e-ISSN:2602-2079

Volume 3
Issue 10
2019

JOURNAL of Surgery and Medicine

International Medical Journal

JOSAM

Volume: 3 - Issue: 10

Contents

Case report

ULAKBİM Dergi Sistemleri (//dergipark.org.tr/en/)

J Surg Med. 2019;3(10):715-717.
DOI: 10.28982/josam.623768

Research article
Araştırma makalesi

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

Evaluation of the prevalence of gestational diabetes mellitus in Kayseri city hospital: A cross-sectional study

Kayseri şehir hastanesinde gestasyonel diabetes mellitus prevalansının değerlendirilmesi: Kesitsel bir çalışma

Mefkure Eraslan Şahin [1], İlknur Çöl Madendağ [1]

[1] Department of Obstetrics and Gynecology, Kayseri City Hospital, Kayseri, Turkey

ORCID ID of the author(s)
MEŞ: 0000-0001-6484-9132
İÇM: 0000-0001-6700-2236

Abstract

Aim: Gestational diabetes mellitus (GDM) is an important disease worldwide and its incidence is rising with increasing maternal age and obesity. The aim of this study is to investigate the prevalence of GDM in accordance with International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria by obtaining data from a single center in Kayseri.

Methods: All pregnant women between the ages of 18 and 45 who were referred to the clinic for routine pregnancy follow-up visits between January 2018-2019 at Kayseri City Hospital's Gynecology and Obstetrics Department were included in this study. Their records were obtained from the hospital registry and retrospectively examined. A single stage 75g oral glucose tolerance test (OGTT) was performed to all patients and IADPSG criteria were used for diagnosis.

Results: 2652 pregnant women were included in this study and screened for GDM with a single-step 75-g OGTT. The mean age of all pregnant women was 26.42 (22-31) years. The mean gravid, parity and gestational weeks at the time of testing were 3 (range 1-5), 3 (range 1-4), 26 (range 24-28), respectively. The prevalence of GDM, detected in 424 of 2652 patients, was 16% (424/2652).

Conclusion: The prevalence of GDM among pregnant women who were referred to our clinic for routine pregnancy follow-up was 16% according to the IADPSG criteria, as determined with a single-step 75-g OGTT.

Keywords: Gestational diabetes mellitus, Prevalence, Kayseri

Öz

Amaç: Gestasyonel diyabet (GDM) dünya genelinde önemli bir sağlık problem olup obezitenin ve maternal yaşın artmasıyla sıklığı giderek artmaktadır. Bu çalışmada, Kayseri'deki tek bir merkezden veri kullanarak International Association of Diabetes and Pregnancy Study Group (IADPSG) kriterlerine göre GDM prevalansını araştırmayı amaçladık.

Yöntemler: Ocak 2018 ile Ocak 2019 arasında, 18-45 yaş arası, 24-28. gebelik haftaları arasında, Kayseri Şehir Hastanesi Kadın Hastalıkları ve Doğum Kliniğinde rutin gebelik takibi için başvuran tüm gebeler retrospektif olarak bilgisayar hastane sistemi kayıtları ile incelendi. Hastalar tek aşamalı 75 g oral glikoz tolerans testi (OGTT) ile tarandı ve tanı için IADPSG kriterleri kullanıldı.

Bulgular: Çalışmaya toplam 2652 gebe dahil edildi ve tek adımlı 75 g OGTT ile GDM taraması yapıldı. Tüm gebelerin yaş ortalaması 26,42 (22-31) idi. Ortalama gravid değeri 3 (1-5 arasında), ortalama parite 3 (1-4 arasında) ve test sırasındaki ortalama gebelik haftası 26 idi (24-28 aralığı). GDM 2652 hastanın 424'ünde tespit edildi. GDM prevalansı %16 olarak bulundu (424/2652).

Sonuç: Kliniğimize başvuran gebelerde, tek adımlı 75 g OGTT ile IADPSG kriterlerine göre GDM prevalansı %16 olarak bulundu.

Anahtar kelimeler: Gestasyonel diabetes mellitus, Prevalans, Kayseri

Corresponding author / Sorumlu yazar:
Mefkure Eraslan Şahin
Address / Adres: Kayseri Şehir Hastanesi, Kadın Hastalıkları ve Doğum Bölümü, Kayseri, Türkiye
e-Mail: mefkureee@hotmail.com

Ethics Committee Approval: The study was approved by the Erciyes University Ethics Committee (Approval no: 2019/616).
Etik Kurul Onayı: Çalışma Erciyes Üniversitesi Etik Kurulu tarafından onaylandı (Onay no: 2019/616).

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.

Published: 10/4/2019
Yayın Tarihi: 04.10.2019

How to cite / Atıf için: Şahin ME, Madendağ İÇ. Evaluation of the prevalence of gestational diabetes mellitus in Kayseri city hospital: A cross-sectional study. J Surg Med. 2019;3(10):715-717.

Introduction

Gestational diabetes mellitus (GDM) does not usually begin until the second trimester of pregnancy, but it is extremely common and continues throughout pregnancy once it begins. Glucose intolerance and elevated blood glucose levels are key to the diagnosis of this pregnancy complication [1,2].The increase in obesity and older pregnancy age contribute to GDM's increasing prevalence, and public health systems bear this burden [3]. GDM may cause various complications for the offspring, including neonatal hypoglycemia, stillbirth, preterm birth, macrosomia, shoulder dystocia, and affect the mother in many ways, ranging from hypoglycemia to a need for caesarean section [4]. Besides these risks associated with pregnancy and delivery, women with GDM are also at increased risk for type 2 diabetes and cardiovascular diseases later in life [5]. The women at highest risk for GDM are those with a family history of type 2 diabetes, a previous personal history of GDM or a macrosomic infant, obesity, and those of advanced age [6].

In the literature, the prevalence of GDM varies between 1.2 and 27.9% in different studies conducted regionally in Turkey [7-20]. Since there has been no multicenter study in our country, there is no data on the national prevalence of GDM today. The use of different diagnostic criteria may be associated with the detection of a wide prevalence range. For this reason, we aimed to investigate the prevalence of GDM in accordance with the criteria of International Association of Diabetes and Pregnancy Study Groups (IADPSG) by using the data from a single center in Kayseri, which is a reference center in Turkey.

Materials and methods

Pregnant women between the ages of 18 and 45 who were referred to the clinic for routine pregnancy follow-up visits between January 2018 and 2019 at Kayseri City Hospital's Gynecology and Obstetrics Department were included in this study. Their records were obtained from the hospital registry and retrospectively examined. All research was conducted in accordance with the Helsinki Declaration, and ethics approval was obtained from Erciyes University Ethics Committee (No: 2019/616). Patients with previously diagnosed diabetes mellitus (type 1 and type 2), those with a history of endocrine diseases (Cushing's disease, Addison's disease, pituitary failure, acromegaly, etc.) or drug use that could affect blood glucose levels were excluded from the study. The date of last menstrual period was used to determine the gestational week of the patients. The gestational age of any patient who did not know the date of her last menstrual period was calculated according to ultrasonographic measurements performed in the first trimester. Patients were screened with single-stage 75-g OGTT, and the IADPSG criteria were used for diagnosis.

Inclusion criteria included the following risk factors for gestational diabetes: diabetes mellitus in the family, particularly in first degree relatives, a body mass index (BMI) >30 kg/m2 or excessive gestational weight gain, gestational diabetes or birth of a macrosomic baby >4.1 kg, a syndromic infant, unexplained perinatal loss in a previous pregnancy, a history of impaired glucose tolerance, glycosuria during prenatal examination, and conditions leading to diabetes, such as metabolic syndrome, polycystic ovary syndrome or actual use of glucocorticoids [21] Following 12 hours of fasting, the plasma glucose of the patients were measured, after which 75 mg glucose was ingested orally by the patients. Venous blood samples were obtained one and two hours later. The upper limit of plasma glucose values for fasting state, and at the first- and second hours following ingestion of glucose were 91, 179 and 152 mg/dL, respectively (Table 1) [22]. Any value crossing the threshold was considered positive. GDM prevalence was determined according to these one-step screening test results.

Table 1: Proposed diagnostic criteria for gestational diabetes mellitus*

Status	Plasma or serum glucose levels (mg/dl)
Fasting	92
1 hour	180
2 hours	153

*Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, et al. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. International Association of Diabetes and Pregnancy Study Groups Consensus Panel. Diabetes Care.2010;33:676–82.

Statistical analysis

For statistical analysis of the study data, PASW Statistics 18 (SPSS version 18, 2009, Chicago, IL, USA) was used, and percentages were determined. Data were expressed as mean (standard deviation), median (25-75%), or n (%). Descriptive statistics was performed.

Results

Two thousand, six hundred and fifty-two pregnant women were included in this study and screened for GDM with a single-step 75-g OGTT. The mean age of all pregnant women was 26.42 (22-31) years. The mean gravid, parity and gestational weeks at the time of testing were 3 (range 1-5), 3 (range 1-4), 26 (range 24-28), respectively. The demographic data, fasting, 60th minute and 120th minute plasma glucose levels are presented in Table 2.

Table 3 shows the prevalence of GDM and the higher rates of fasting, 60-min, and 120-min plasma glucose levels. The prevalence of GDM, detected in 424 of 2652 patients, was 16% (424/2652).

