truncated protein), Epigenetic factors like Loss of imprinting, Loss of heterozygosity, Methylation, Histone acetylation, sRNAs, siRNAs.

Retinoblastoma is a neuroectodermal tumor of primitive cells of retina. A "benign" variant of retinoblastoma is known as retinoma or retinocytoma which is a differentiated tumor with no growth potential. It is the commonest intraocular malignancy in children. More than 90% of cases are diagnosed before the age of 5 years with the average age of diagnosis at 1 year in bilateral cases and 2 years unilateral cases [9]. The presentation of retinoblastoma in adults is extremely rare [10]. In adults, it always present with atypical manifestations such as decreased vision, floaters, and pain. It rarely presents with classic manifestations [11].

Retinoblastoma gene was the first tumor suppressor gene identified, a recessive gene located on chromosome 13q and thus both the genes must be inactivated before their functional derangement. Retinoblastoma gene produces Rb protein which can be inactivated by mutation or deletion, thus leading to loss of cell cycle control and genomic instability.

Clinical presentation and indirect ophthalmoscopic examination are insufficient for the diagnosis. CT scan is still the study of choice in the diagnosis of retinoblastoma showing intraocular calcification, but when MRI is available it should be performed for better differentiation from lesions such as Coat's disease. In doubtful cases, FNAC is performed. Cytological smears show predominantly discrete population of small round cells with occasional rosette- like structures as Flexner-wintersteiner rosettes and homer wright rosettes. Flexner-Wintersteiner rosettes are seen as cells around the lumen whereas in case of Homer-Wright rosettes, the cells are arranged around cobweb-like material. The nuclei are round, monomorphic and hyperchromatic with fine nuclear chromatin. Occasional prominent nucleoli are also seen. The distinct cytological features of retinoblastoma are tight cohesion and nuclear molding among the tumor cells.

Grossly, retinoblastomas are usually creamy white with chalky areas of calcification and yellowish necrotic regions. They may grow inward toward the vitreous cavity (endophytic retinoblastoma) presenting as one or more isolated or coalesced tumors of variable size or may grow outward towards the choroid (exophytic retinoblastoma)causing retinal detachment, or in a mixed pattern. Thus, vitreous and subretinal seeding along with calcifications are virtually pathognomonic of retinoblastoma. Rarely, retinoblastomas thicken the retina diffusely without forming a discrete mass (diffusely infiltrative retinoblastoma). Whereas retinocytoma (retinoma) is characterized by homogenous, more or less translucent greyish masses, calcifications, with pigment migration and proliferation bordering the tumor with spontaneous remission. Tumor may invade the optic nerve and extend along it towards the brain or individual neoplastic cells may reach the CSF by penetrating into the subarachnoid space surrounding the optic nerve. Thus, the resection margin of optic nerve in an enucleated eye should be given careful attention [10].

Retinoblastomas infrequently spread extraocularly through sclera channels that contain blood vessels and nerves (emissarial canals), but the spread mainly occurs through the optic nerve and choroid. A risk of trilateral involvement is seen in the hereditary form of retinoblastoma. There is association of retinoblastoma, usually bilateral (90%) but not exclusively, with an intracranial neuroblastic tumor commonly in the region of the pineal gland (pinealoblastoma). Since these cells are being linked to the RB1 gene and of the same phylogenic origin as retinal tissues. Under the St. Jude's staging system, intraocular retinoblastoma is classified into four stages: Stage I: the tumor is confined to the retina. Stage II: it is confined to the eyeball. Stage III: the cancer has spread to areas in the region around the eye. Stage IV: the cancer has spread through the optic nerve to the brain, or through the blood to soft tissues, bone, or lymph nodes [11].

Persistent hyperplastic primary vitreous (PHPV) and Coats' disease are the most common conditions (benign) to mimic retinoblastoma. Coats' disease also known as primary (congenital) retinal telangiectasia is a rare non hereditary probably congenital exudative retinopathy. The exudates are responsible for a luminous leukocoria but in the presence of retinal detachment, it takes on a greyer hue. Clinically, coat's disease shows three major features: retinal telangiectasia in the form of strings of fusiform dilatations of the retinal vessels; massive yellowish exudates within and underlying an edematous retina, sometimes giving a pseudo-tumoral appearance; exudative, sometimes leading to total retinal detachment.

PHPV is a non-hereditary, congenital malformation. Normally, regression of the embryonic vascular connective tissue (hyaloid artery, vasa hyaloidea propria, tunica vasculosa lentis) occurs after 4 months of gestation. The arrest of this normal regression leads to PHPV. It is almost always unilateral often presenting with moderate microphthalmia and other associated

malformations such as failure of cleavage of the anterior segment or uveal coloboma.

Retinoblastoma should also be differentiated from various small round cell tumors, such as lymphoma or leukemia and metastatic neuroblastoma involving the orbit. Fundus examination does not enable diagnosis to be made with certainty. Ultrasonography is the next method of choice which is an inexpensive and is highly specific means of detecting the calcifications [12]. Other methods of diagnosis include ocular coherence topography (commonly used for macular lesions) and CT scan (involves X rays and thus is potentially dangerous). Immunocytochemistry is helpful in the differential diagnosis of small blue round cell tumors [13]. Treatment strategies aim to salvage the eye and preserve vision. Currently, the methods available for treatment include laser treatment, cryotherapy, radiotherapy, chemotherapy and enucleation. Enucleation is the treatment of choice for advanced uniocular retinoblastoma or the worse eye in bilateral cases [12].

Neuroblastoma is an undifferentiated malignant tumor of the primitive neuroblasts. Neuroblastoma is a pediatric neoplasm which is the most common cancer diagnosed during infancy [13]. It represents second most common orbital tumor in children after rhabdomyosarcoma. It arises from the sympathetic system and ganglia and represents the peripheral nervous system counter part of retinoblastoma. Neuroblastoma occurs primarily in abdomen in 60% cases but in only 8% cases the tumor arises in the orbit from ciliary ganglion [14]. Most of the cases are reported before the age of 4 years.

Neuroblastoma commonly spreads via lymphatics to regional lymph nodes, often in the para-aortic chain, and less commonly to the next echelon of lymphatics, such as the left supraclavicular fossa (Virchow node) in patients with abdominal tumors. Hematogenous spread often occurs to bone marrow, bone, and liver. Neuroblastoma appears to have a proclivity for the bones of the skull and especially the posterior orbit, which can cause the clinical presentation of “raccoon eyes” from periorbital ecchymosis within three months after diagnosis. 40% of orbital metastasis is bilateral. Other possible ophthalmic manifestations of metastatic neuroblastomas are Horner's syndrome, papilledema, retinal striae, anisocoria, nystagmus and cranial nerve paralysis.

The typical neuroblastoma is composed of small, uniform cells containing dense, hyperchromatic nuclei and scant cytoplasm. The presence of neuritic processes (neuropil) is pathognomonic. Numerous markers have been used for the diagnosis of neuroblastomas including NE markers, cytoskeletal proteins, catecholamine-synthesizing enzymes, and neuroblastoma-“specific” antibodies (such as NB84, that is raised to neuroblastoma cells) to differentiate from common possible differentials such as desmoplastic small round cell tumor, Ewing’s sarcoma/primitive neuroectodermal tumor, rhabdomyosarcoma, ganglioneuroblastoma [15].

Desmoplastic small round cell tumors grow and spread uninhibited within the abdominal cavity. First symptoms of the disease often include abdominal distention, abdominal mass, abdominal or back pain, gastrointestinal obstruction, lack of appetite. They reveal well circumscribed solid tumor nodules with areas of central necrosis within a dense desmoplastic stroma. Cells have hyperchromatic nuclei with increased nuclear/cytoplasmic ratio. On immunohistochemistry, these cells have trilinear coexpression- epithelial marker cytokeratin, the mesenchymal markers- desmin, vimentin and the neuronal marker- neuron-specific enolase. A multi-modality approach of high-dose chemotherapy, aggressive surgical resection, radiation, and stem cell rescue improves survival for some patients but prognosis remains poor [16,17].

Rhabdomyosarcomas (RMS) of the orbit are usually found in children. Majority of these tumors are of the embryonal followed by alveolar subtype developing from primitive mesenchymal cells that go on to differentiate into striated muscle cells. They are found in the orbit, eyelid, conjunctiva and uveal tract [18]. Orbital RMS should be considered in the differential diagnosis of any child with a progressive unilateral proptosis [18].These tumors typically present with a rapid enlarging mass, often in the upper inner quadrant of orbit. It is usually painless but causes proptosis and diplopia. Often the mass invades the eyelid causing marked edema. CT scan shows homogeneous soft tissue masses isodense to normal muscle. The mainstay of treatment is a combination of radiotherapy and chemotherapy.

Ewing's sarcoma rarely occurs in children under 5 years and the peak incidence is between 10 and 15 years. Earlier it was thought that Ewing's sarcoma only occurred in the bone, however other tumors were found within the soft tissues and is thought to be similar microscopically. These include extraosseous Ewing's sarcoma and peripheral primitive neuroectodermal tumor (PNET) and are now grouped together as the Ewing's sarcoma family of tumors. They primarily occur in non head and neck sites. Only 2-10% develops in head and neck sites, most commonly involving skull and jaw, other less common sites includes the sinonasal tract, orbit and various mucosal sites. There is reciprocal translocation between chromosome 11(FLI1 gene) and chromosome 22(EWSR1 gene). HPE shows uniform small cells with round to oval nuclei, fine chromatin (powdery) with pale to clear cytoplasm and indistinct cell borders. These tumors give diastase sensitive PAS positive reaction and express CD99. Prognosis depends on the extent of the disease at initial presentation, size of the tumor and response to therapy [19].

Ganglioneuroblastomas are neuroectodermal in origin and is the fourth most common tumor in childhood within first 4 years of life. They occur anywhere in anatomic distribution of sympathoadrenal neuroendocrine system. They behave in a benign fashion are composed primarily of mature ganglion cells, neuropil, and Schwann cells. Ganglioneuroblastomas have histopathologic characteristics of both neuroblastomas and ganglioneuromas [20].

Conclusions

Accurate diagnosis of pediatric small round cell tumors has become crucial, as disparate approaches to therapy are used for distinct tumor types. Immunohistochemistry can be helpful in narrowing the differential diagnosis of small-round-cell tumors. Despite recent advances in immunohistochemistry and molecular pathology, some cases of small-round-cell tumors of childhood remain diagnostically problematic.

Acknowledgements

The technicians of Cytopathology Lab.