Table 2: Mean age, fasting, 60-min, and 120-min. plasma glucose levels of the patients

	Mean (SD)	25-75 percentile
Maternal age	26.42 (6.02)	(22-31)
Fasting plasma glucose (mg/dL)	79.6 (12.35)	(74-84)
60 min plasma glucose (mg/dL)	130.8 (36.93)	(106-153)
120 min plasma glucose (mg/dL)	104.8 (31.40)	(86-119)

Table 3: Prevalence of GDM and the higher rates of fasting, 60-min and 120-min plasma glucose levels

	Number of patients	%
Fasting plasma glucose ≥92 mg/dL	232/2652	8.7
60-min plasma glucose ≥180 mg/dL	242/2652	9.1
120-min plasma glucose ≥153 mg/dL	158/2652	6
GDM prevalence	424/2652	16

Discussion

There is no clear international consensus on GDM screening and diagnosis. The World Health Organization and the Endocrine Society suggest a one-step approach using the IADPSG diagnostic criteria. The American College of Obstetricians and Gynecologists (ACOG) and the National Institutes of Health (NIH) suggest a two-step approach, while The American Diabetes Association (ADA) has stated that any one of the one- or two-step approaches may be used. In the literature, the prevalence of GDM in our country is reported as 1.2-27.9% [6-19]. In our study, GDM screening with a single step 75g OGTT revealed that the prevalence in Kayseri was 16%

according to the IADPSG criteria. The difference in GDM prevalence in different regions of our country may be caused by differences in dietary groups, nutritional status, age groups, and diverse diagnostic tests.

Although a large amount of research was conducted in central Anatolia in Turkey, the vast majority have been conducted in Ankara. In a study conducted by Altay et al. [14] with 6909 pregnant women in 2010, the prevalence of GDM was determined as 10.4%. They used two-step screening according to the National Diabetes Data Group (NDDG) criteria. Ozdemir et al. [16] prospectively researched GDM prevalence and found it to as 8.4% according to single-step screening and IADPSG criteria. The prevalence of GDM among 1434 pregnant women by Karcaaltıncaba et al. [18] revealed it as 11.1% according to IADPSG criteria with single-step screening. Recently, Ozgu et al. [19] found that the prevalence of GDM was 21% according to IADPSG criteria with single-step screening. The prevalence of GDM is increasing within Ankara, another reference city for the Central Anatolia region. In Kayseri, two-step screening of pregnant women in 2008 revealed that the prevalence of GDM, according to the NDDG criteria, was 6.2% [10]. The single-step GDM screening performed in accordance with the IADPSG criteria in the USA revealed 18% prevalence, which was at least

twice as high as what was calculated in two-step screening following ACOG recommendations [23]. The high prevalence of GDM in Kayseri may be explained by the usage of the single-step screening method. Many risk factors, including obesity, increased urbanization, sedentary lifestyle, and advanced maternal age increase GDM prevalence. It has been shown that the prevalence of GDM in the province of Kayseri is higher than the other central regions of Turkey. GDM is an important health problem causing both maternal and perinatal complications with increasing incidence in our country and all over the world. This situation calls for immediate action: Improving maternal nutrition and exercise may decrease the rate of death of both mothers and infants due to GDM.

Limitations

The evaluation of the prevalence of GDM in a single center is the main limitation of our study, despite the fact the Kayseri City Hospital is a reference hospital. Additionally, we did not compare maternal demographic and delivery outcomes between GDM positive and negative groups, which is another limitation. Further studies are needed.

Conclusion

The prevalence of GDM was 16% according to the IADPSG criteria with a single-step 75-g OGTT in pregnant women in Kayseri.

References

1. Sahin E, Col Madendag I, Sahin ME, Madendag Y, Acmaz G, Muderris, II. Effect of vitamin D deficiency on the 75 g oral glucose tolerance test screening and insulin resistance. Gynecol Endocrinol. 2019;35(6):535-8. Epub 2019/01/10. doi: 10.1080/09513590.2018.1554038.
2. Aydın A, Atadağ Y, Öksüz A, Kaya D, Aydın NE. Comparison of the effects of impaired fasting glucose and impaired glucose tolerance on diabetic development risks on HbA1c levels: A retrospective study. J Surg Med. 2008;1(1):1-4.
3. American Diabetes A. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2019. Diabetes Care. 2019;42(Suppl 1):S13-S28. Epub 2018/12/19. doi: 10.2337/dc19-S002.
4. Metzger BE, Coustan DR, Trimble ER. Hyperglycemia and Adverse Pregnancy Outcomes. Clin Chem. 2019;65(7):937-8. Epub 2019/04/19. doi: 10.1373/clinchem.2019.303990.
5. Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet. 2009;373(9677):1773-9. Epub 2009/05/26. doi: 10.1016/S0140-6736(09)60731-5.
6. Reece EA, Leguizamon G, Wiznitzer A. Gestational diabetes: the need for a common ground. Lancet. 2009;373(9677):1789-97. Epub 2009/05/26. doi: 10.1016/S0140-6736(09)60515-8.
7. Erem C, Cihanyurdu N, Deger O, Karahan C, Çan G, Telatar M. Screening for gestational diabetes mellitus in northeastern Turkey (Trabzon City). European journal of epidemiology. 2003;18(1):39-43.
8. Tanir H, Sener T, Gürer H, Kaya M. A ten-year gestational diabetes mellitus cohort at a university clinic of the mid-Anatolian region of Turkey. Clinical and experimental obstetrics & gynecology. 2005;32(4):241-4.
9. Akış N, Pala K, Seçkin R. Gestational diabetes mellitus prevalence and related risk factors. Uludag Medical Journal. 2008;34(3):93-6.
10. Gürel C, Özgün M, Batukan C, Başbuğ M. Prevalence of gestational diabetes among pregnant women attending Erciyes University Medical Faculty. Erciyes Medical Journal. 2009;31(4):323-30.
11. Karcaaltincaba D, Kandemir O, Yalvac S, Güvendag-Guven S, Haberal A. Prevalence of gestational diabetes mellitus and gestational impaired glucose tolerance in pregnant women evaluated by National Diabetes Data Group and Carpenter and Coustan criteria. International Journal of Gynecology & Obstetrics. 2009;106(3):246-9.
12. Akbay E, Torun Sİ, Yalçınkaya H, Uzunçakmak C, Toklucu G. Prevalence of gestational diabetes among pregnant women attending in MD SadiKonuk Training and Research Hospital. TürkiyeKlinikleriJinekolojiObstetrik. 2010;20(3):170-5.
13. Özyurt R, Aşıcıoğlu O, Gültekin T, Güngördük K, Boran B. The Prevelance of Gestational Diabetes Mellitus In Pregnant Women Who Administered to İstanbul Teaching and Research Hospital Obstetrics and Gynecology Department. İstanbul Kanuni Sultan Süleyman Tip Dergisi (IKSST). 2013;5(1):7-12.
14. Altay MM, Özdoğan S, Tohma A, Esin S, Erol O, Gelişen O, et al. Can the 3rd Hour Value of 100 g Oral Glucose Tolerance Test Be Ignored in the Diagnosis of Gestational Diabetes Mellitus? Gynecology Obstetrics & Reproductive Medicine. 2016;19(3):157-61.
15. Sevket O, Ates S, Uysal O, Molla T, Dansuk R, Kelekci S. To evaluate the prevalence and clinical outcomes using a one-step method versus a two-step method to screen gestational diabetes mellitus. The Journal of Maternal-Fetal & Neonatal Medicine. 2014;27(1):36-41.
16. Özdemir Ö, Sari ME, Ertuğrul FA, Şakar VS, Özcanli G, Atalay C. Ankara numuneeğitimvearaştırmahastanesikadınhastalıklarıvedoğumkliniğinebaşvurangebelerdegestasyoneldiyabetsıklığı. Journal of Clinical Obstetrics & Gynecology. 2014;24(1):24-9.
17. Balık G, Şahin SB, TekinYB, Şentürk Ş, Kağıtcı M, Şahin FK. The prevalence of gestational diabetes mellitus in pregnants who applied to the maternity outpatient clinic of a university hospital. Ege Journal of Medicine. 2016;55(2):55-8.
18. Karcaaltincaba D, Calis P, Ocal N, Ozek A, AltugInan M, Bayram M. Prevalence of gestational diabetes mellitus evaluated by universal screening with a 75-g, 2-hour oral glucose tolerance test and IADPSG criteria. International Journal of Gynecology & Obstetrics. 2017;138(2):148-51.
19. Ozgu-Erdinc AS, SertUY, BuyukGN, Engin-Ustun Y. Prevalence of gestational diabetes mellitus and results of the screening tests at a tertiary referral center: A cross-sectional study. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2019;13(1):74-7.
20. Gürlek B, Kale İ. RizeİlindeGestasyonel Diabetes Mellitus Prevalansı. Jinekoloji-ObstetrikveNeonatolojiTıpDergisi. 2019;16(1).
21. Madendag Y, Sahin E, Madendag Col I, Eraslan SM, Tayyar A, Ozdemir F, et al. The effect of hyperemesis gravidarum on the 75 g oral glucose tolerance test screening and gestational diabetes mellitus. The Journal of Maternal-Fetal & Neonatal Medicine. 2018;31(15):1989-92.
22. International Association of D, Pregnancy Study Groups Consensus P, Metzger BE, Gabbe SG, Persson B, Buchanan TA, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010;33(3):676-82. Epub 2010/03/02. doi: 10.2337/dc09-1848.
23. Practice CoO. Practice bulletin no. 137: gestational diabetes mellitus. Obstet Gynecol. 2013;122:406-16.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):718-721.
DOI: 10.28982/josam.631161

Research article
Araştırma makalesi

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

Effect of peri-operative milrinone on pulmonary artery pressure in patients undergoing mitral valve replacement

Mitral kapak değişimi yapılan hastalarda milrinon kullanımının pulmoner basınç üzerine etkisi

Ahmet Dolapoğlu [1], Eyüp Avcı [2]

[1] Department of Cardiovascular Surgery, Medical School, Balikesir University, Balikesir Turkey
[2] Department of Cardiology, Medical School, Balikesir University, Balikesir Turkey

ORCID ID of the author(s)
AD: 0000-0001-9161-2632
EA: 0000-0002-7790-8450

Abstract

Aim: Increased pulmonary artery pressure is associated with higher surgical risk in patients undergoing mitral valve replacement. The aim of this study was to investigate the effect of milrinone on the pulmonary artery pressures of patients with mitral valve disease (stenosis or regurgitation) who underwent mitral valve replacement surgery.