References

1. Odogu V, Udoye E, Azonobi IR. Retinoblastoma in a 12 year old girl: a case report. Int J Med Res Health Sci. 2014;3(2):441-4.
2. Zhao J, Li S, Shi J, Wang N. Clinical presentation and group classification of newly diagnosed intraocular retinoblastoma in China. Br J Ophthal. 2011;95(10):1372-5.
3. Ayotunde A, Effiong A and Bolutife O. Retinoblastoma presenting with a cheek mass. J Nat Med Assoc. 2005;97(11):1553-5.
4. Shields CL, Schoenberg E, Kocher K, Shukla SY, Kaliki S, Shields JA. Lesions simulating retinoblastoma (pseudoretinoblastoma) in 604 cases. Am Acad of Ophthal. 2013;120(2):311-6.
5. Chawla B, Tomar A, Sen S, Bajaj MS, Kashyap S. Intraocular fine needle aspiration cytology as a diagnostic modality for retinoblastoma. Int J Ophthal. 2016;9(8):1233-5.
6. Timmerman R. Raccoon eye and neuroblastoma. N Eng J Med. 2003;4:349-50.
7. Ahmed S, Goel S, Khandwala M, Agrawal A, Simmons IG. Neuroblastoma with orbital metastasis: ophthalmic presentation and role of ophthalmologists. Eye. 2006;20:466-70.
8. Rakesh K, Binay R, Manjul V. Neuroblastoma with eye involvement. J Paed Oncol. 2013;10(5):25-6.
9. Aerts I, Lumbroso-Le Rouic L, Gauthier-Villars M, Brisse H, Doz F, Desjardins L. Retinoblastoma. Orphanet J Rare Dis. 2006;1(8):31-2.
10. Karcioglu ZA, Abboud EB, Al-Mesfer SA, Al-Rashed W, Pilapil DH. Retinoblastoma in older children. J Am Assoc Paed Ophthal and Strabismus. 2002;6(1):26-32.
11. Zhang Z, Shi JT, Wang NL and Ma JM. Retinoblastoma in a young adult mimicking coat's disease. Int J Ophthal. 2012;5(5):625-9.
12. Parulekar MV. Retinoblastoma - current treatment and future direction. Early Hum Dev. 2010;86(10):619-25.
13. Zhang N and Lin LK. Presumed primary orbital neuroblastoma in a 20 month old female. Ophthal Plast Reconstr Surg. 2010;26(5):383-5.
14. Sofi RA, Khanday SB, Keng MQ, Wani JS, Goel A, Shafi T. A case of primary orbital neuroblastoma. Int J Case Reports and Images. 2012;3(3):16-8.
15. Talarico F, Iusco D, Negri L, Belinelli D. Combined resection and multi agent adjuvant chemotherapy for intra-abdominal desmoplastic small round cell tumor: case report and review of literature. G Chir. 2007;28(10):367-70.
16. Lal DR, Su WT, Wolden SL, Loh KC, Modak S, La Quaglia MP. "Results of multimodal treatment for desmoplastic small round cell tumors". J Paed Surg. 2005;40(1):251-5.
17. Shields CL, Shields JA, Honavar SG, Demirci H.Clinical spectrum of primary ophthalmic rhab-domyosarcoma. Ophthal. 2001;108(12):2284-92.
18. Zareifar S, Abdolkarimi B, Ashraf MJ, Kamali K. Bilateral intraocular rhabdomyosarcoma: A Case Report. Mid East J Cancer. 2016;7(2):93-5.
19. Saral SD and Nirmala AJ. Pathology of Ewing's sarcoma/PNET: Current opinion and emerging concepts. Ind J Orthop. 2010;44(4):363-8.
20. Alessi S, Grignani M, Carone L. Ganglioneuroblastoma: Case report and review of the literature. J Ultrasound. 2011;14(2):84-8.

J Surg Med. 2018;2(3):396-398.
DOI: 10.28982/josam.431576

Journal of Surgery and Medicine
e-ISSN: 2602-2079

A case of pancreatic cyst hydatid misdiagnosed as pancreatic cancer

Pankreatik kanser olarak yanlış tanı konan bir pankreatik kist hidatik olgusu

Anas Belhaj [1], Ouazzani Et-Tayeb [1], Zerhouni Ahmed [1], Souiki Tarik [1], Karim Ibn Majdoub Hassani [1], Imane Toughrai [1], Khalid Mazaz [1]

[1] Department of Visceral Surgery B, Hassan II University Hospital, Fez, Morocco

ORCID ID of the authors
AB: 0000-0002-1118-1594
OET: 0000-0003-2977-2904
ZA: 0000-0001-8441-016X
ST: 0000-0002-2416-4355
KIMH: 0000-0002-0421-7296
IT: 0000-0003-0401-3012
KM: 0000-0001-7779-7802

Corresponding author / Sorumlu yazar:
Anas Belhaj
Address / Adres: Department of Visceral Surgery B, Hassan II University Hospital, Fez, Morocco
e-Mail: dr.anasbelhaj@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 07.06.2018
Accepted / Kabul tarihi: 29.06.2018
Published / Yayın tarihi: 14.07.2018

Abstract
Hydatid disease, is a zoonotic infection caused by the Echinococcus parasite, localized especially at the liver, herein we described a case which presented with epigastric pain and Hydatid cyst of the pancreas. 19-year-old female with a history of stage B pancreatitis one month ago presented with epigastric pain, and her physical examination showed an epigastric mass 5 cm in diameter. Abdominal computed tomography showed a pancreatic tumor: Cystadenoma or Cystadenocarcinoma. Magnetic resonance imaging showed a mucinous intra-papillary tumor of the pancreas without signs of degeneration. Echo endoscopy realized talks about an aspect of a pseudo papillary solid tumor of the pancreas or false cyst of the pancreas. Surgery discovered finally a hydatid cyst of the pancreas, then a medial pancreatectomy was performed with anastomosis between the tail of the pancreas and the stomach. In conclusion, hydatid cyst of the pancreas should be considered in the differential diagnosis of cystic lesion of the pancreas, and in some cases surgery remains the only definitive diagnostic and therapeutic tool.
Keywords: Hydatid disease, Pancreas, Medial pancreatectomy

Öz
Hidatik hastalık, özellikle karaciğerde lokalize olan Echinococcus parazitinin neden olduğu zoonotik bir enfeksiyondur. Burada epigastrik ağrı ve pankreasın hidatik kisti ile başvuran bir olguyu tanımladık. Bir ay önce evre B pankreatit öyküsü olan 19 yaşında kadın hasta epigastrik ağrı ile başvurdu ve fizik muayenesinde 5 cm çapında epigastrik kitle saptandı. Abdominal bilgisayarlı tomografide pankreas tümörü görüldü: kistedenom yada kistadenokarsinom. Manyetik rezonans görüntülemede dejenerasyon belirtileri olmaksızın pankreasın intra-papiller tümörüne rastlandı. Eko endoskopi pankreasın pseudo papiller solid tümörünün veya pankreasın yanlış kistinin bir yönüyle ilgili görüşmelerde bulundu. Ameliyat sonunda nihayetinde pankreas kist hidatiği saptandı, daha sonra pankreas ve midenin kuyruğu arasında anastomoz ile medial pankreatektomi yapıldı. Sonuç olarak, pankreasın kistik lezyonunun ayırıcı tanısında pankreasın hidatik kisti düşünülmeli ve bazı olgularda cerrahi tek kesin tanı ve tedavi aracı olarak kalmaktadır.
Anahtar kelimeler: Hidatik hastalık, Pankreas, Medial pankreatektomi

Introduction

Hydatid disease, or echinococcal disease, is a zoonotic infection caused by the Echinococcus parasite, it's endemic to regions where stock-breeding and agriculture are a common occupation, and these include the Mediterranean region, Africa, South America, Australia, Middle East and India. Hydatid cysts are localized especially at the liver (84%), lung (15%–47%), spleen (12%) [1]. But it can be found in all body organs. We describe a case which presented with epigastric pain and cystic pancreatic mass.

Case presentation

Young 19-year-old female housewife, rural resident and having contact with dogs. With a history of stage B pancreatitis one month ago. The clinical symptomatology dates back to 2 years by the occurrence of intermittent epigastric pain which has been aggravated since a month by a permanent character, all evolving in a context of apyrexia and conservation of the general state. The physical examination showed an epigastric mass 5 cm in diameter, painless and mobile. The biological assessment was without particularity in particular negative tumor markers and negative hydatid serology.

Abdominal computed tomography (CT) showed a cystic mass of the body of the multi-localized pancreas measuring 7 cm in diameter with dilation of wirsung at 2.4 cm, this mass is in favor of a pancreatic tumor Cystadenoma or Cystadenocarcinoma (Figure 1).

How to cite / Atıf için: Belhaj A, Et-Tayeb O, Ahmed Z, Tarik S, Hassani KIM, Toughrai I, Mazaz K. A case of pancreatic cyst hydatid misdiagnosed as pancreatic cancer. J Surg Med. 2018;2(3):396-398.

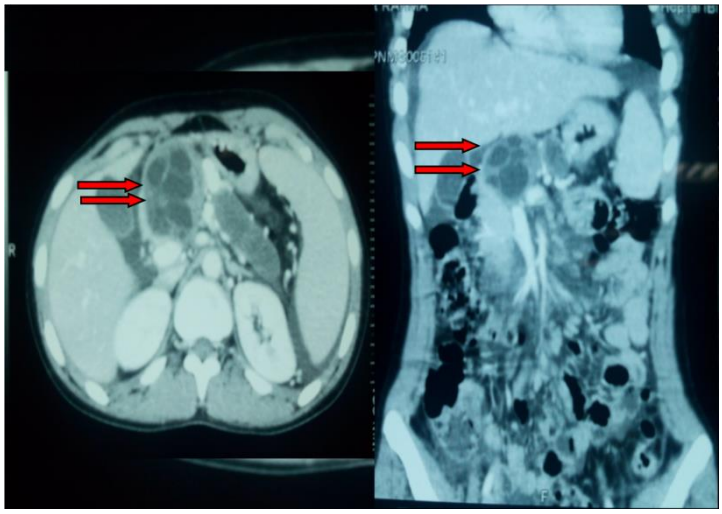


Figure 1: Computed tomography scan shows the hydatid cyst of the pancreas.

On the other hand an abdominal magnetic resonance imaging shows of a mass of the pancreatic isthmus of 5 cm clearly communicating with the wirsung which is dilated at the level of its corporal-caudal part measuring 16 mm of diameter, no fleshy bud either in the mass or in the wirsung this aspect is in favor of a mucinous intra-papillary tumor of the pancreas without signs of degeneration (Figure 2).

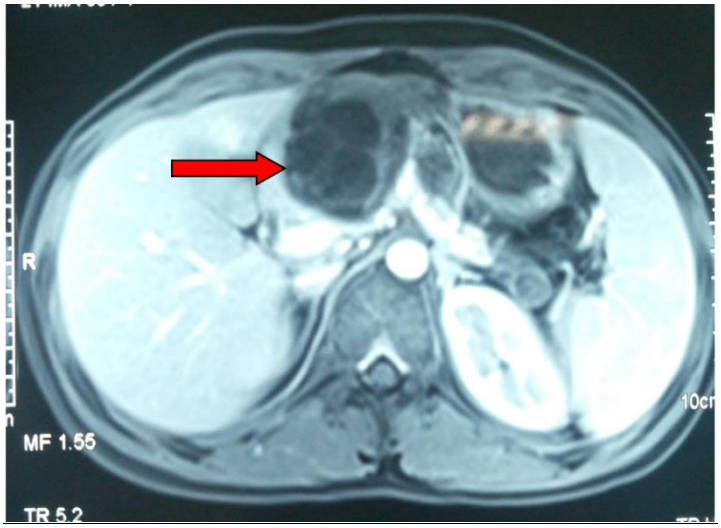


Figure 2: Magnetic resonance imaging of the hydatid cyst occupying the body of the pancreas

In front of the doubt diagnosis an echo endoscopy was realized: aspect in favor of a pseudo papillary solid tumor of the pancreas or false cyst of the pancreas. The patient's file was discussed in multidisciplinary meeting and the decision was a surgical exploration.

Surgical exploration showed the presence of a cystic mass at the expense of the pancreatic isthmus and extending towards the tail of the pancreas, while the head was intact, the dissection showed that the portal vein is taken in the mass. The dissection was at the cost of a wound of the portal vein difficult to control hence the decision to open the mass to quickly control the bleeding. The opening of the mass finally objectified a hydatid cyst type III with vesicles and a cavity that continues with the wirsung duct towards the tail of the pancreas, after bleeding control a medial pancreatectomy with wirsung-to-gastric anastomosis was performed. Drainage by two drains (Figure 3). The evolution was marked by the occurrence of a pancreatic fistula which has dried up.

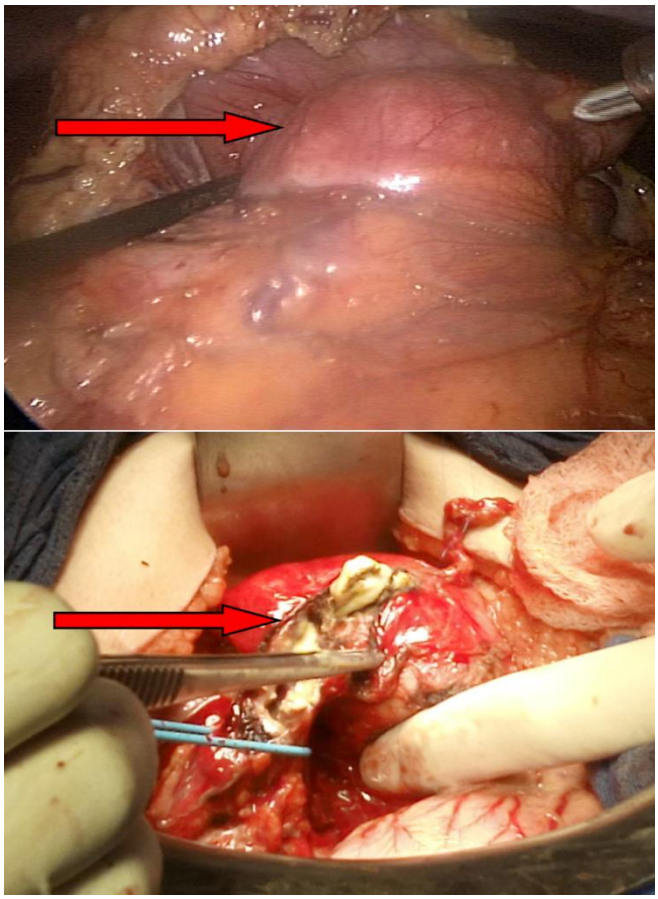


Figure 3: Intraoperative image showing the hydatid cyst and the vesicle outlet after opening.

Discussion

Primary hydatid disease of the pancreas is indeed rare [2]. So the diagnosis of pancreatic hydatid cyst may be a challenge. Usually, hydatid cysts are usually asymptomatic; however, patients may present with abdominal pain, vomiting or complications such as obstructive jaundice or pancreatitis. The Enzyme-Linked Immunosorbent Assay (ELISA) Echinococcus antigens is a useful tool with a global specificity about 85%, which is not always positive in the presence of hydatid cyst. [3]. Definitive diagnosis can be made only at surgery. The differential diagnosis of hydatid cyst of the pancreas includes pseudocyst, serous cystadenoma and mucinous cystic neoplasm. The difference between a hydatid cyst and a cystic lesion of the pancreas must be made.

Abdominal sonography is considered the most sensitive tool detecting the floating membranes, hydatid sand and floating daughter cysts. Water lily sign, water attenuation and calcifications detected by CT scanning are also highly suggestive of hydatid cyst [4]. Endoscopic ultrasound can provide characterization of cystic lesions of the pancreas. While EUS morphology alone has limitations regarding definitive diagnosis fluid aspirates can help in differentiating malignant cystic lesions. Serology is more specific but less sensitive than imagery [5]. The surgical treatment of the pancreatic hydatid cyst depends on its location, as in our case the cyst is located at the level of the body of the pancreas with wide communication with the wirsung so a medial pancreatectomy with pancreatic gastric anastomosis was performed, while the cysts in the body and the head pancreas without communication with the wirsung can be treated by a good evacuation, pericystectomy and omentoplasty.

We conclude that hydatid cyst of the pancreas should be considered in the differential diagnosis of cystic lesion of the pancreas, and in some cases surgery remains the only definitive diagnostic and therapeutic tool.

References

1. Derfoufi O, Ngoh Akwa E, Elmaataoui A, Miss E, Esselmani H, Lyagoubi M, et al. Epidemiological profile of echinococcosis in Morocco from 1980 to 2008. Ann Biol Clin (Paris). 2012 Jul-Aug;70(4):457-61.
2. Masoodi MI, Nabi G, Kumar R, Lone MA, Khan BA, Naseer Al Sayari K. Hydatid cyst of the pancreas: a case report and brief review. Turk J Gastroenterol. 2011 Aug;22(4):430-2.
3. Sorogy ME, El-Hemaly M, Aboelenen A. Pancreatic body hydatid cyst: A case report. Int J Surg Case Rep. 2015;6C:68-70.
4. Masoodi I, Nabi G, Kumar R, Lone MA, Khan BA, Naseer Al Sayari K. Hydatid cyst of the pancreas: a case report and brief review. Turk J Gastroenterol. 2011;22(4):430–2.
5. Babba H, Messedi A, Masmoudi S, et al. Diagnosis of human hydatidosis: comparison between imagery and six serologic techniques. Am J Trop Med Hyg. 1994;50:64-8.

J Surg Med. 2018;2(3):399-400.
DOI: 10.28982/josam.428890

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Occlusion of the small bowel on a virgin abdomen: Case report

Ameliyatsız karın vakasında ince bağırsağın tıkanıklığı: Olgu sunumu

Eddy Oleko Ekuke [1], Meriem Lhaine [1], Hicham El Bouhadoutti [1]

[1] Department of Visceral Surgery, Hassan II University Hospital, Fez, Morocco Hospital, Fez, Morocco

ORCID ID of the authors
EOE: 0000-0003-0381-4870
ML: 0000-0003-2661-6949
HEB: 0000-0001-8881-0101

Abstract
Peritoneal flanges on virgin abdomen are of uncommon etiology of occlusive syndrome. In particular, congenital bridles represent 0.7 to 2% of small bowel and colon occlusions, from all causes. We report a case of a pelvic occlusion in a 22-year-old patient.
Keywords: Occlusion, Virgin abdomen

Öz
Ameliyatsız batındaki peritoneal flanşlar tıkayıcı sendromun nadir bir etiyolojisidir. Özellikle, konjenital bridler, tüm nedenlerden % 0,7 ila % 2 ince bağırsak ve kolon oklüzyonunu temsil eder. Biz 22 yaşında bir hastada pelvik oklüzyon olgusunu sunuyoruz.
Anahtar kelimeler: Oklüzyon, Ameliyatsız karın

Introduction

Acute intestinal obstruction (AIO) can be functional due to peristalsis disorders related to the disruption of the motor nervous system of the intestine, more often paralytic than spasmodic. AOI can also be mechanical by obstruction, necking or strangulation. These last two AOI mechanisms, especially in adults, are most often secondary to postoperative flanges and / or adhesions [1-3].

However, these flanges and adhesions may occur in patients who have no history of laparotomy [4]. In these cases they are either congenital or spontaneous or initial. Congenital flanges and adhesions are due to abnormal adhesion of peritoneal leaflets during embryogenesis or to an abnormality of the omphalo-mesenteric duct [4]. They are said to be spontaneous or initial when they occur in persons who have no history of abdominal surgery or congenital anomalies, nor any other obvious inflammatory site of interest to organs of the abdominal cavity [5].

Case presentation

Patient aged 23 years without significant antecedents pathologies admitted to the emergency for stopping matter without stopping gas accompanied by vomiting all evolving in a context apyrexia and conservation of the general state. Patient's examination revealed stable hemodynamic and respiratory functions and normal colored conjunctiva. The abdominal examination showed no scar laparotomy, abdomen distended, tympanic but flexible.

The hernia orifices were free to rectal touch stool trace. An X-ray of the abdomen without preparation showed typical hydroaeric levels. A realized abdominal computed tomography (CT) which spoke of appearance in favor of a volvulus of the grele with a distension of the grelic handles of upstream reaching 5cm (Figure 1). The patient was operated by median laparotomy with the presence of extensive grelic distension upstream of a flange performing a grelike volvulus (Figure 2). We performed resection carrying the volvated part (Figure 3) with the completion of a manual terminal grelogrelic anastomosis. Patient declared outgoing four days postoperative without complications.

Corresponding author / Sorumlu yazar:
Eddy Oleko Ekuke
Address / Adres: Department of Visceral Surgery, Hassan II University Hospital, Fez, Morocco Hospital, Fez, Morocco
e-Mail: olekoekuke20121982@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 11.06.2018
Accepted / Kabul tarihi: 18.07.2018
Published / Yayın tarihi: 26.07.2018

How to cite / Atıf için: Ekuke EO, Lhaine M, Bouhadoutti HE. Occlusion of the small bowel on a virgin abdomen: Case report. J Surg Med. 2018;2(3):399-400.

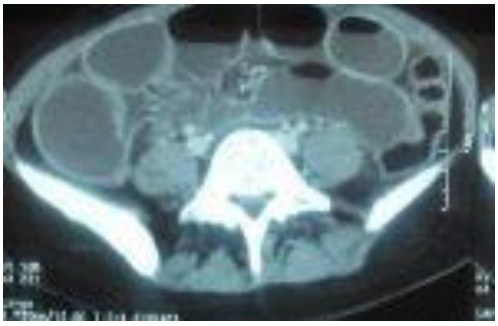


Figure 1: Abdominal computed tomography of the case

Figure 2: Operation view of the intestine showing a grelike volvulus

Figure 3: Resected specimen

Discussion

Congenital bridles are an infrequent pathology of small bowel occlusions, they represent about 0.7 to 2 small bowel and colon occlusions, all causes combined. Congenital bridles are of two types according to:

Lorimier [6] stated that either a persistence of the omphalo-mesenteric canal that has not completely invoked but persists in the form of a fibrous tract, a remnant of vitelline vascularization. Involution of the omphalo-mesenteric duct forms a bridle to the anti-mesenteric edge of the terminal small bowel, either free in the peritoneum or attached to the umbilicus or any other intra-peritoneal viscus. The most common complication is hail volvulus. Lorimier [6] also recalls that among the congenital etiologies, there are omental malformations real bridles called Ladd flanges. They are happy associated with other congenital anomalies including the ring pancreas and mesentery common. None of these situations were found in our case. What made us remember the origin "Spontaneous" or rather initial of this flange?

Very few studies are concerned with initial flanges. Clinical signs are often marked by premature vomiting and stopping of material without stopping gas. X-ray of the abdomen without preparation in the standing or lateral decubitus position was considered gold-standard. This quick and inexpensive examination can confirm the diagnosis of occlusion in more than half of the cases. The main signs observed are a small distention, hydro-air levels and possibly free intra-abdominal fluid by erasing the contours of the psoas-iliac muscles. In a context of acute occlusion of the loess, the sub-diaphragmatic free air image is pathognomonic of perforation and is an indication for urgent surgery [7,8].

X-rays can sometimes reveal the etiology of the occlusion episode, such as biliary ileus or the presence of a foreign body. This examination, however, has its limitations and is not very sensitive for assessing the presence of ischemia or small necrosis. Although the place of abdominal radiography is questionable in the event of an emergency abdominal CT scan, the literature recommends it as the initial baseline examination for screening and selection of patients requiring CT scan [7,8].

CT-scan has become an almost unavoidable examination in the evaluation of patients with suspected hail obstruction. It answers the questions of the presence of an occlusion, its location, its cause and the severity of the attack with a sensitivity of 90 to 96% and a specificity of 96% [9,10]. This examination indicates in the first place the presence of dilated proximal loops and loops of normal diameter or collabées. There is also a local risk, that of necrosis or intestinal perforation resulting from mechanical ulcerations (ileus biliary) or parietal ischemia, either on the obstacle (flange, strangulation, volvulus) or upstream of the obstacle (diastatic perforation due to gas distension).

The primary flange occlusion treatment is surgical. It may consist of a simple section of the flange or a resection of the part responsible for occlusion with a termino-terminal grelogelic anastomosis as was our case.

Conclusion

Occlusion on bridles or spontaneous adhesions is observed in young patients without any history of laparotomy, presenting with a table of free occlusive syndrome. It is only during laparotomy that the spontaneous or initial etiology of the flanges is observed. The flange is often unique. Morbidity and mortality are negligible due to early surgery guided by good medical resuscitation.