Methods: In this case-control study, 48 patients with mitral valve disease who underwent mitral valve replacement surgery were included. The patients were divided into a control group of 30, who were not administered milrinone, and a study group of 18 who received milrinone perioperatively. Systolic pulmonary artery pressures (SPAP), left ventricle ejection fractions (LVEF) and the following postoperative outcomes were recorded: low cardiac output syndrome, stroke, renal failure, bleeding, ventricular arrhythmia and mortality occurring within 30 days of surgery either in or out of the hospital.

Results: In the study group, preoperative LVEFs and postoperative low cardiac output syndrome were lower (72.0 (6.1) vs 62.5(8.4) $P<0.001$ and $P=0.007$, respectively), SPAPs were higher (45.50 (7.0) vs 55.06 (5.5), $P<0.001$), and length of stay in intensive care unit was significantly shorter (4.7 (2.2) vs 3.2 (0.5), $P=0.008$). Also, reduction in both postoperative SPAP and 30-day SPAP were significantly higher [-11.40(-13.25-(-8.63)) vs -4.42(-5.89-(-2.80)), $P<0.001$; -13.6(-15.6-(-9.75)) vs -5.56 (-7.20-(-3.30)), $P<0.001$, respectively].

Conclusion: We found that using perioperative milrinone reduces the systolic pulmonary artery pressure and lowers the rate of low cardiac output syndrome. Milrinone can be used as an effective therapy to reduce to pulmonary pressure in patients with pulmonary hypertension undergoing mitral valve replacement surgery.

Keywords: Mitral valve disease, Pulmonary artery pressure, Mitral valve replacement

Öz

Amaç: Pulmoner arter basıncının yüksek olduğu durumlarda mitral kapak değişimi operasyonlarında cerrahi risk yükselmektedir. Bu çalışmada mitral kapak hastalığı nedeniyle cerrahi tedavi uygulanan hastalarda milrinon kullanımının pulmoner basınlar üzerine etkisini araştırmayı amaçladık.

Yöntemler: Mitral kapak hastalığı nedeniyle kapak değişimi uygulanan 48 hasta çalışmaya dahil edildi. Hastalar cerahide milrinon kullanımına göre milrinon kullanılan (n=18) ve milrinon kullanılmayan (n=30) olarak ikiye gruba ayrıldı. Cerrahi sonrası 30 günlük süre içinde sistolik pulmoner arter basıncı ve sol ventrikül ejeksiyon fraksiyonları ile birlikte cerrahi sonrası mortalite, düşük kardiyak debi sendromu, inme, böbrek yetmezliği, kanama ve ventrikül aritmileri kaydedildi.

Bulgular: Milrinon kullanan grupta cerrahi öncesi sol ventrikül ejeksiyon fraksiyonu kullanmayan gruba göre daha düşükken (72,0 (6,1) vs 62,5 (8,4) $P<0,001$) sistolik pulmoner arter basınçları daha yüksekti (45,50 (7,0), 55,06 (5,5), $P<0,001$). Cerrahi sonrası milrinon kullanılan grupta düşük kardiyak debi sendromu daha az görülürken ($P=0.007$), yoğun bakımda kalış süreleri kullanmayan gruba göre daha kısaydı (4,7 (2,2) vs 3,2 (0,5), $P=0,008$). Hem cerrahi sonrası hem de 30. gün sistolik pulmoner arter basınçlarında ki düşme değerleri milrinon kullanılan grupta istatistik açıdan daha anlamlıydı [-11,40(-13,25-(-8,63)) vs -4,42(-5,89-(-2,80)), $P<0,001$; -13,6(-15,6-(-9,75)) vs -5,56 (-7,20-(-3,30)), $P<0,001$, sırasıyla].

Sonuç: Çalışmamızda milrinon kullanımı cerrahi sonrası pulmoner basınçları düşürürken düşük kardiyak debi oluşumun azalttığı gözlenmiştir. Bu sonuca göre pulmoner arter hipertansiyonu olan ve mitral kapak değişimi yapılacak hastalarda milrinon kullanımının pulmoner basınçları düşürmede etkili bir tedavi seçeneği olduğunu düşünmekteyiz.

Anahtar kelimeler: Mitral kapak hastalığı, Pulmoner arter basıncı, Mitral kapak değişimi

Corresponding author / Sorumlu yazar:
Ahmet Dolapoğlu
Address / Adres: Balikesir Universitesi Tip Fakultesi Hastanesi, Balikesir, Türkiye
e-Mail: ahmetdolapoglu@yahoo.com

Ethics Committee Approval: The study was approved by the Ethics Committee of Balıkesir University Medical School (date: 25.09.2019; no: 2019/128).
Etik Kurul Onayı: Çalışma, Balıkesir Üniversitesi Tıp Fakültesi Etik Kurulu tarafından onaylandı (tarih: 25.09.2019; no: 2019/128).

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.

The study was previously presented as an oral presentation in 2th National ADHAD Congress / Pulmoner Hypertension 2018, at Bodrum, Antalya, Turkey, 26-29 April 2018 with the number of SS30.

Published: 10/14/2019
Yayın Tarihi: 14.10.2019

How to cite / Atıf için: Dolapoğlu A, Avcı E. Effect of peri-operative milrinone on pulmonary artery pressure in patients undergoing mitral valve replacement. J Surg Med. 2019;3(10):718-721.

Introduction

Increased systolic and diastolic pulmonary pressures are frequently seen in mitral valve disease [1]. Pulmonary hypertension (PHT) occurs due to the retrograde transmission of increased left atrial pressure. In patients with mitral valve disease, PHT indicates compensated heart failure along with left ventricular dysfunction.

Higher pulmonary artery pressure is associated with increased risk of mortality and morbidity during mitral valve surgery [2]. Medical options to decrease pulmonary vascular resistance in PHT patients undergoing cardiac surgery include nitric oxide, sildenafil, and isoproterenol, none of which have long-lasting effects [3].

Milrinone, a phosphodiesterase inhibitor, is commonly used in cardiopulmonary bypass during the weaning process to decrease the pulmonary vascular resistance [4]. It exerts inotropic effects by increasing myocardial contractility. Milrinone's advantages include lowering coronary artery resistance and increasing coronary perfusion.

In this study we aimed to investigate the effect of milrinone on postoperative outcomes in patients with mitral valve disease undergoing mitral valve replacement.

Materials and methods

We identified 48 patients with mitral valve disease (regurgitation or stenosis) who electively underwent mitral valve replacement surgery from September 2015 to July 2019. Clinical characteristics, laboratory findings, surgical details and postoperative outcomes were obtained from the patients' files. Patients with a history of kidney disease requiring dialysis, right-heart failure, poor morbidity, patients in critical preoperative state, those who had active endocarditis and concomitant aortic valve disease requiring surgical intervention were excluded from the study.

All patients were divided into two groups according to perioperative milrinone usage. The study group consisted of 18 patients who received milrinone and the control group comprised 30 patients who did not. The following postoperative outcomes were recorded: low cardiac output syndrome, stroke, renal failure, bleeding, ventricular arrhythmia, and mortality occurring within 30 days of surgery either in or out of hospital. Additionally, left ventricle ejection fraction (LVEF) and systolic pulmonary artery pressure (SPAP) within the postoperative period were recorded just before discharge from hospital-between the 5^{th}-7^{th} post-operative days and during the first month follow-up.

Echocardiographic analysis

All patients were examined with two-dimensional trans-thoracic echocardiography (TTE) before and after their surgical procedures. TTE was performed pre-operatively, between the 5^{th} and 7^{th} postoperative days (just before discharge from hospital) and one month following the surgery. A modified Simpson`s method was used to assess left-ventricular ejection fractions and Bernoulli equation by Doppler was used to measure pulmonary artery systolic pressures.

30-day mortality was considered as death within 30 days of surgery. Postoperative stroke was defined as newly occurring neurological deficit with radiological confirmation. Renal failure was defined as deterioration of kidney function requiring hemodialysis. Ventricular arrhythmia was occurrence of any ventricular arrhythmias which needed medical or electrical cardioversion, i.e., ventricular tachycardia and ventricular fibrillation. Low output syndrome was defined as a decrease in systemic perfusion secondary to myocardial dysfunction requiring inotropic agents other than milrinone or intra-aortic balloon pump implantation during the peri-operative period. Postoperative bleeding was massif drainage of blood requiring surgical revision. Length of stay (LOS) was defined by days spent in the intensive care unit (ICU) and in the hospital after surgery.

Surgical technique

All mitral valve replacement (MVR) procedures were performed with median sternotomy. Cardiopulmonary bypass was established with ascending aortic and bicaval cannulation. Cold blood cardioplegia was administered to stop and protect the heart. The mitral valve was exposed through a left atriotomy in the interatrial groove, and the anterior and posterior leaflets were excised. A mechanical or bioprosthetic valve was then implanted according to the patient's condition. Concomitant procedures included coronary artery bypass graft (CABG), cryo-ablation with maze procedure and tricuspid annuloplasty depending on indication.