References

1. Miller G, Boman J, Shrier I, Gordon PH. Etiology of small bowel obstruction. Am J Surg. 2000;180:336.
2. Parker MC, Ellis M, Moran BJ, Thompson JN, Wilson MS, Menzies D, et al. Postoperative adhesions: ten-year follow-up of 12,584 patients undergoing lower abdominal surgery. Dis Colon Rectum. 2001;44:822-29.
3. Miller G, Boman J, Shrier I, Gordon PH. Readmission for small-bowel obstruction in the early post-operative period: etiology and outcome. Can J Surg. 2002;45:255-8.
4. Akgur FM, Tanyel FC, Büyükpamukçu N, Hiçsönmez A. Anomalous congenital band causing intestinal obstruction in children. J Pediatr Surg. 1992;27:471-3.
5. Nemir P. Intestinal obstruction, Ten-year statistical survey at the hospital of the University of Pennsylvania. Ann Surg. 1952;135:367-75.
6. Lorimier G, Coppo B, Delay J, Guntz M. Occlusion of hail by spontaneous bridles. Med Chir Dig. 1990;19:163-5.
7. Lappas JC, Reyes BL, Maglinte DD. Abdominal radiography findings in small-bowel obstruction : Relevance to triage for additional diagnostic imaging. AJR Am J Roentgenol. 2001;176:167-74.
8. Thompson WM, Kilani RK, Smith BB, et al. Accuracy of abdominal radiography in acute small-bowel obstruction: Does reviewer experience matter? AJR Am J Roentgenol. 2007;188:W233-8.
9. Maglinte DD, Heitkamp DE, Howard TJ, et al. Current concepts in imaging of small bowel obstruction. Radiol Clin North Am. 2003;41:263-83.
10. Qalbani A, Paushter D, Dachman AH. Multidetector row CT of small bowel obstruction. Radiol Clin North Am. 2007;45:499-512.

J Surg Med. 2018;2(3):401-402.
DOI: 10.28982/josam.444053

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Spigelian hernia after laparoscopic hysterectomy: Case report

Laparoskopik histerektomi sonrası spigelian herni: Olgu sunumu

Zeynep Öztürk İnal [1], Hasan Ali İnal [1], Ender Alkan [2]

[1] Konya Education and Research Hospital, Departmant of Obstetric and Gynecology, Konya, Turkey
[2] Aksaray University Medical Faculty, Departmant of Radiology, Aksaray, Turkey

ORCID ID of the authors
ZÖİ: 0000-0002-8766-2079
HAİ: 0000-0002-8361-7908
EA: 0000-0002-8401-2193

Corresponding author / Sorumlu yazar:
Hasan Ali İnal
Address / Adres: Konya Eğitim ve Araştırma Hastanesi, 42090 Meram Yeni Yol Konya, Türkiye
e-Mail: dr.hasanaliinal@yahoo.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 15.07.2018
Accepted / Kabul tarihi: 04.08.2018
Published / Yayın tarihi: 11.08.2018

Abstract

A Spigelian hernia, which may be congenital or acquired, is a rarely seen (0.12–2%) defect of the anterior wall of the abdomen, often causing pain or swelling. Surgical treatment is recommended because of complications such as ileus and strangulation. In this presentation, a case of Spigelian hernia in a 57-year-oldwomen who presented with abdominal pain and ileus and was diagnosed using a computerized tomography scan in the trocar entry is discussed in light of the literature.

Keywords: Hysterectomy, Ileus, Spigelian hernia

Öz

Konjenital veya edinsel olabilen Spigelian herni, genellikle karın ağrısı veya karında şişkinliğe neden olabilen, karın ön duvarının nadir görülen (%0,12–2) bir defektidir. İleus ve strangülasyon gibi komplikasyonlar nedeniyle cerrahi tedavi önerilmektedir. Bu sunumda, 57 yaşında, karın ağrısı - ileus ile başvuran ve bilgisayarlı tomografi ile trokar girişi yerinde tanı konulan bir kadın hastadaki Spigelian herni literatür eşliğinde tartışılmıştır.

Anahtar kelimeler: Histerektomi, İleus, Spigelian herni

Introduction

A Spigelian hernia, which arises from transverse aponeurosis failure of abdominal fascia, may be seen from the ninth costal cartilage, called the semilunar line, extending from the lateral edge of the rectus abdominis to the symphysis pubis [1,2]. Any hernia between the fascial leaves may not be detected as an apparent mass with examination via inspection or palpation [3]. Laparoscopic surgery is mostly used in the treatment of hernias, and conventional methods may also be preferred [4,5].

Case presentation

In a 57-year-old female patient who was admitted to the emergency department with flatulence and abdominal pain on the 5th postoperative day after a laparoscopic hysterectomy operation, laboratory findings showed no leukocytosis, a potassium level of 3.2 mEq/L (3.5–5.1), dilated intestine, and free intraperitoneal fluid on ultrasonography (USG) examination. An abdominal computed tomography (CT) examination with oral and intravenous contrast showed dilatation of the stomach, duodenum, and jejunum, and a hernia incision with a diameter of about 4x3 cm containing small intestine was observed in an 18 mm diameter fascial defect (Figure 1, 2).

How to cite / Atıf için: İnal ZÖ, İnal HA, Alkan E. Spigelian hernia after laparoscopic hysterectomy: Case report. J Surg Med. 2018;2(3):401-402.

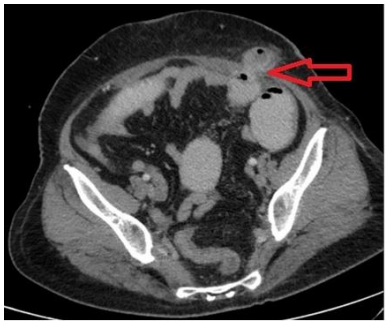


Figure 1: A Spigelian hernia, which extends under the skin from the lateral part of the left rectus muscle and contains the intestine, in the axial section of the abdominal CT scan.

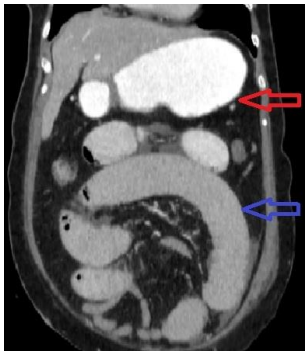


Figure 2: Contrast filled dilated stomach (red arrow) and small intestine (blue arrow) on coronal reformatted CT section.

The patient was diagnosed with Spigelian hernia with current clinical and imaging findings, and surgical intervention was decided. Primarily, laparoscopic surgery was tried, but the intestine was not reduced. Open surgical intervention was then performed, and the defect was covered with a mesh after the intestine was reduced. There was no necrosis of the intestine in the hernia incision, and no resection was needed because peristalsis of the intestine was observed (Figure 3). The patient, who could be fed orally on the 2nd postoperative day and had gas and fecal discharge, was discharged on the 4th postoperative day. There were no adverse effects in the control examination performed on the 10th postoperative day.

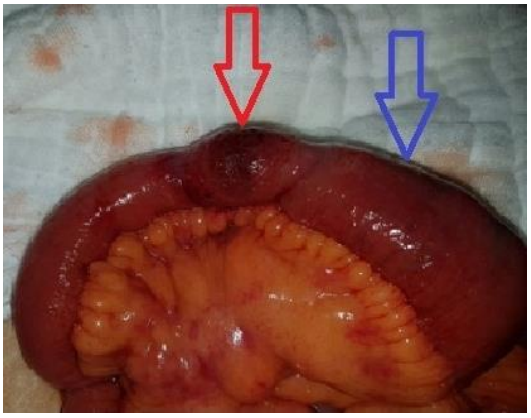


Figure 3: Strangulated intestine (red arrow) and the image of the dilated proximal intestine (blue arrow).

Discussion

Herniation of the linea alba, known as the Spigelian line, was first described by Klinkosch in 1764 and may occur as congenital or acquired [2,6]. Risk for Spigelian hernia peaks in the sixth and seventh decades and is slightly higher in females at 1.18/1 than in males [7].

Congenitally, the perforating veins can weaken the abdominal wall fascia and hernia can occur at these points. Acquired causes include obesity, which can cause tension on the abdominal wall, multiple pregnancies, and previous surgical intervention [3]. In our case, Spigelian hernia was observed as acquired in the trocar entry after a laparoscopic hysterectomy operation.

Spigelian hernias can be missed because of a lack of specific symptoms, difficult detection in the fascial leaves, or difficult mass detection with palpation. Only half of cases are diagnosed preoperatively [8]. In our case, the Spigelian hernia could not be detected with physical examination but was diagnosed with abdominal CT.

Surgical intervention is recommended for all Spigelian herniated patients because sharp edges of the fascia increase the risk of strangulation [2]. The operation can be performed by open surgery (laparotomy) or laparoscopic surgery. The first laparoscopic surgery for Spigelian hernia was performed by Carter and Mizes in 1992 via suturing the hernia incision [3]. Currently, meshes are used to close the hernia sac [4]. Laparoscopic surgery is preferred because the hospitalization time is shorter than open surgery, and patients' comfort is better than with laparotomy [9]. In our case, the laparoscopic approach was first tried to reduce the bowel. When this failed, open surgical repair was performed, and the fascial defect was closed with mesh.

In conclusion, if the hernia sac is between the fascial leaves, the diagnosis of hernia by physical examination is very difficult. Because of the high risk of strangulation in patients with Spigelian hernia, surgical closure of the fascial defect is recommended and a laparoscopic procedure with fewer postoperative complications is preferred.

References

1. Nagarsheth KH, Nickloes T, Mancini G, Solla JA. Laparoscopic repair of incidentally found Spigelian hernia. JSLS. 2011;15(1):81-5. doi: 10.4293/108680811X13022985131372.
2. Weiss J. Lernan OZ, Nilson S. Spigelian hernia. Ann Surg. 1974;180:836-9.
3. Mittal T, Kumar V, Khullar R, Sharma A, Soni V, Baijal M, et al. Diagnosis and Management of Spigelian hernia: A review of literature and our experience. J Min Access Surg. 2008;4:95-98.
4. Carter JE, Mizes C. Laparoscopic diagnosis and repair of Spigelian hernia: report of case and technique. Am J Obstet Gynecol. 1992;167:77-8.
5. Chowbey PK, Sharma A, Khullar R, Baijal M, Vashistha A. Laparoscopic ventral hernia repair. J Laparoendoscopy Adv Surg Tech. 2000;10:79-84.
6. Klinkosch JT. Programma Quo Divisionem Herniarum, Novumque Herniae Ventralis Specium Proponit. Rotterdam: Benam; 1764.
7. Spangen L. Spigelian hernia. World J Surg. 1989;13(5):573-80.
8. Opson RO, Davis WC. Spigelian hernia: Rare or obscure? Am J Surg. 1968;116:842-6.
9. Moreno-Egea A, Carrrasco L, Girela E, Martin JG, Aguayo JL, Canteras M. Open vs. laparoscopic repair of spigelian hernia: A prospective randomized trial. Arch Surg. 2002;137:1266-8.

J Surg Med. 2018;2(3):403-405.
DOI: 10.28982/josam.437453

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Solitary involvement of multiple myeloma in the upper thoracic spine, and anterior approach to thoracic region without full sternotomy: A case report

Üst torasik omurgada multipl miyelomun soliter tutulumu ve tam sternotomi olmaksızın torasik bölgeye anterior yaklaşım: Olgu sunumu

Mehmet Bülent Önal [1], Atilla Kırçelli [2], Erdinç Civelek [3]

[1] Acibadem University, Vocational School of Health Sciences, Istanbul, Turkey
[2] Neurosurgery Department, Baskent University, Istanbul, Turkey
[3] Neurosurgery Department, Taksim Gaziosmanpasa Education and Research Hospital, Istanbul, Turkey

ORCID ID of the authors
MBÖ: 0000-0003-0563-3221
AK: 0000-0003-2109-1274
EC: 0000-0002-3988-4064

Corresponding author / Sorumlu yazar:
Mehmet Bülent Önal
Address / Adres: Eskişehir Acıbadem Hastanesi, Beyin Cerrahi Bölümü, Eskibağlar Cad., Tepebaşı, Eskişehir, Türkiye
e-Mail: bulentonal@hotmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 26.06.2018
Accepted / Kabul tarihi: 12.08.2018
Published / Yayın tarihi: 19.08.2018

Abstract

Multiple myeloma is cancer that starts in the plasma cells in bone marrow. Bone x- rays may show fractures or hollowed out areas of bone. The most common skeletal sites are pelvis, skull, spine, ribs and femoral and humeral shafts. The unique anatomy of thoracic spine creates challenging surgery approaches. Treatment choices of hematological malignancies of the spine are surgery, chemotherapy and radiotherapy. Unilateral L-shaped manubriotomy does not require full sternotomy for upper thoracic segment pathologies. We present a case of multiple myeloma patient in the upper thoracic area and the surgical management. We present an approach to anterior pathology of the upper thoracic spine that obviates the need for sternotomy.

Keywords: Multiple myeloma, Unilateral L-shaped manubriotomy, Anterior approach, Cervicothoracic junction

Öz

Multipl miyelom kemik iliğindeki plasma hücrelerinden başlayan bir kanser türüdür. Kemik grafileri kemikteki kırıkları ve oyukları gösterebilir. En sık tutulan iskelet alanları pelvis, kafatası, kaburgalar ve femur- humerus kemikleridir. Torasik omurganin özellikli anatomisi, bu bölgenin cerrahi yaklaşımlarını oldukça zorlaştırır. Omurgadaki hematolojik hastalıkların tedavi seçenekleri arasında cerrahi, kemoterapi ve radyoterapi seçenekleri yeralmaktadır. Tek taraflı L- şekilli manubriyotomi sayesinde üst torasik bölge patolojilerine yaklaşımlarda tam sternotomi gerekmemektedir. Üst torasik omur multiple myeloma hastasının cerrahi yönetimini sunmayı amaçladık. Sunulan cerrahi yöntem üst torasik bölgeye yaklaşımda sternotomi ihtiyacını ortadan kaldırmaktadır.

Anahtar kelimeler: Multipl Miyelom, Tek taraflı L-şekilli manubriyotomi, Anterior yaklaşım, Servikotorasik bileşke

Introduction

Multiple myeloma is the prototype of malignant monoclonal gammopathies. Radiographic presentation is lytic skeletal lesions classically. Also can present sclerotic and porotic changes. The most common skeletal sites are pelvis, skull, spine, ribs and femoral and humeral shafts. The unique anatomy of thoracic spine creates challenging surgery approaches. Exposure of the upper two thoracic vertebrae is most compelling of all [1]. Created rigidity of this area by rib cage provides tightness so the spondylotic changes do not occur as in the cervical or lumbar spine [2].

Traumatic injuries, infections, spondilopathies or malignancies can require anterior corpectomy of the thoracic spine. These approaches permit the surgeon a wide decompression of the corpus but can be critical to uncover complications associated with entering the thorax and working around aorta [3].

How to cite / Atıf için: Önal MB, Kırçelli A, Civelek E. Solitary involvement of multiple myeloma in the upper thoracic spine, and anterior approach to thoracic region without full sternotomy: A case report. J Surg Med. 2018;2(3):403-405.

Case presentation

A 44-year-old woman with localized back pain went under x- ray to thoracic spine and T3 region localized compression fracture was found at another hospital. Magnetic resonance imaging was performed. Pre- diagnosis of the MRI was spinal tumor so she went under PET scan, but no primary tumor was found. She underwent posterior T3- 4 laminectomy and T3 corpus biopsy procedure but the pathology did not give any result of a tumor so she was discharged from hospital with analgesic treatment (figure 1). She admitted to our emergency service with continued severe back pain. Recent MRI of the thoracic spine revealed severe impression of T3 to the spinal cord (figure 2). So she underwent anterior T2-3 corpectomy followed by anterior spinal stabilization by corpectomy cage and anterior plate (figure 3). Manubro-sternotomy for anterior approach was performed. Pathological diagnosis was kappa monoclonal plasmacytoma. Bone marrow biopsy performed by oncology department showed none plasma cell increase. FISH study results showed 13q, 17p, t84:14 negativity. She was given radiotherapy treatment to the thoracic spine. She remains neurologically intact at 1 year postoperatively without evidence of disease recurrence. Patient has given consent for this report.

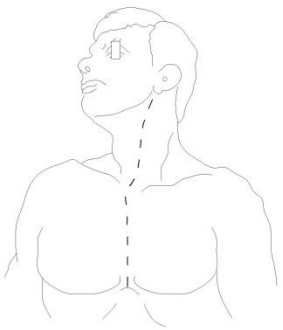
Figure 1: Thoracic spine sagittal tomography image after outer clinic operation

Figure 2: Spinal cord impression of T3 vertebrae on the MRI two months after first operation

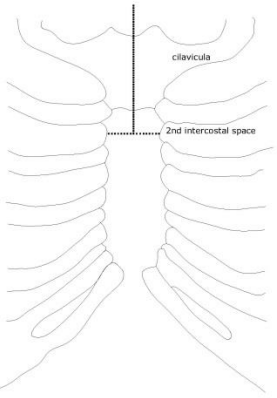
Figure 3: Early postoperative sagittal 3- dimension tomography image showing placement of corpectomy cage with T1-2 anterior plating after T2-3 anterior corpectomy

Technique

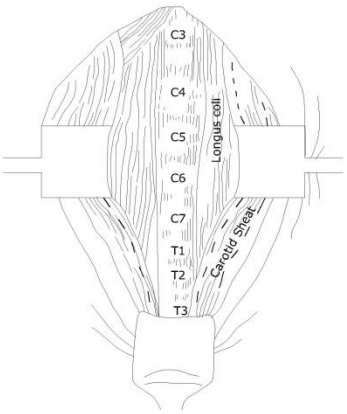
The patient is positioned supine, the trunk 10° flexed and the head slightly rotated to the right (picture 1). We used an incision cranially from the medial side of the sternocleidomastoid muscle to the manubrium notch, which extended 5 cm downwards on the midline. A L-shaped osteotomy is made over the manubrium sterni (picture 2) and a retractor was placed (picture 3). With blunt dissection, eusophagus and trachea retracted to the left (medial) side and the common carotid artery to the right side laterally (picture 4, 5). T3 vertebrae was exposed, but because of the thoracic kyphosis and the deep angled vision, T2 corpectomy is also required together with T3 corpectomy. Stabilization with expandable corpectomy cage [medicon r] and anterior plating is done (figure 2).



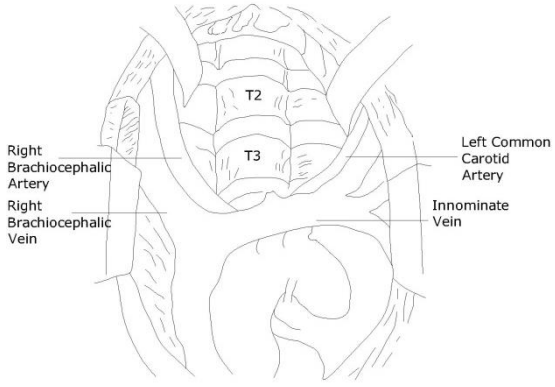
Picture 1: Patient positioning and incision area decision before surgery. First half of the incision (cranial half) is used for this case. Whole incision is necessary for sternotomy



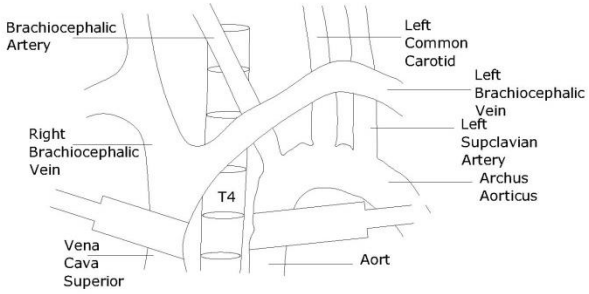
Picture 2: L-shaped skin incision is showed in the drawing



Picture 3: Surgical area is shown after bilaterally m. longus coli dissection



Picture 4: The relationship with T2-3 is shown in the drawing.



Picture 5: The drawing shows the surgical area anatomy

Discussion

Multiple myeloma is characterized by the accumulation of malignant plasma cells in the bone marrow followed by impaired hematopoiesis and bone disease, which includes mainly lytic lesions, pathological fractures, hypercalcemia and osteoporosis [4].

Thoracotomy to access the anterior thoracic spine was first described in 1950s [2]. Hematological malignancies such as myeloma and lymphoma incidence in spinal localizations varies from 6 to 20%. Treatment choices are surgery, chemotherapy and radiotherapy. Place of surgery in spinal hematological malignancies treatment takes up less space. According to Lachaniette et al. [5], surgical treatment must be considered in case of acute vertebral collapse, or if the diagnosis is uncertain and a biopsy is needed, or if the neurological symptoms increase under medical treatment of the hematological malignancy.

The cervicothoracic junction is defined as an area between C7 to T4 mostly and varied approaches to this area have been described, including low anterior cervical approach alone or combined with sternotomy, unilateral or bilateral manubriotomy or with clavicular dissection and lateral parascapular thoracotomy. Anterior approach is defined as the best surgical strategy for this region, because it allows better decompression of neural structures [6,7].

Surgical approaches from the seventh cervical to the fourth thoracic vertebrae is always challenging because of the regular kyphosis of the higher thoracic segments requires deep surgical area [8,9]. Traditional approaches to this region includes thoracotomy or at least limited sternotomy [10]. Huang et al [11] described the region in their cadaveric study recently. As they reported that, when an access to T2 and above is required, the traditional low cervical approach is usually enough, but the manubrium sterni and clavicles often hinder access to T3, T4 and below, so trans-sternal, trans-clavicular and trans-manubrial approaches are defined.

Sundaresan et al [1] first described a T-shaped incision on 1984, with the vertical limb extending over the body of sternum for the anterior approach to upper thoracic region. Accordingly to his method, medial third of the clavicula is resected and disconnected from the sternum which improves exposure and also used as a strut graft for the fusion after corpectomy. Height of the manubrium, shape of the thoracic aperture and the degree of cervicothoracic kyphosis may limit this approach. The most caudal lesion level was T2 in their study.

Subsequent to Sundaresan [1], Darling et al [12] used a modified trans- manubrial approach [unilateral manubriotomy] to access T4- T5 level, however it provided a narrow operation field. Luk et al [9] used bilateral manubriotomy for more extensive exposure of this area. The transverse limb of the osteotomy of the manubrium sterni should exit at the second intercostal space and can be unilateral (L-shaped) or bilateral [inverted T-shaped] [5].

Conclusion

We used the unilateral L-shaped manubriotomy. This approach is useful to expose upper thoracic spine until fifth thoracic vertebrae so there is no need for full sternotomy for these segment pathologies. It also provides the patient from postoperative pain and potential morbidity of full sternotomy. It provides an 8-cm interval between the split manubrium and allows access to both sides of the vertebrae. The deep localization of the vertebral bodies due to kyphosis of the upper thoracic spine and the presence of neurovascular and osseous obstacles over the operation area are out limitation factors for this approach.