Milrinone usage

All patients with high systolic pulmonary artery pressures received intravenous milrinone. A loading dose of 25 μgr/kg milrinone during weaning from cardiopulmonary bypass was followed by a maintenance dose of 0.25 μgr/kg/min administered for 24 hours following the operation.

Statistical analysis

Statistical tests were performed with SPSS version 16 (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean (standard deviation), and categorical variables were shown with percentages. Either the Student's t-test or the Mann-Whitney U test was used to compare parametric values between the two groups. Chi-square test was used to compare categorical variables.

Results

Among 48 patients, 18 (37.5%) were males and 30 (62.5%) were females. Table 1 shows the demographic, clinical and laboratory characteristics of the population. Preoperative LVEFs were lower (72.0 (6.1) vs 62.5(8.4) $P<0.001$) and SPAPs were higher in the study group (45.50 (7.0) vs 55.06 (5.5), $P<0.001$). The operative details of the patients, which are presented in Table 2, did not differ among groups.

While mortality and other complications were similar, postoperative low cardiac output syndrome was significantly lower ($P=0.007$) and length of stay in the intensive care unit was significantly shorter in the study group (4.7 (2.2) vs 3.2 (0.5), $P=0.008$).

Reductions in both postoperative SPAP and 30-day SPAPs were more significant in patients who received milrinone [-11.40(-13.25-(-8.63)) vs -4.42(-5.89-(-2.80)), $P<0.001$; -13.6(-15.6-(-9.75)) vs -5.56 (-7.20-(-3.30)), $P<0.001$, respectively] (Table 3).

Table 1: Baseline characteristics of the study population

Variable	Control group (n=30)	Study group (n=18)	*P*-value
Age (years)	63.3 (9)	64.6 (11)	0.654
Female n (%)	18 (60%)	12 (67%)	0.644
Male n (%)	12 (40%)	6 (33%)	0.644
History of COPD n (%)	6 (20%)	2 (11%)	0.424
Hypertension n (%)	12 (40%)	10 (56%)	0.295
Diabetes mellitus n (%)	5 (17%)	4 (22%)	0.633
Current smoking n (%)	9 (30%)	2 (11%)	0.132
Type of additional surgery			
Ablation n (%)	3 (10%)	4 (22%)	0.245
Tricuspid annuloplasty	5 (17%)	5 (28%)	0.359
CABG	4 (13%)	4 (22%)	0.424
Preop-NYHA > 2 n (%)	8 (27%)	7 (39%)	0.376
Postop-NYHA > 2 n (%)	1 (3%)	1 (6%)	0.728
Postop-30-day-NYHA > 2 n (%)	3 (11%)	1 (6%)	0.545
Post-op LCOS (%)	22 (73%)	6 (33%)	0.007
Postop-Ventricular Tachycardia n (%)	3 (10%)	3 (17%)	0.499
30-day mortality n (%)	2 (7%)	1(6%)	0.878
Dialysis requirement (%)	3 (10%)	1 (7%)	0.590
Stroke n (%)	1 (3%)	1 (6%)	0.709
Postoperative bleeding n (%)	1 (3%)	1 (6%)	0.709

COPD: Chronic obstructive pulmonary disease, CABG: Coronary artery bypass graft, LCOS: Low cardiac output syndrome, NYHA: New York Heart Association

Table 2: The laboratory findings of study population

Variable	Control group (n=30)	Study group (n=18)	*P*-value
BMI ((kg/m^2))	22.2 (1.4)	22.7 (1.7)	0.321
SCr (mg/dl)	1.06 (0.2)	1.04 (0.2)	0.825
Glucose (mg/dl)	107.2 (15.4)	105.6 (12.4)	0.712
WBC ($\times 10^3/\mu L$)	7.42 (1.0)	7.84 (1.5)	0.242
Hemoglobin (g/dl)	11.3 (1.3)	11.9 (1.8)	0.208
CPB time (min)	97 (15)	101 (17)	0.416
X-Clamp time (min)	73 (11)	75 (10)	0.675
Los ICU	4.7(2.2)	3.2 (0.5)	0.008
Los overall	11.8 (3.9)	9.6 (1.4)	0.024

BMI: Body mass index, SCr; Serum creatinine at admission, WBC: White blood cell, CPB: Cardiopulmonary bypass, ICU: Intensive care unit, Los: Length of stay

Table 3: Echocardiographic findings of study population

Variable	Control group (n=30)	Study group (n=18)	*P*-value
Preoperative LVEF (%)	50.40 (4.8)	44.22 (6.2)	<0.001
Postoperative LVEF (%)	43.07 (3.9)	42.60 (4.9)	0.716
30^{th} day LVEF (%)	49.48 (2.7)	47.24 (4.5)	0.046
Preoperative PASP (mmHg)	45.50 (7.0)	55.06 (5.5)	<0.001
Postoperative PASP (mmHg)	41.25 (4.8)	44.00 (3.6)	0.048
30. day PASP (mmHg)	40.4 (3.8)	42.29 (2.7)	0.083
ΔLVEF* (postop-preop)	-7.3 (-10.2-(4.4))	-2.4 (-3.6-(-1.4))	0.001
ΔLVEF* (30^{th} day-preop)	-7.3 (-10.2-(4.4))	-2.4 (-3.6-(-1.4))	0.001
ΔLVEF* (30^{th} day-postop)	5.8 (4.2-8.8)	4.6 (3.4-5.8)	0.250
ΔPASP* (postop-preop)	-4.42(-5.89-(-2.80))	-11.40(-13.25-(-8.63))	<0.001
ΔPASP* (30^{th} day-preop)	-5.56 (-7.20-(-3.30))	-13.6(-15.6-(-9.75))	<0.001
ΔPASP* (30^{th} day-postop)	-1.17(-1.92-(-0.30))	-1.67(-2.81-(-0.36))	0.746

LVEF: Left ventricle ejection fraction, PASP: Pulmonary artery systolic pressure, these values were presented by median with inter-quartile range (25th and 75th percentile)

Discussion

This study showed that perioperative milrinone administration reduces postoperative SPAP and LCOS occurrence in patients with pulmonary hypertension undergoing mitral replacement surgery.

Pulmonary hypertension is a common sequel of mitral valve disease and is associated with poor prognosis during surgical repair or replacement [5,6]. Chronically elevated left atrial pressure causes alveolar stress, and pulmonary vascular remodeling due to elevation of pulmonary vascular resistance accounts for the pathophysiological mechanism underlying PHT in mitral disease [1]. Increased pulmonary vascular resistance (PVR) is detrimental to cardiac output in postoperative cardiac-surgery patients.

The treatment of increased pulmonary vascular resistance has not been fully established due to the lack of selectivity of drugs for pulmonary vasculature. Many agents, such as dobutamine, norepinephrine, levosimendan, nitric oxide and nitroglycerin, were used to relieve pulmonary hypertension during cardiovascular surgery [7-10]. However, these inotropic drugs have possible systemic or cardiac side effects, like arrhythmia and increased myocardial oxygen consumption resulting in cardiac ischemia and renal failure [11,12].

Milrinone, a phosphodiesterase inhibitor, exerts positive inotropic effects by increasing cyclic adenosine monophosphate in the myocardium, thereby increasing stroke volume. It is widely used in cardiac surgery during the weaning process from cardiopulmonary bypass [13]. The drug is also commonly used in congenital cardiac surgery or in patients with heart failure [14,15]. Milrinone is also a potent pulmonary vasodilator that reduces pulmonary vascular resistance, for which reason it is particularly preferred in patients with low cardiac output and higher pulmonary artery pressure undergoing cardiac surgery.

Only a couple of studies have previously examined milrinone in pulmonary hypertension occurring during mitral valve surgery. Oztekin et al. [16] reported that using milrinone caused significant reduction in pulmonary artery pressure, central venous pressure and pulmonary capillary wedge pressure in patients with mitral valve stenosis and PHT undergoing mitral valve replacement. They also found that it facilitated weaning from cardiopulmonary bypass with less side effects. Wang et al. [17] showed that mean pulmonary artery pressure and PVR were significantly reduced by the administration of milrinone in the same population. In our study, postoperative SPAP had similarly reduced in the study group at the first postoperative week and month.

Previous studies have shown that compared with dobutamine, milrinone causes greater reduction in left and right ventricular filling pressures owing to greater reduction in vascular resistance, which makes it superior to dobutamine in the treatment of low cardiac output syndrome following cardiac surgery [18]. We similarly found that the occurrence of postoperative LCOS reduced with milrinone administration.

In our study, pre-operative LVEF were lower and SPAP was higher in patients who received milrinone. Although postoperative mortality and morbidity were similar in both groups, we found that in the study group, systolic pulmonary artery pressures reduced significantly during the postoperative week and remained low at one-month follow up.

Limitation

The retrospective and unicentered nature as well as the small sample size were the primary limitations of this study. The exact measurement of the pulmonary artery pressure is performed by right heart catheterization; however, we assessed pulmonary pressures with echocardiography. Further research is needed to evaluate the effects of milrinone following MVR in patients with mitral valve disease.

Conclusion

Milrinone effectively reduces SPAP and LCOS and appears to be an alternative promising approach in addressing the problem of pulmonary hypertension in patients undergoing mitral valve replacement surgery.

References

1. Maeder MT, Weber L, Buser M, Gerhard M, Haager PK, Maisano F, et al. Pulmonary Hypertension in Aortic and Mitral valve Disease. Front Cardiovasc Med. 2018;5:40.
2. Ghoreishi M, Evans CF, DeFilippi CR, Hobbs G, Young CA, Griffith BP, et al. Pulmonary hypertension adversely affects short- and long-term survival after mitral valve operation for mitral regurgitation: implications for timing of surgery. J Thorac Cardiovasc Surg. 2011;142(6):1439-52.
3. Hernandez AF, Li S, Dokholyan RS, O'Brien SM, Ferguson TB, Peterson ED. Variation in perioperative vasoactive therapy in cardiovascular surgical care: data from the society of thoracic surgeons. Am Heart J. 2009;158:47–52.