References

1. Sundaresan N, Shah J, Foley KM, Rosen G. An anterior surgical approach to the upper thoracic vertebrae. J Neurosurg. 1984;61(4):686-90.
2. Lall RR, Smith ZA, Wong AP, Miller D, Fessler RG. Minimally invasive thoracic corpectomy: surgical strategies for malignancy, trauma, and complex spinal pathologies. Minim Invasive Surg. 2012;2012:213791.
3. Gokaslan ZL, York JE, Walsh GL, McCutcheon IE, Lang FF, Putnam JB Jr, Wildrick DM, Swisher SG, Abi-Said D, Sawaya R. Transthoracic vertebrectomy for metastatic spinal tumors. J Neurosurg. 1998;89(4):599-609.
4. Tamburrelli FC, Proietti L, Scaramuzzo L, De Stefano V, Logroscino CA. Bisphosphonate therapy in multiple myeloma in preventing vertebral collapses: preliminary report. Eur Spine J 21 Suppl. 2012;1:141-5.
5. Flouzat-Lachaniette CH, Allain J, Roudot-Thoraval F, Poignard A. Treatment of spinal epidural compression due to hematological malignancies: a single institution's retrospective experience. Eur Spine J (E Pub). 2012;10.
6. Tarantino R, Donnarumma P, Marruzzo D, Landi A, Giacomo T, Delfini R. Anterior surgical approaches to the cervicothoracic junction: when to use the manubriotomy? Spine J. 2013 Mar 30. doi:pii: S1529-9430(13)00249-0.
7. Donnarumma P, Nigro L, Tarantino R, De Giacomo T, Delfini R. The Manubriotomy is a safe option for the anterior approach to the cervico-thoracic junction. Journal of Spine Surgery. 2017;3(3):426-8.
8. Pointillart V, Aurouer N, Gangnet N, Vital JM. Anterior approach to the cervicothoracic junction without sternotomy: a report of 37 cases. Spine. 2007;32(25):2875-9.
9. Luk KD, Cheung KM, Leong JC. Anterior approach to the cervicothoracic junction by unilateral or bilateral manubriotomy. A report of five cases. J Bone Joint Surg Am. 2002;84(6):1013-7.
10. Comey CH, McLaughlin MR, Moossy J. Anterior thoracic corpectomy without sternotomy: a strategy for malignant disease of the upper thoracic spine. Acta Neurochir (Wien). 1997;139(8):712-8.
11. Huang Y, Tian N, Chi Y, Wang S, Pan J, Xu H. Mini open anterior approach to the cervicothoracic junction: a cadaveric study. Eur Spinr J. 2013 doi:10.1007/s00586-2766-9.
12. Darling GE, McBroom R, Perrin R. Modified anterior approach to the cervico- thoracic junction. Spine. 1995;20:1519-21.

J Surg Med. 2018;2(3):406-407.
DOI: 10.28982/josam.437945

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Achromobacter xylosoxidans infection in urinary tract in a secondary kidney stone patient: Case Report

Sekonder böbrek taşı hastasında idrar yolunda Achromobacter xylosoxidans enfeksiyonu: Vaka sunumu

Sercan Sarı [1], Emine Yeşilyurt [2], Neziha Yılmaz [2], Abdullah Gürel [1], Emin Gürtan [1], Laser Şanal [2]

[1] Bozok University Faculty of Medicine, Department of Urology, Yozgat, Turkey
[2] Bozok University Faculty of Medicine, Department of Microbiology, Yozgat, Turkey

ORCID ID of the authors
SS: 0000-0002-0994-3799
EY: 0000-0002-6100-0480
NY: 0000-0001-9027-079X
AG: 0000-0003-3112-448X
EG: 0000-0002-1992-3556
LŞ: 0000-0003-4280-8895

Corresponding author / Sorumlu yazar:
Sercan Sarı
Address / Adres: Bozok Üniversitesi, Üroloji Anabilim Dalı, Yozgat, Türkiye
e-Mail: sercansari92@hotmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 27.06.2018
Accepted / Kabul tarihi: 14.08.2018
Published / Yayın tarihi: 20.08.2018

Abstract

Achromobacter xylosoxidans formerly named as Alcaligenes xylosoxidans is an aerobic, non-fermenting, oxidase positive, catalase positive gram negative bacillus. It is seen especially in immunosuppressed patients, patients with tumors, hypogamaglobulinemia or transplant patients. A. xylosoxidans infection in urinary system is very rare. 56 year old male patient was presented to our clinic with bilateral flank pain. He had not immunodeficiency and tumor history. He had diabetes mellitus. He had shock wave lithotripsy history for bilateral kidney stone. He had previous open surgery for right kidney stone and retrograde intrarenal surgery for left kidney stone. In the urine culture, Achromobacter xylosoxidans infection was detected. Ciprofloxacin, ceftriaxone and methenamine hippurate treatment were firstly applied to the patient. Patient was followed and 15 days later he admitted our clinic. 38 white blood cells and 8 red blood cells were present in urinalysis and the control urine culture was sterile. In conclusion, A. xylosoxidans infection is rarely seen and it has high resistance to antibiotics. Clinicians must be careful about the infection and treatment of A. xylosoxidans infection.

Keywords: Achromobacter xylosoxidans, Urinary tract

Öz

Achromobacter xylosoxidans Alcaligenes xylosoxidans olarak bilinir. Aerobik, non-fermentative, oksidaz pozitif, katalaz pozitif gram negatif bir basildir. Immun yetmezlikli, tümörlü, hipogamaglobulinemili ve transplantlı hastalarda genellikle görülür. Uriner sistem enfeksiyonu nadirdir. 56 yaşında erkek hasta bilateral flank ağrı ile kliniğimize başvurdu. Hastanın immunyetmezlik ve tümör öyküsü yoktu. Bilateral böbrek taşı için şok dalga litotripsi öyküsü mevcuttu. Sağ böbrek taşı için açık cerrahi, sol böbrek taşı için retrograt intrarenal cerrahi öyküsü mevcuttu. İdrar kültüründe Achromobakter xylosoxidans enfeksiyonu tespit edildi. Ciprofloksasin, seftriakson ve methenamin hippurat tedavileri hastaya ilk olarak uygulandı. Hasta takip edildi ve 15 gün sonra kliniğe kabul edildi. 38 beyaz küre hücresi ve 8 kırmızı küre hücresi idrar analizinde görüldü ve idrar kültürü sterildi. Sonuç olarak A. xylosoxidans enfeksiyonu nadir görülür ve antibiyotiklere yüksek dirence sahiptir. Klinisyenler A. xylosoxidans enfeksiyonu ve tedavisi konusunda dikkatli olmalıdır.

Anahtar kelimeler: Achromobacter xylosoxidans, İdrar yolu

Introduction

Achromobacter xylosoxidans formerly named as Alcaligenes xylosoxidans is an aerobic, non-fermenting, oxidase positive, catalase positive gram negative bacillus. In 1971, it was firstly reported by Yabuchi and Ohyama [1] in patients with chronic otitis media. It is rarely seen in human. It is seen especially in immunosuppressed patients, patients with tumors and hypogamaglobulinemia, or transplant patients [2]. A. xylosoxidans infection in urinary system is very rare. In this study, we reported urinary tract infection due to A. xylosoxidans in a secondary kidney stone patient.

How to cite / Atıf için: Sarı S, Yeşilyurt E, Yılmaz N, Gürel A, Gürtan E, Şanal L. Achromobacter xylosoxidans infection in urinary tract in a secondary kidney stone patient: Case Report. J Surg Med. 2018;2(3):406-407.

Case presentation

56 year old male patient was presented to our clinic with bilateral flank pain. He had not immunodeficiency and tumor history. He had diabetes mellitus (DM). He had shock wave lithotripsy (SWL) history for bilateral kidney stone. He had previous open surgery for right kidney stone and retrograde intrarenal surgery (RIRS) for left kidney stone. Operation was planned. Informed consent was taken before operation. In the laboratory tests, blood urea nitrogen (BUN) was 9 mg/dl, creatinine was 0.81 mg/dl. In the common blood count test, White blood cell (WBC) was 9.7 K/uL, hemoglobin was 15.6 g/dl. 6 red blood cells (RBC) and 151 WBCs were present in urinalysis. There were kidney stones and the largest one was 32 mm sized in the radiological imaging. Urine analysis and urine culture was ordered to indicate any possibility of urinary tract infection. Urine was inoculated in to Sheep blood agar (SBA) utilized for quantitative urine culture and MacConkey agar utilized as selective differential agar for gram-negative bacteria, A single species of gram negative bacillus recovered at >105 cfu‟s/mL urine were identified as Achromobacter xylosoxidans by the Vitek 2 Compact system using Gram-negative cards (bioMérieux, France) and were subjected to antibiotic sensitivity test.. It was susceptible to ceftazidime, meropenem and piperacilline tazobactam. Ciprofloxacin, ceftriaxone and methenamine hippurate treatment were firstly applied to the patient. Patient was followed and 15 days later he admitted to our clinic. 38 WBCs and 8 RBCs were present in urinalysis and the control urine culture was sterile.

Discussion

A. xylosoxidans is a rarely seen opportunistic gram negative non-fermenting bacillus [3]. It is seen in immunocompromised patients, transplant patients and patients with hematological malignancy and blood diseases [4]. Otitis media, skin infections, intravenous catheter related and surgery site infections are typical infections of A. xylosoxidans [2]. Urinary tract infections (UTI) are rarely seen. In a study, UTI rate was % 0.04. 9 cases were reported. These cases had history of hematologic or solid malignancy, DM, chronic renal failure and renal transplantation [5]. Six patients had kidney anomaly.8 patients had cystitis symptoms and one patient was asymptomatic [5]. In another study, a patient with septic shock after SWL due to A. xylosoxidans was reported. Patient didn't have immunodeficiency, chronic disease, UTI and kidney stone history. Septic shock caused by A. xylosoxidans was appeared in the patient and after treatment in intensive care unit patient was healthy and discharged [6]. In our study patient complained with flank pain. Patient had DM. He had previous surgery and SWL history for kidney stone. A. xylosoxidans infection was detected in preoperative urine culture.

A. xylosoxidans infection treatment is difficult due to high resistance to antibiotics. In the literature, A. xylosoxidans is susceptible to imipenem, piperacillin tazobactam, ceftazidime and trimethoprim sulfamethoxazole [4,7,8]. Studies about mixed treatments are carried out [4,8].

In conclusion, A. xylosoxidans infection is rarely seen and it has high resistance to antibiotics. Clinicians must be careful about the infection and treatment of A. xylosoxidans infection.

References

1. Yabuuchi E, Oyama A. Achromobacter xylosoxidans n sp. From human ear discharge. Jpn J Microbiol. 1971;15:477-81.
2. Mandell WF, Garvey GJ, Neu HC. Achromobacter xylosoxidans bacteremia. Rev Infect Dis. 1987;9:1001-5.
3. Eshwara VK, Mukhopadhyay C, Mohan S, Prakash R, Pai G. Two unique presentations of Achromobacter xylosoxidans infections in clinical settings. J Infect Dev Ctries. 2011;5:138-41.
4. Duggan JM, Goldstein SJ, Chenoweth CE, Kauffman CA, Bradley SF. Achromobacter xylosoxidans bacteraemia: report of 4 cases and review of the literature. Clin Infect Dis. 1996;23:569-76.
5. Tena D, Gonzales- Praetorius A, Perez-Balsalobre M, Sancho O, Bisquert J. Urinary tract infection due to Achromobacter xylosoxidans: report of 9 case. Scand J Infect Dis. 2008;40:84-7.
6. Lee JH, Lee SY, Park IY, et al. A Case of Septic Shock caused by Achromobacter xylosoxidans in an Immunocompetent Female Patient after Extracorporeal Shock Wave Lithotripsy for a Ureteral Stone. Infect Chemother. 2016 Mar;48(1):47-50. https://doi.org/10.3947/ic.2016.48.1.47
7. Aisenberg G, Rolston KV, Safdar A. Bacteraemia caused by Achromobacter and Alcaligenes species in 46 patients with cancer (1989–2003). Cancer. 2004;101:2134–40.
8. Shie SS, Huang CT, Leu HS. Characteristics of Achromobacter xylosoxidans bacteraemia in northern Taiwan. J Microbiol Immunol Infect. 2005;38:277–82.

J Surg Med. 2018;2(3):408-409.
DOI: 10.28982/josam.442268

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Case of an atypical located leiomyoma arising from rectus sheath

Rektus kılıfından kaynaklanan atipik yerleşimli leiomyom olgusu

Görker Sel [1]

[1] **Bülent Ecevit University, Department of Obstetrics and Gynecology, Kozlu, Zonguldak, Turkey**

ORCID ID of the authors:
GS: 0000-0001-8653-5687

Abstract
Fibroids or leiomyomas are the commonest benign tumor of the female reproductive tract, occurring most commonly in the uterus. Abdominal wall fibroids are uncommon; we present a rare case of an isolated leiomyoma of the anterior abdominal wall in a patient with no previous history of any abdominal surgeries. We present a case of a 54-year-old female. She was first admitted to the general surgery clinic with a complaint of vague abdominal pain. Abdominal ultrasound and computed tomography revealed the mass, measuring 10x9x7cm, located at the left adnexal area, reported as complex ovarian cyst. She had no history of an abdominal surgery. Laparoscopic surgery was planned. We located the mass, with the help of abdominal palpation and laparoscopic observation at the same time that located anterior to the abdominal parietal peritoneum, beneath the rectus muscle. We extracted the mass, which was capsulated, fine bordered, tender, slightly mobile; with sharp and blunt dissection without any complication. Leiomyomas are the commonest benign tumor of the reproductive tract and found in 20-40% of women of reproductive age. Abdominal wall fibroids are really rare, thought to follow seeding following surgical resection of uterine fibroids. There are very few reported cases of isolated abdominal wall fibroids in the literature, without having previous abdominal surgeries or presence of uterine fibroids as reported in our case.
Keywords: Abdominal wall, Fibroids, Leiomyoma, Rectus sheath

Öz
Fibroidler veya leiomyomlar, en sık uterusta izlenen, dişi üreme sisteminin en yaygın benign tümörüdür. Abdominal duvar fibroidleri nadirdir. Bu olgu sunumunda, herhangi bir abdominal cerrahi öyküsü olmayan bir hastada anterior abdominal duvarda izole bir leiomiyom vakasını sunuyoruz. 54 yaşında bayan olgu, ilk önce genel cerrahi kliniğine müphem karın ağrısı şikayeti ile başvuran hastanın abdominal ultrasonografi ve bilgisayarlı tomografi ile sol adneksiyal alanda 10x9x7 cm boyutlarında kitle imajı veren over kisti saptanmıştır. Geçirilmiş batın ameliyatı öyküsü yoktu. Laparoskopik cerrahi planlandı. Abdominal paryetal peritonun ön tarafında, rektus kasının altında yerleşen; abdominal palpasyon ve laparoskopik gözlem yardımıyla kitle lokalize edildi. Kapsüllü, düzgün sınırlı, yumuşak kıvamda, kısmen mobil kitle; herhangi bir komplikasyon olmadan keskin ve künt diseksiyon ile çıkartıldı. Leiomyomlar üreme sisteminin en sık görülen benign tümörüdür ve üreme çağındaki kadınların % 20-40'ında bulunur. Abdominal duvar fibroidleri nadirdir ve uterin fibroidlerinin cerrahi rezeksiyonunu takiben, seeding, oluştuğu düşünülmektedir. Literatürde; bizim olgumuzdaki gibi daha önce batın operasyonu geçirmediği halde batın ön duvarında izole fibroid saptanması, az rastlanan bir durumdur.
Anahtar kelimeler: Karın duvarı, Fibroidler, Leiomyom, Rektus kılıfı

Introduction

Fibroids or leiomyomas are the commonest benign tumor of the female reproductive tract, occurring most commonly in the uterus, estimated incidence of 20%–40% in women during their reproductive years [1,2]. The commonest site is the uterus, but they are also found in the broad ligament, ovaries, vagina and rarely on the anterior abdominal wall like our case [3-7]. Uterine fibroids are associated with infertility, menorrhagia, pain and compression symptoms when very large [3,8]. Abdominal wall fibroids are uncommon; we present a rare case of an isolated leiomyoma of the anterior abdominal wall in a patient without having history of any abdominal surgeries.

Corresponding author / Sorumlu yazar:
Görker Sel
Address / Adres: Bülent Ecevit Üniversitesi, Kadın Hastalıkları ve Doğum Kliniği, Kozlu, Zonguldak, Türkiye
e-Mail: gorkersel@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 10.07.2018
Accepted / Kabul tarihi: 28.08.2018
Published / Yayın tarihi: 28.08.2018

How to cite / Atıf için: Sel G. Case of an atypical located leiomyoma arising from rectus sheath. J Surg Med. 2018;2(3):408-409.

Case presentation

We present a case of a 54-year-old (parity: 4) female. She was first admitted to the general surgery clinic with a complaint of vague abdominal pain. Abdominal ultrasound and computed tomography (CT) revealed the mass, measuring 10x9x7cm, located at the left adnexal area, reported as complex ovarian cyst. She had no history of an abdominal surgery. Ca-125 was at normal range. After preoperative evaluation and preparation for anesthesia and surgery was done and informed consent was taken, she was taken to the operating room for surgical evaluation. Laparoscopic surgery was planned. The abdomen was entered via Veress needle and pneumoperitoneum was created, then 5-mm optic was inserted through the 5 mm trocar. General observation of the abdominopelvic organs was done, but no ovarian cyst or pelvic mass were observed, also uterus was observed as normal. We looked for the mass, which was revealed by ultrasound and CT. We located the mass, with the help of abdominal palpation and laparoscopic observation at the same time, located anterior to the abdominal parietal peritoneum, beneath the rectus muscle. Laparotomy via transverse 4 cm incision was performed. Subcutaneous tissues were normal, and transversalis fascia was incised, beneath the left rectus muscle and also beneath the pubic bone we figured out the mass (Figure 1). There was not any connection to the uterus or any pelvic structure, since while dissecting the mass we also observed if any connection existed or not, via laparoscope. We extracted the mass, which was capsulated, fine bordered, tender, slightly mobile; with sharp and blunt dissection without any complication. Layers of the abdomen were closed and abdomen was desuflated, operation was done. The immediate post-operative period was uneventful. Patient was discharged on the postoperative 3th day. Pathology revealed the mass as leiomyoma.

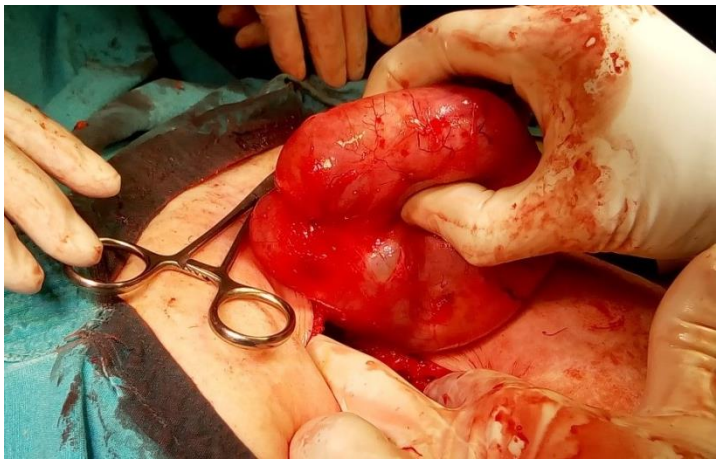


Figure 1: Extraction of the mass located beneath the rectus sheath and anterior to parietal peritoneum

Discussion

Leiomyomas are the commonest benign tumor of the reproductive tract and found in 20-40% of women of reproductive age [1,2]. They are usually asymptomatic, but if symptomatic, are associated with cyclical pain in relation to the menstrual cycles. A combination of hyper-responsiveness to estrogen and progesterone, and a variety of secondary paracrine and autocrine mediators is responsible for the increased pain and growth of the fibroid [9].

Leiomyomas are commonly seen in the uterus, but they are also found in the broad ligament, ovaries, and vagina and rarely on the anterior abdominal wall [1-3]. Abdominal wall fibroids are really rare, thought to follow seeding following surgical resection of uterine fibroids. There are very few reported cases of isolated abdominal wall fibroids in the literature without previous abdominal surgeries or presence of uterine fibroids as reported in our case [6,7].

The commonest primary diseases of the rectus muscle sheath are desmoid tumor and rectus sheath hematoma. Leiomyoma of the rectus muscle sheath is extremely rare [10]. Our case differs with its counterparts with the patient's non-surgery history, which is thought to be important for seeding process for this kind of rare localizations of leiomyomas.

Also we would like to mark the importance of intraoperative decision making in these kind of extraordinary cases. For instance if we did not search for the mass, which was reported on the CT scan, and thought that the mass that mentioned at CT had been a misdiagnosed image; then we would close the patient without identifying and extracting the mass. In these kinds of issues it is really important for a surgeon to be skeptical and obsessive about the inconsistent intraoperative and preoperative findings. If abdominal palpation or bimanual physical examination does not work, then intraoperative vaginal or abdominal ultrasound scanning could be another alternative in these kinds of odd situations not to disregard the preoperatively diagnosed mass.

As a conclusion, while evaluating a patient with an abdominal mass, which was revealed prior to the operation, extraordinary located leiomyomas such as in the vicinity of rectus sheath should be kept in mind.

References

1. Stewart EA. Uterine fibroids. Review Lancet. 2001;357(9252):293–8. doi: 10.1016/S0140-6736(00)03622-9.
2. Moon HS, Koo JS, Park SH, Park GS, Choi JG, Kim SG. Parasitic leiomyoma in the abdominal wall after laparoscopic myomectomy. Fertil Steril. 2008 Oct;90(4):1201.e1-2. doi: 10.1016/j.fertnstert.2007.08.068..
3. Muffly T, Vadlamani I, Weed JC. Massive leiomyma of the broad ligament. Obstet Gynecol. 2007;109(2 pt 2):563–5.
4. Igberase GO, Mabiaku TO, Ebeigbe PN, Abedi HO. Solitary anterior abdominal wall leiomyoma in a 31-year-old multipara woman: a case report. Cases Journal. 2009;2:113. doi:10.1186/1757-1626-2-113.
5. Andersen J. Growth factors and cytokines in uterine leiomyomas. Semin Reprod Endocrinol. 1996;14(3):269–82.
6. Lambroza A, Tighe MK, DeCosse JJ, Dannenberg AJ. Disorders of the rectus abdominis muscle and sheath: a 22-year experience. Am J Gastroenterol. 1995;90(8):1313-7.
7. Ryan GL, Syrop CH, Van Voorhis BJ. Role, epidemiology, and natural history of benign uterine mass lesions. Clin Obstet Gynecol. 2005;48(2):312–24.
8. Wallach EE, Vlahos NF. Uterine myomas: an overview of development, clinical features, and management. Obstet Gynecol. 2004;104(2):393–406.
9. D'souza C, Bhat S, Purushothaman, Dhanej. De novo growth of leiomyoma from rectus sheath: A rare presentation. Ann Trop Med Public Health 2012;5(4):390-2.
10. Khan AT, Shehmar M, Gupta JK. Uterine fibroids: current perspectives. International Journal of Women's Health. 2014;(6):95-114. doi:10.2147/IJWH.S51083.