4. Zangrillo A, Biondi-Zoccai G, Ponschab M, Greco M, Corno L, Covello RD, et al. Milrinone andmortality in adult cardiac surgery:a meta-analysis. J Cardiothorac Vasc Anesth. 2012;26:70–7.
5. Le Tourneau T, Richardson M, Juthier F, Modine T, Fayad G, Polge AS, et al. Echocardiography predictors and prognostic value of pulmonary artery systolic pressure in chronic organic mitral regurgitation. Heart. 2010;96(16):1311-7.
6. Alsancak Y, Gurbus AS, Duzenli MA.Transcatheter mitral valve repair and replacement; current therapies and general evaluation of new approaches. J Surg Med. 2017;1(3):56-8.
7. Landoni G, Lomivorotov VV, Alvaro G, Lobreglio R, Pisano A, Guarracino F, et al. Levosimendan for hemodynamic support after cardiac surgery. N Engl J Med. 2017;376:2021–31.
8. Feneck RO, Sherry KM, Withington PS, Oduro-Dominah A, European Milrinone Multicenter Trial Group. Comparison of the hemodynamic effects of milrinone with dobutamine in patients after cardiac surgery. J Cardiothorac Vasc Anesth. 2001;15:306–15.
9. Carmona MJ, Martins LM, Vane MF, Longo BA, Paredes LS, Malbouisson LM. Comparison of the effects of dobutamine and milrinone on hemodynamic parameters and oxygen supply in patients undergoing cardiac surgery with low cardiac output after anesthetic induction. Rev Bras Anestesiol. 2010;60:237–46.
10. Sardo S, Osawa EA, Finco G, Gomes Galas FRB, de Almeida JP, Cutuli SL, et al. Nitric Oxide in Cardiac Surgery: A Meta-Analysis of Randomized Controlled Trials. J Cardiothorac Vasc Anesth. 2018;32(6):2512-9.
11. Indolfi C, Piscione F, Perrone-Filardi P, Prastaro M, Di Lorenzo E, Sacco L, et al. Inotropic stimulation by dobutamine increases left ventricular regional function at the expense of metabolism in hibernating myocardium. Am Heart J. 1996;132:542–9.
12. Schulz R, Rose J, Martin C, Brodde OE, Heusch G. Development of short-term myocardial hibernation. its limitation by the severity of ischemia and inotropic stimulation. Circulation. 1993;88:684–95.
13. Levy JH, Bailey JM, Deeb GM. Intravenous milrinone in cardiac surgery. Thorac Surg. 2002;73(1):325-30.
14. Burkhardt BE, Rücker G, Stiller B. Prophylactic milrinone for the prevention of low cardiac output syndrome and mortality in children undergoing surgery for congenital heart disease.Cochrane Database Syst Rev. 2015;(3):CD009515.
15. Hashim T, Sanam K, Revilla-Martinez M, Morgan CJ, Tallaj JA, Pamboukian SV, et al. Clinical Characteristics and Outcomes of Intravenous Inotropic Therapy in Advanced Heart Failure.Circ Heart Fail. 2015;8(5):880-6.
16. Oztekin I, Yazıcı S, Oztekin DS, Goksel O, Issever H, Canık S. Effects of low-dose milrinone on weaning from cardiopulmonary bypass and after in patients with mitral stenosis and pulmonary hypertension. Yakugaku Zasshi. 2007;127(2):375-83.
17. Wang H, Gong M, Zhou B, Dai A. Comparison of inhaled and intravenous milrinone in patients with pulmonary hypertension undergoing mitral valve surgery. Adv Ther. 2009;26(4):462-8.
18. Ushio M, Egi M, Wakabayashi J, Nishimura T, Miyatake Y, Obata N, et al. Impact of Milrinone Administration in Adult Cardiac Surgery Patients: Updated Meta-Analysis. Cardiothorac Vasc Anesth. 2016;30(6):1454-60.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):722-724.
DOI: 10.28982/josam.626520

Research article
Araştırma makalesi

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

Evaluation of trauma patients admitted to the emergency department of in Mogadishu Training and Research Hospital, Somalia: Cross-sectional study of 1106 patients

Somali Mogadişu'daki eğitim ve araştırma hastanesi acil servisine başvuran travma hastalarının değerlendirilmesi: 1106 hastanın kesitsel çalışması

Mustafa Enes Demirel [1], Ibrahim Hussein Ali [2]

[1] Anamur Public Hospital, Clinics of Emergency, Mersin, Turkey
[2] Mogadishu Turkey Education and Research Hospital, Mogadishu, Somalia

ORCID ID of the author(s)
MED: 0000-0001-5187-5737
IHA: 0000-0002-9794-6649

Abstract

Aim: Trauma-related injuries are among the most pressing issues today, causing economic, social, and healthcare burdens. The aim of this study is to better manage and approach trauma patients by comparing our results with the literature, and reach standards set by developed countries.

Methods: Data of patients who were admitted to the emergency service of Mogadishu Somalia Turkish Training and Research Hospital with trauma between 1 September 2017 and 30 April 2018 were retrospectively obtained from the hospital registry and patient files. Demographic data such as the age, gender, means of injury, site of injury, department of hospitalization and discharge/death records were recorded and analyzed. Descriptive statistics and chi-square test were used. $P<0.05$ was considered statistically significant.

Results: Among 11225 patients admitted to the emergency department, 1106 were trauma patients. 29.3% were females and 70.7% were males. 49.9% of the patients (n=551) were discharged from the emergency service after follow-up, and 50.1% (n=541) were admitted to various departments. 14 patients died in the emergency service.

Conclusion: Traumas constitute about a quarter of referrals to the emergency service in developed countries. In Somalia, this ratio was about 1:10. Proper management during the pre-hospitalization and hospitalization periods and transferal of patients when needed may help reduce the morbidity and mortality of trauma patients.

Keywords: Emergency medicine, Trauma patients, Somalia

Öz

Amaç: Yaralanmalar günümüzde en önemli konular arasındadır ve ekonomik, sosyal ve sağlıkla ilgili sorunlara neden olmaktadır. Bu çalışmanın amacı hastaneye başvuran travma hastalarına yaklaşım ve yönetiminin, bu çalışma sonuçları ve literatür bilgileri ile kıyaslama yaparak daha iyi hale getirilmesi ve gelişmiş ülkelerdeki standardizasyonu yakalaması için katkı sağlamaktır.

Yöntemler: 01 Eylül 2017 ve 30 Nisan 2018 tarihleri arasında 8 aylık dönemde hastanemiz acil servisine başvuran hastaların verileri hastane bilgi otomasyon ve dosya kayıtlarından yararlanılarak retrospektrif olarak toplandı. Çalışmaya alınan hastaların yaş, cinsiyet, yaralanma mekanizmaları, yaralanma bölgesi ve yatış verilen servis, taburculuk / eksitus kayıtları değerlendirmeye alındı. Analiz için SPSS 22 programı kullanıldı. Descriptives, Chi-Square istatistik testleri kullanılarak $P<0,05$ anlamlı olacak şekilde kabul edildi.

Bulgular: Hastanemize başvuran 11225 hastanın 1106 tanesi travma hastası olarak acil servisimize başvurmuşlardır. Çalışmaya alınan hastaların yüzde 29,3'ü kadın hasta 70,7%'i ise erkek hasta olduğu görülmüştür. Çalışmamızda alınan hastalardan 551 (49,9%) hasta acil servisten takipleri sonrası taburcu edilmişlerdir. 541 hasta ise çeşitli bölümlere yatışı yapılmıştır. Başvuran hastalarımızdan 14 hastamız ise acil serviste eksitus oldu.

Sonuç: Travmalar gelişmiş ülkelerde acil servise başvuruların yaklaşık olarak dörtte birini oluşturmaktadır. Somali'de yaptığımız bu çalışmada ise yaklaşık 10'da 1 oranında olduğu görülmüştür. Travma hastalarının yönetiminde hastane öncesi ve hastane döneminin iyi yönetilmesi, uygun hastaneye uygun şekilde transport edilmesi travma hastalarında morbidite ve mortaliteyi azaltmaya yardımcı olabilir.

Anahtar kelimeler: Acil servis, Travma hastaları, Somali

Corresponding author / Sorumlu yazar:
Mustafa Enes Demirel
Address / Adres: Anamur Devlet Hastanesi Acil Klinikler, Saglık Mah., 33640 Anamur, Mersin, Türkiye
e-Mail: mnsdmrl@hotmail.com

Ethics Committee Approval: The study was approved by Mogadishu Somalia Turkish Education and Research Hospital ethics committee (decision number 116/5550-615).
Etik Kurul Onayı: Çalışma Mogadişu Somali Türk Eğitim ve Araştırma Hastanesi etik kurulu tarafından onaylandı (karar numarası 116 / 5550-615).

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.

Published: 10/16/2019
Yayın Tarihi: 16.10.2019

How to cite / Atıf için: Demirel ME, Ali IH. Evaluation of trauma patients admitted to the emergency department of in Mogadishu Training and Research Hospital, Somalia: Cross-sectional study of 1106 patients. J Surg Med. 2019;3(10):722-724.