J Surg Med. 2018;2(3):410-412.
DOI: 10.28982/josam.438745

Journal of Surgery and Medicine
e-ISSN: 2602-2079

A rare form of the lung cancer: Mucoepidermoid carcinoma: A case report

Akciğer kanserinin nadir bir formu: Mukopepidermoid karsinom: Olgu sunumu

Göktan Temiz [1], Özgür Ömer Yıldız [2], Ömer Cenap Gülyüz [3], Nurettin Karaoğlanoğlu [4]

[1] Department of Thoracic Surgery, Adana City Education and Research Hospital, Adana, Turkey
[2] Department of Thoracic Surgery, Yildirim Beyazit University, Yenimahalle Education and Research Hospital, Ankara, Turkey
[3] Department of Thoracic Surgery, Adiyaman University Education and Research Hospital, Adiyaman, Turkey
[4] Department of Thoracic Surgery, Yildirim Beyazit University, Faculty of Medicine, Ankara, Turkey

ORCID ID of the authors:
GT: 0000-0002-8025-5315
ÖÖY: 0000-0001-8995-5644
ÖCG: 0000-0001-8528-5567
NK: 0000-0003-2827-6044

Corresponding author / Sorumlu yazar:
Özgür Ömer Yıldız
Address / Adres: Yıldırım Beyazıt Üniversitesi, Yenimahalle Eğitim ve Araştırma Hastanesi, Göğüs Cerrahisi Anabilim Dalı, Ankara, Türkiye
e-Mail: dr.ooyildiz@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş tarihi: 29.06.2018
Accepted / Kabul tarihi: 28.08.2018
Published / Yayın tarihi: 28.08.2018

Abstract
Mucoepidermoid carcinoma (MEC) of the lung is a rare form of lung cancer that is classified into low grade and high grade based on histological features. For Mucoepidermoid Carcinoma of the Lung, surgery is the most commonly used and most effective form of treatment. Surgical resection is the primary treatment for low-grade MEC with excellent outcomes but high-grade MEC is a more aggressive form of this malignancy.
Keywords: Lung cancer, Mucoepidermoid carcinoma

Öz
Akciğerin mukoepidermoid karsinomu (MEC), histolojik özelliklerine göre düşük ve yüksek gradeli olarak sınıflandırılan nadir bir akciğer kanseri türüdür. Akciğerdeki Mukoepidermoid Karsinom için cerrahi en sık kullanılan ve en etkili tedavi şeklidir. Cerrahi rezeksiyon, mükemmel sonuçlara sahip düşük dereceli MEC için birincil tedavidir, ancak yüksek gradeli MEC bu malignitenin daha agresif bir şeklidir.
Anahtar kelimeler: Akciğer kanseri, Mukoepidermoid karsinom

Introduction

Mucoepidermoid carcinoma (MEC) is a rare tumor of the lung that accounts for 0.1 to 0.2% of all pulmonary tumors [1]. Mucoepidermoid carcinoma of the salivary gland is relatively common but mucoepidermoid carcinoma arising from the mucous glands of the bronchus is rare. Mucoepidermoid carcinoma of the bronchus occurs in patients with a wide age range from 3 to 78 years [1]. Bronchial mucoepidermoid carcinoma usually presents as an intraluminal mass producing luminal occlusion. The symptoms displayed are caused due to irritation and/or obstruction of the trachea and airways. The tumors are usually well differentiated and contain a combination of mucus-secreting, squamous, and intermediate cells. The prognosis of localized low-grade disease is excellent but in high-grade tumors, metastasis to adrenal glands, liver, brain, and bone is indicative of a poor prognosis. Here we report a MEC case located in middle lobe of the right lung.

Case presentation

A 63-year-old man was admitted to our hospital for routine physical examination. He was asymptomatic. The mass of the lung encountered on routine chest X-ray. Chest radiography revealed a mass shadow measuring 30 mm in diameter in the middle lobe of the lung field, and chest computed tomography (CT) showed a lobulated mass shadow measuring 30 mm in diameter in the middle lobe (Figure 1, 2).

Figure 1: Post contrast axial computed tomography image shows a lesion in the middle lobe of right lung

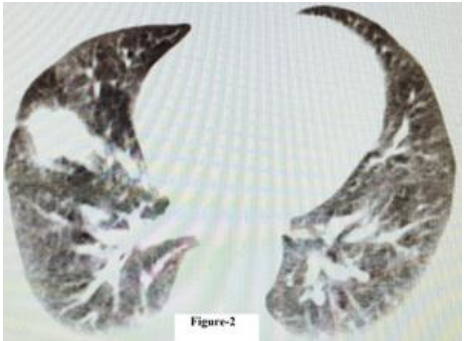


Figure 2: Computed tomography revealing the mass in the middle lobe of the right lung

How to cite / Atıf için: Temiz G, Yıldız ÖÖ, Gülyüz ÖC, Karaoğlanoğlu N. A rare form of the lung cancer: Mucoepidermoid carcinoma: A case report. J Surg Med. 2018;2(3):410-412.

No mediastinal lymph node metastasis or other organ metastases were observed on positron emission tomography (PET) scan. The patient had smoking history. Blood tests showed no abnormal tumor markers. His past was unremarkable with no history of tuberculosis, recurrent respiratory infections. Flexible bronchoscopy was performed for further evaluation of this mass. Bronchoscopy revealed normal airways. Transthoracic needle biopsy was done to evaluate middle lobe mass. Biopsy result of the mass was reported as mucoepidermoid carcinoma. The patient underwent a thoracotomy with middle lobectomy and mediastinal lymph node dissection. Diameter of resected tumor's size was approximately 3 cm. Histologically, tumor is comprised of a mixture of different cell types including mucin-secreting glandular cells, squamous cells, and intermediate cells with cytological atypia and necrosis. Sections from the tumor were stained with hematoxylin and eosin (Figure 3a). The mucus-secreting cells are demonstrated by staining with mucicarmine (Figure 3b). Immunohistochemical staining for p63 and TTF-1 showed positive (Figure 3c, 3d). Histopathological examination of the tissue reported the diagnosis as high-grade MEC. All resection margins were negative for tumor involvement, and the lymph nodes were free of metastatic disease. There was not any complication during the operation period. He recovered well post- surgery. The patient did not require any chemotherapy or radiotherapy post-operatively and remained well after the operation. He has been scheduled for a surveillance CT scan.

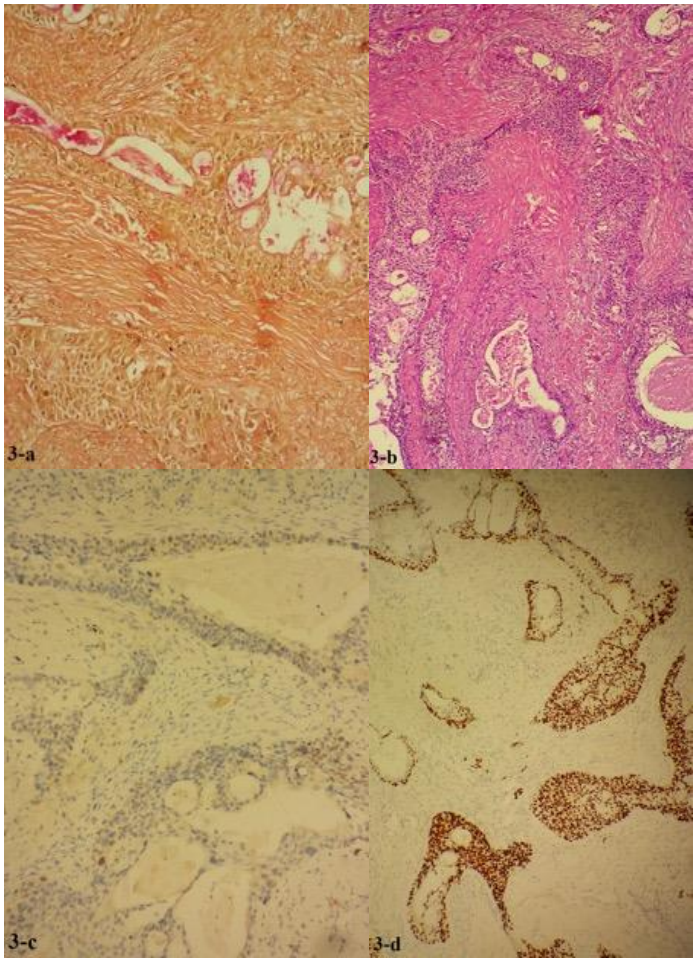


Figure 3: a) Haematoxylene & Eosin X100 b) Mucicarmine X100 c) TTF1 X100 d) P63 X100

Discussion

MEC is a tumor characterized by a combination of mucus-secreting, squamous, and intermediate cell types. It is a recognized form of malignancy arising from the salivary glands; however, it can present as a primary lung cancer. The estimated frequency of MEC is 0.1% to 0.2% of all primary lung tumors [1]. The age range reported extends from 3 to 78 years with equal sex distribution [1-3]. Our case was old aged, male and had similar histological findings. It presents as an endobronchial exophytic mass that can be either sessile and broad-based or pedunculated with a well-formed stalk [2]. The size of the tumor varies from several millimeters to up to 6 cm in diameter [2]. It is usually located in the lumen of a main, lobar, or segmental bronchus [3]. In our case, there was not observed any endobronchial lesion in the tracheobronchial tree. Diameter of the mass was about 3 cm. Histologically, it is classified as high grade or low grade. The high-grade features include necrosis, nuclear pleomorphism, and active mitosis. The low-grade tumors are usually confined to the bronchus and lack those histologic features associated with high-grade tumors [3]. Our case was reported as low-grade tumor. The presenting symptoms include cough, hemoptysis, and wheezing. MEC can be an incidental finding, with no clinical symptoms in up to 25% of patients [5]. In our case, the mass was detected incidentally on routine physical examination. The chest x-ray may show evidence of pneumonia or atelectasis. Other radiologic findings include a solitary lung nodule or mass [4]. The findings on chest CT scan include a well-defined endobronchial mass, with or without obstructive pneumonia or atelectasis [6]. In our case, chest CT showed a lobulated mass shadow measuring 30 mm in diameter in the middle lobe. A definitive diagnosis of MEC requires bronchoscopic or transthoracic adequate biopsy [2]. In most cases, MEC is diagnosed at an early stage with low-grade features. Surgical resection is usually curative and this carries an excellent prognosis [5]. In contrast, high-grade tumors show a poor prognosis with an estimated 5-year survival of 31% [5]. In our case, there was no endobronchial lesion, so transthoracic biopsy was performed for diagnosis. The possibility of secondary MEC to a primary salivary tumor should be ruled out. The approach ranges from simple clinical examination of the head and neck to advanced imaging studies such as 2-(18F)-fluoro-2-deoxy-D-glucose positron emission tomography scan [7]. On positron emission tomography, any secondary tumor findings were not detected in our case. In conclusion, Mucoepidermoid tumors have to be treated by radical surgery with lymph node sampling and dissection. Patients with low grade tumors can be expected to be cured following complete resection. Careful histological typing plays a key role in prediction of late results, and further studies are needed.

References

1. Colby T, Koss M, Travis W. Tumors of salivary gland type. Tumors of the Lower Respiratory Tract. Atlas of Tumor Pathology; 3rd series, fascicle 13. 1995 Washington, DC Armed Forces Institute of Pathology:65–89.
2. Liu X, Adams AL. Mucoepidermoid carcinoma of the bronchus: a review. Arch Pathol Lab Med. 2007;131:1400–4.
3. Kim TS, Lee KS, Han J, et al. Mucoepidermoid carcinoma of the tracheobronchial tree: radiographic and CT findings in 12 patients. Radiology. 1999;212:643–8.

4. Yousem SA, Hochholzer L. Mucoepidermoid tumors of the lung. Cancer. 1987;60:1346–52.
5. Vadasz P, Egervary M. Mucoepidermoid bronchial tumors: a review of 34 operated cases. Eur J Cardiothorac Surg. 2000;17:566–9.
6. Li X, Zhang W, Wu X, et al. Mucoepidermoid carcinoma of the lung: common findings and unusual appearances on CT. Clin Imaging. 2012;36:8–13.
7. Chua AP, Joshi M, Mehta AC. Bronchial mucoepidermoid carcinoma. J Bronchol Intervent Pulmonol. 2009;16:39–40.