Introduction

Trauma-related injuries are among the most pressing issues today, causing economic, social and healthcare burdens [1]. In addition to being one of the major causes of death, they constitute an integral public health problem since young people are more commonly affected, which leads to concomitant material and psychological/spiritual losses [2]. Trauma is ranked third to fourth among all mortality causes in the world, first in mortality between ages 1 and 44 [3], and first in mortality in the emergency service [4]. Injury may occur due to thermal, radiation-related, explosive or mechanical causes. Mechanical traumas may present as blunt or penetrating injuries, and include traffic accidents, falls, firearms and knife injuries [5]. Approach to patients with multiple injuries is examined with regards to the pre-hospitalization and hospitalization periods. Pre-hospitalization period includes arrival to the hospital, communication and information exchange with the patient, detailed anamnesis about the injury, triage and carrying out the appropriate transport protocol to the most suitable hospital [6]. Delayed treatment of a patient with multiple injuries not only extends the hospitalization period of the patient, but can also lead to organ failure and death [7].

In this study, we aimed to retrospectively classify trauma patients referred to the emergency department of Mogadishu Somalia Turkish Training and Research Hospital (MSTERH) from a demographic and epidemiological perspective, identify the needs and deficiencies of our emergency department and improve the service quality in our hospital while contributing to the literature.

Materials and methods

Study population

The data of 11225 patients who were admitted to MSTERH Emergency Department between 01.09.2017 and 30.04.2018 were examined retrospectively. Using the Hospital Information Management System (HIMS) software, the ages, genders, date, reason and department of admissions, mechanism of injuries, injury sites and ICD-10 codes of trauma patients were obtained. Consultation notes and death records of patients did not exist, hence were not included. The data of patients injured in the major explosion in October were excluded from the study since they had missing elements compared with the data we used in our study. Ethics committee approval was obtained from Mogadishu Somalia Turkish Training and Research Hospital on 20.02.2019 (No:116 /5550-615) and the study was conducted in accordance with the Declaration of Helsinki and its later amendments.

Study design

1106 patients out of 11225 were admitted to the emergency department due to trauma, and classified based on gender, medical condition, department of admission, the localization and extent of injury and discharge/death status. Location of injuries included the head and neck region, thorax, abdomen, and extremities. Patients were admitted to Orthopedics and Traumatology, Neurosurgery, General and Pediatric surgery, Cardiovascular and Thoracic Surgery, Plastic Surgery and Otorhinolaryngology and Ophthalmology (the latter two were classified as "other") departments. The "Abbreviated Injury Scale" (AIS) was used for patients with multiple traumas, which was defined as trauma in two or more sites [8, 9], and a severity code was used to classify each injury as minor, moderate, serious, severe, critical, virtually unsurvivable maximum injury and unknown.

Statistical analysis

The SPSS 22.0 software was used for data analysis. Descriptive statistics were performed. Data was presented in percentages. Chi-square test was used to compare data and $P<0.05$ was considered statistically significant.

Results

Out of 1106 trauma patients who were referred to the emergency department of MSTTRH in Somalia, 29.3% (n=324) were female and 70.7% (n=782) were male ($P<0.001$). Mean ages of female, male and all patients were 30.7 (22.34), 27.3 (16.86) and 28.34 (18.68), respectively. Youngest and oldest of all patients were 1 and 91 years old. The mean ages of all categories are presented in Table 3. Traffic accidents were the most common cause of trauma among all patients and males were more frequently injured with gunshot and explosions compared to females (Table 1). The mean age of patients who died in the emergency service was 12.8 (3.5).

The injury sites in decreasing order of frequency were lower and upper extremities (34.2%, n=379), the head and neck region (32.7%, n=362), abdomen (13.6%, n=149), multiple sites (11.1%, n=123) and thorax (8.4%, n=93) (Table 4). The frequency of patients admitted to the Orthopedics and Traumatology and Neurosurgery departments were 18.2% and 20.3%, respectively (Table 5).

Table 1: Injury mechanisms of patients according to gender

Gender	Explosion	Gun-shot	Burn, penetrant, dog bite, electric shock	Car accident	Fall	Violence, Other blunt trauma, etc.	Total	P-value
Female	27	23	19	144	95	16	324	<0.001
Male	121	109	74	308	129	41	782	
Total	148	132	93	452	224	57	1106	

Table 2: Injury mechanisms of patients

Injury mechanism	Frequency	%
Explosion	148	13.4
Gun shot	132	11.9
Burn, penetrant, dog bite, electrical crush	93	8.3
Car accident	452	40.9
Fall	224	20.3
Violence and other blunt trauma	57	5.1

Table 3: Relationship between age and cause of trauma

Trauma mechanism	Age Mean	Age Min - Max	*P*-value
Explosion	29.65	1 - 67	0.091
Gun shot	31.25	12 – 65	
Burn, penetrant, dog bite, electrical crush	15.65	1 - 48	
Car accident	25.64	2 - 83	
Fall	37.21	1 - 91	
Violence and other blunt trauma	25.42	10- 60	

Table 4: Distribution of patients according to injury site

Injury site	Frequency	%
Extremities	379	34.2
Head	362	32.7
Thorax	93	8.4
Abdomen	149	13.6
Multiple sites	123	11.1
Total	1106	100.0

Table 5: Admission service of patients

Department of admission	Frequency	%
Discharge	551	49.8
Mortality in the emergency Department	14	1.4
Orthopedics and Traumatology	202	18.2
General & Pediatric Surgery	36	3.3
Neurosurgery	224	20.2
Thoracic–Cardiovascular Surgery	37	3.3
Plastic Surgery	36	3.3
Otorhinolaryngology, ophthalmology, etc.	6	0.5
Total	1106	100.0

Discussion

Traumas constitute approximately one-fourth of emergency service admissions in developed countries [10]. In a study conducted in the United States, the rate of admissions to the emergency department was reported as 14.3% [4], while another study in the US revealed that 37% of these admissions were due to trauma [11]. Akoglu et al. [12] stated that trauma patients constituted 3% of all patients admitted to the emergency department in Turkey. This rate was 9.86% in our study. The significantly higher rate of males in our study may be explained by the fact that men in Somalia spend more time in social environments where they are exposed to trauma.

A previous study reported that the most common cause of trauma in the US was falling (44.9%) [13], while in our study, falling came second (20.3%) to car accidents (40.9%). In a country such as Somalia where bombing and shooting are frequent, we would argue that these rates are low.

In younger patients, assaults and motor vehicle injuries are among the most common causes of traumatic injury. Large international studies have reported that trauma patients aged >80 years are the largest contributors to the increase in mortality among all trauma cases [14]. In contrast, young adults remaining at the scene in Somalia, where bombings and sporadic fighting are extensive, have contributed to the increase in mortality. Less serious cases are admitted to the emergency departments, and injured children are more susceptible to hypovolemia after trauma.

In their study conducted in Turkey, Durdu et al. [15] reported that 44.8% of injuries (n=567) were in the upper extremity, 34.7% (n=440) in the head and neck, 27.2% (n=344) in the lower extremity, 15.7% (n=198) in the face, 11.5% (n=146) in the thorax, and 7.4% (n=93) in the abdomen. The difference between these results and ours was attributed to different injury mechanisms in Somalia and Turkey arising from contrasting socio-cultural structures.

Varol et al. [16] stated that among patients injured by traffic accident who were examined in their study, 54.2% of those admitted to the emergency service were discharged, 8.5% were admitted to the Orthopedics and Traumatology department and 8.2% were admitted to the Neurosurgery department. In our study, 18.2% of all trauma patients were admitted to the Orthopedics and Traumatology department and 20.3% to the Neurosurgery department. In Durdu et al.'s study [15], 85% of the patients admitted to the emergency services were discharged after monitoring and treatment. Akin to the above-mentioned studies, the discharge rate from the emergency department was 49.8% (n= 551) in our study. 14 patients died in the emergency department. Local trauma patients who were not admitted to the external services were discharged after being managed in accordance with their indications in the emergency service examination room.

Although patients older than 65 years constitute 6.7% of the total population in Turkey, 22% of all hospitalized trauma patients are older than 65 years. The same rates for the US are 12% and 23%, respectively. Our results revealed that the rate of hospitalized trauma patients older than 65 years in Somalia was only 6.7% [12]. It is known that elderly patients are generally more prone to trauma. However, the lower mean age in our study, unlike in the other countries, can be explained by the shorter life expectancy in Somalia compared to other developed countries.

Limitation

The numbers of local trauma and multiple trauma patients are similar. However, as stated in the "Methods" section, several difficulties were encountered during the identification of multiple traumas. Although a multiple trauma patient is defined as having an Injury Severity Score (ISS) of ≥16, this definition has been designed to determine the long-term mortality and morbidity rather the classification of patients [17]. It was determined that there was not enough file information to use the ISS during our retrospective review. Similarly, all scoring systems such as "Comprehensive Research Injury Scale" [18], "Trauma Injury Severity Score" [19] and "A Severity Characterization Of Trauma" recommended by the trauma committee of the American College of Surgeons required more information than the data we obtained during our retrospective review [20]. We believe that classification of multiple and local trauma patients we performed using the multiple and local trauma conditions specified in the AIS system may give different results with the use of ISS.

Conclusion

Traumas constitute about a quarter of referrals to the emergency service in developed countries. In Somalia, this ratio was about 1:10. Proper management during the pre-hospitalization and hospitalization periods and transferal of patients when needed may help reduce the morbidity and mortality of trauma patients.

References

1. Ertekin C. Multipl Travmalı Hastaya Yaklaşım. Yoğun Bakım Dergisi. 2002;2(2):77-87.
2. Battistella F, Benfield JR. Blunt and penetrating injuries of the chest wall, pleura and lungs. General thoracic surgery 5th ed Philadelphia: Lippincott Williams & Wilkins. 2000:815-31.
3. Miniño AM, Heron MP, Smith BL. Deaths: preliminary data for 2004. National vital statistics reports. 2006;54(19):1-49.
4. Burt CW, Fingerhut LA. Injury visits to hospital emergency departments: United States, 1992-95: Department of Health and Hu Ol and Prevention Nati; 1998.
5. Mackenzie E, Fowler C. Epidemiology of injury. Trauma 5th ed New York, NY: McGraw-Hill Companies, Inc. 2003.
6. Mattox KL, Maningas PA, Moore EE, Mateer JR, Marx JA, Aprahamian C, et al. Prehospital hypertonic saline/dextran infusion for post-traumatic hypotension. The USA Multicenter Trial. Annals of surgery. 1991;213(5):482.
7. Edition TS. Mc Graw Hill Medical. Feliciano, D, Mattox K, Moore E. 2008.
8. Greenspan L, McLELLAN BA, Greig H. Abbreviated Injury Scale and Injury Severity Score: a scoring chart. The Journal of trauma. 1985;25(1):60-4.
9. Rating the severity of tissue damage. I. The abbreviated scale. Jama. 1971;215(2):277-80. Epub 1971/01/11. doi: 10.1001/jama.1971.03180150059012.
10. Becher RD, Meredith JW, Kilgo PD. Injury severity scoring and outcomes research. Mattox KL, Moore EE, Feliciano DV, editors Trauma 7th ed New York: McGraw-Hill. 2013.
11. Nourjah P. National hospital ambulatory medical care survey: 1997 emergency department summary. Advance data from vital and health statistics. 1997(304).
12. Akoğlu H, Denizbaşı A, Ünlüer E, Güneysel Ö, Onur Ö. Marmara Üniverstesi Hastanesi acil servisine başvuran travma hastalarının demografik özellikleri. Marmara Medical Journal. 2005;18(3):113-22.
13. Burt CW. Injury-related visits to hospital emergency departments: United States, 1992. 1995.
14. Eachempati SR, Reed RL, Louis JES, Fischer RP. "The Demographics of Trauma in 1995" Revisited: An Assessment of the Accuracy and Utility of Trauma Predictions. Journal of Trauma and Acute Care Surgery. 1998;45(2):208-14.
15. Durdu T. Analysis of trauma cases admitted to the emergency department. Journal of Clinical and Analytical Medicine. 2013;5(93):182-5.
16. Varol O, Eren ŞH, Oğuztürk H, Korkmaz İ, Beydilli İ. Acil servise trafik kazası sonucu başvuran hastaların incelenmesi. CÜ Tıp Fakültesi Dergisi. 2006;28(2):55-60.
17. Linn S. The injury severity score—importance and uses. Annals of epidemiology. 1995;5(6):440-6.
18. Rating the severity of tissue damage. I. The abbreviated scale. JAMA. 1971 Jan 11;215(2):277-80.
19. Boyd CR, Tolson MA, Copes WS. Evaluating trauma care: the TRISS method. Trauma Score and the Injury Severity Score. The Journal of trauma. 1987;27(4):370-8.
20. Champion HR, Copes WS, Sacco WJ, Frey CF, Holcroft JW, Hoyt DB, et al. Improved predictions from a severity characterization of trauma (ASCOT) over Trauma and Injury Severity Score (TRISS): results of an independent evaluation. Journal of Trauma and Acute Care Surgery. 1996;40(1):42-9.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):725-728.
DOI: 10.28982/josam.559559

Research article
Araştırma makalesi

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

The effect of laparoscopy courses in laparoscopy practice after urology resident training: A questionnaire-based observational study

Laparoskopi kurslarının üroloji asistan eğitimi sonrası laparoskopi uygulamalarına etkisi: Ankete dayalı gözlemsel çalışma

Gökhun Özmerdiven [1], Onur Kaygısız [2], Çağatay Çiçek [2], Kadir Ömür Günseren [2], Hakan Vuruşkan [2]

[1] Istanbul Aydın University, School of Medicine, Department of Urology, Department of Urology, Istanbul, Turkey
[2] Uludag University, School of Medicine, Department of Urology, Bursa, Turkey

ORCID ID of the author(s)
GÖ: 0000-0002-0142-0897
OK: 0000-0002-9790-7295
ÇÇ: 0000-0002-0471-5404
KÖG: 0000-0001-8673-3093
HV: 0000-0001-9549-8435

Abstract

Aim: Laparoscopy is an important part of surgical training. Laparoscopy courses are organized to increase competence of laparoscopy. This aim of this paper is to evaluate the laparoscopic surgery competence of Turkish urologists and the effectiveness of laparoscopy courses.

Methods: In 2014, an online survey consisting of 11 questions was sent to 180 urologists via e-mail, among which 78 responded. The survey questions aimed at gathering information about where the urologists worked, their laparoscopic surgical experience, how long they attended laparoscopy courses, and whether they considered themselves to be competent in laparoscopic surgeries.

Results: 41.2% of the respondents who considered themselves to be competent in laparoscopy and 84.1% of those who did not, stated that they wanted to attend laparoscopy courses (P<0.001). 100% of the respondents who could perform Level-1 laparoscopy surgeries stated that they did not consider themselves to be competent and wanted to receive laparoscopic training (P<0.001). 54.9% of those who did not receive laparoscopy training during their residency and 48.1% of those who received training during residency stated that they attended courses in the past. All respondents who attended long-term courses and 73.6% of those who attended short-term courses could perform laparoscopic surgeries (P<0.001). It was also determined those who attended long-term courses could perform complicated laparoscopic surgeries (P<0.001).

Conclusion: This study revealed that the courses contributed a lot to laparoscopic surgical competence after residency. The study stresses that if the urologists who did not receive laparoscopy training during their residency attend long-term courses, they can increase their competence in laparoscopy.

Keywords: Laparoscopy, Course, Survey, Competence

Öz

Amaç: Laparoskopi, cerrahi eğitimin önemli bir parçasıdır. Laparoskopi yeterliliğini arttırmak için laparoskopi kursları düzenlenmektedir. Bu yazıda Türk ürologların, laparoskopik cerrahi yeterliliği ve laparoskopi kurslarının etkinliğinin değerlendirilmesi planlandı.

Yöntemler: 2014 yılında Türkiye'de üroloji alanındaki 180 uzmana e-mail anket formu gönderildi. Sorulara yanıt veren 78 üroloji uzmanının, çalıştığı kurum, laparoskopik deneyimi, aldıkları laparoskopi kurs süresi ve laparoskopi cerrahisindeki yeterlilikleri 11 soruluk anket ile sorgulanmıştır.

Bulgular: Laparoskopi konusunda kendini yeterli gören uzmanların %41,2'si, yeterli görmeyenlerin %84,1'i kurs almak istediğini belirtti (P<0,001). Zorluk seviyesi 1 kabul edilen laparoskopi vakaları yapabilen uzmanların %100'ü kendini yeterli görmeyip, laparoskopi eğitimi almak istediğini belirtti (P<0,001). Asistanlığında laparoskopi eğitimi almayanların %54,9'u ve alanların %48,1'i kurs almış. Uzun süreli kurs alanların hepsi, kısa süreli kurs alanların %73,6'sı laparoskopi yapabiliyordu (P<0,001). Uzun süreli kurs alanlar daha zor vaka yapabildiği izlenmektedir (P<0,001).

Sonuç: Yapılan anketin sonucunda, asistanlık sonrası laparoskopik cerrahi yeterliliğinde kursların büyük yarar sağladığı görülmektedir. Asistanlığında laparoskopi eğitimi almayan ürologların, uzun süreli eğitim veren merkezlerde bulunması laparoskopi becerilerini arttıracağını düşünmekteyiz.

Anahtar kelimeler: Laparoskopi, Kurs, Anket, Yeterlilik

Corresponding author / Sorumlu yazar:
Gökhun Özmerdiven
Address / Adres: İstanbul Aydın Üniversitesi Tıp Fakültesi, Üroloji Anabilim Dalı, Turgut Özal str. No: 1, Küçükçekmece 34303 İstanbul, Türkiye
e-Mail: gozmerdiven@gmail.com

Ethics Committee Approval: Ethics Committee of Uludag University was approved this study (2017-13/54).
Etik Kurul Onayı: Uludağ Üniversitesi Etik Kurulu bu çalışmayı onayladı (2017-13/54).

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.

Published: 10/16/2019
Yayın Tarihi: 16.10.2019

How to cite / Atıf için: Özmerdiven G, Kaygısız O, Çiçek Ç, Günseren KÖ, Vuruşkan H. The effect of laparoscopy courses in laparoscopy practice after urology resident training: A questionnaire-based observational study. J Surg Med. 2019;3(10):725-728.

Introduction

The laparoscopic approach has been used with increasing frequency in urology during the last 25 years due to technological and technical development. In parallel with the development of suturing techniques and sutures, laparoscopic surgeries have become widespread all over the world and almost all urologic operations are currently performed by laparoscopic technique [1-4]. Compared to open surgery, laparoscopic technique reportedly provides a significant advantage in shortening hospital stay and decreasing postoperative pain [5].

Laparoscopic surgical skills are an integral part of surgical training [6], and laparoscopic surgery is harder than open surgery due to reduced depth perception that arises from two-dimensional vision, reduced tactile sensations, and the need for hand-eye coordination. Therefore, laparoscopic surgery requires a new structured training program that should include clinical practice [7].

Due to the need for laparoscopic training, various centers have invested to promote training through skill-courses [8]. However, acquiring laparoscopic skills, especially stitching skills, is a difficult and lengthy process [9]. The long-term impact of the courses on surgical practice is still unknown. It is also difficult to assess the impact of these courses on surgical practice because training centers do not provide feedback [10].

In the literature, short-term laparoscopy courses have been shown to be an effective and useful method to achieve laparoscopic skills [11]. However, urologists still need to transfer their knowledge and experience to clinical practice. Although short-term courses provide ample experience, the transferal of skills to the clinical practice may be insufficient. For this reason, it is thought that long-term training methods can be developed with the training models developed in short-term courses [12,13].

In this study, we investigated the competence of urology specialists to perform laparoscopy and the period of training courses that are more useful.

Materials and methods

An online survey was sent to 180 urologists between 01.10.2014 and 30.10.2014. The survey response rate was 43.33% (78 persons). All answers were recorded on an Excel form. This 2-page questionnaire was prepared anonymously by Uludag University Faculty of Medicine, department of Urology by the approval of the Ethics Committee of Uludag University (2017-13/54). The survey containing 11 questions is presented in Table 1. Laparoscopy courses after residency were grouped under three headings according to the responses: a short course of maximum three days, a long local course of at least three months, and a long international course of at least three months. All the long courses abroad were certified centers for laparoscopy. The domestic long-term courses attended by four respondents held regular courses while the other centers did not.

Urological laparoscopic cases were divided into 4 levels according to their difficulty and respondents were asked what level of surgery they could perform.

- Level 1: Diagnostic laparoscopy, laparoscopic orchiopexy, laparoscopic cyst excision
- Level 2: Laparoscopic nephrectomy, laparoscopic ureterolithotomy, laparoscopic pyelolithotomy, laparoscopic adrenalectomy
- Level 3: Laparoscopic pyeloplasty, laparoscopic sacrocolpopexy, laparoscopic simple prostatectomy
- Level 4: Laparoscopic radical prostatectomy, laparoscopic partial nephrectomy, laparoscopic radical cystoprostatectomy

Statistical analysis

The information in the survey form was recorded numerically in SPSS version 15 (SPSS Inc, Chicago, Ill, USA) program and analyzed. Chi-square test was used to compare the data. $P<0.05$ was considered statistically significant.

Table 1: Survey form

1.Your title:	a. Specialist b. Assistant Professor c. Associate Professor d. Professor	
2. Where did you receive laparoscopy training?	a. Training and Research Hospital b. University-public c. University-private	
3. Expertise period: (year)		
4. Place of work:	a. Public Hospital b. Training and Research Hospital c. University Hospital d. Private Hospital	
5. Did you receive laparoscopic surgery training during your specialization?	Yes	No
6. Do you perform laparoscopic urological surgeries?	Yes	No
7. Do you consider yourself to be competent in laparoscopic surgeries?	Yes	No
8. Do you want to receive laparoscopy training?	Yes	No
9. Where did you receive laparoscopy training after specialization?	a. Short term course b. Training and practice in a domestic center c. Training and / or practice in a center abroad	
10. What is the name of the institution where you received laparoscopic surgery training after specialization and how long did you train?		
11. What laparoscopic surgeries have you performed in the last two years? (you can mark more than one item)	a. Diagnostic laparoscopy, Laparoscopic orchiopexy b. Laparoscopic nephrectomy, Laparoscopic ureterolithotomy, Laparoscopic pyelolithotomy, Laparoscopic adrenalectomy c. Laparoscopic pyeloplasty, Laparoscopic sacrocolpopexy, Laparoscopic simple prostatectomy d. Laparoscopic radical prostatectomy, Laparoscopic radical cystoprostatectomy, Laparoscopic partial nephrectomy	

Results

The mean duration of specialization was 6.5 years (1-16 years). Respondents included 10 professors, 13 associate professors, 11 assistant professors and 42 specialists. The titles of two respondents were unknown. Fifteen out of 29 respondents with less than 5 years of specialization, six out of 19 respondents with 6-10 years of specialization, five out 13 respondents with 11-15 years of specialization, and one out of 17 respondents with more than 15 years of specialization had received laparoscopy training during their residency ($P=0.004$). Eighteen of the 27 respondents who received laparoscopy training and 24 of the 51 respondents who did not receive laparoscopy training during residency performed laparoscopic surgeries. The difference between the groups was not significant ($P=0.152$).

The rate of performing laparoscopy was 26.7%, 60.6%, 63.2% and 54.5% in public hospitals, university hospitals, training-research hospitals, and private hospitals, respectively. The rate of performing laparoscopic surgeries of the respondents working in public hospitals was lower than that of the respondents working in other hospitals ($P=0.023$). Sixteen (38.1%) of the 42 respondents who stated that they performed laparoscopic surgeries and 35 (97.2%) of the 36 respondents who stated they could not perform laparoscopic surgeries indicated that they wanted to receive laparoscopic training ($P<0.001$).

Based on their responses, 4 urologists could perform Level-1 laparoscopic surgeries, 23 urologists, Level-2 laparoscopic surgeries, 9 urologists, Level-3 laparoscopic surgeries, and 10 urologists, Level-4 laparoscopic surgeries. None of the Level-1 laparoscopic surgery performers, 16 (66.7%) of Level-2 performers, 7 (77.8%) of Level-3 performers and 10 (100%) of Level-4 laparoscopic performers considered themselves competent (P=0.001). Among respondents, all Level-1 performers, 52.17% of Level-2 performers, 33.3% of Level-3 performers and 10% of Level-4 performers indicated that they wanted to receive laparoscopic training (P=0.001) (Figure 1). 41.2% of respondents who considered themselves competent in laparoscopy and 84.1% of those who did not, wanted to receive training (P<0.001). 22 of the 27 urologists who did not want to receive training had previously attended courses.

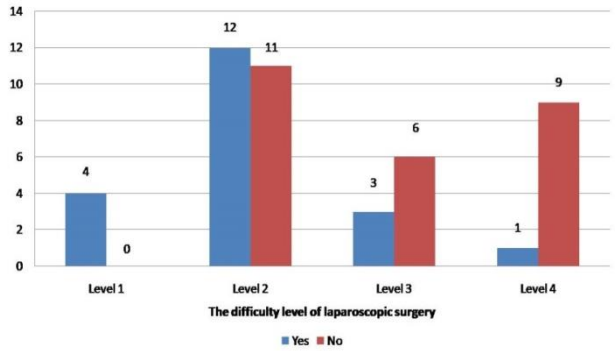

Figure 1: Respondents who want to receive laparoscopy training were asked what level of surgery they could do

Twenty-eight (54.9%) urologists who did not receive laparoscopy training during residency and 13 (48.1%) who did, attended laparoscopy courses after residency (P=0.637). Among those who did not receive training during residency, 14 individuals attended short-term courses, five individuals, local long-term courses and nine individuals, international long-term courses. Among those who received training during their residency, the number of individuals who attended short-term, local long-term, and international long-term courses were five, six and two, respectively (P=0.526). Twenty-three of 28 urologists who attended laparoscopy courses for the first time after residency stated that they could perform laparoscopic surgeries while 24 respondents who did not attend any courses stated that they could not (P<0.001).

Twelve of 13 urologists who received laparoscopic training during residency and again thereafter, and six of the 14 urologists who did not attend any courses could perform laparoscopic surgeries (P=0.013).

While all of the 11 urologists who attended local long-term courses and international long-term courses could perform laparoscopic surgeries, of the 19 urologists who attended short-term courses, 14 could perform laparoscopic surgeries (P<0.001). Four of those who could not perform laparoscopic surgeries and who attended short-term courses stated that they did not receive laparoscopy training during their residency. In addition, those who attended long-term courses were able to perform more difficult laparoscopic surgeries than those who attended short-term courses (P<0.001). Attended course types were presented in figure 2.

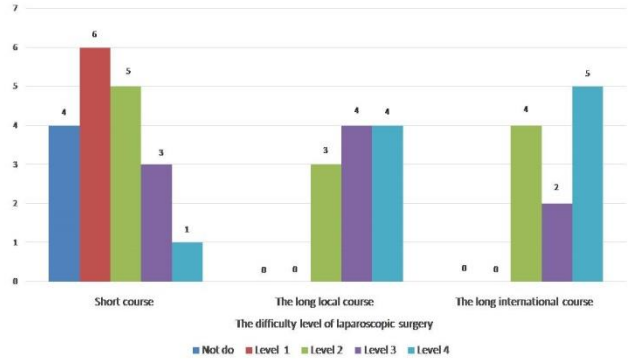

Figure 2: Respondents who perform laparoscopic surgery were asked which course they attended

Discussion

Using the survey method, we investigated the laparoscopic competence of Turkish urologists and the effectiveness of laparoscopy training courses after residency. The majority of the studies on surgery courses to date provide insight into the content of these courses and the attitudes of the participants towards them. However, few studies have been conducted on their clinical implications or educational methods [10]. Therefore, the impact of these courses on health service outcomes, quality of training and resource allocation remains unclear. Research on training shows that between 10% and 40% of the knowledge obtained during training is transferred to clinic practice [14].

In this study, only 27 (34.6%) of 78 urologists and only 1 urologist who had completed their residency before 2005 had received laparoscopic training during residency. This indicates the necessity of additional laparoscopy training for urologists who completed residency training at earlier dates. On the other hand, only half of the urologists who completed their residency in the last 5 years had received laparoscopic training. A survey of urology residents in Europe revealed that laparoscopic surgeries were performed in 74% of the clinics, only 23% of the urologists considered themselves to be competent, and 33% of them received no laparoscopy training or attended no laparoscopy course. It is therefore recommended that urologists are encouraged to attend laparoscopy courses [15].

Nowadays, laparoscopic skills are required of urologists, irrespective of whether they received laparoscopic training. The fact that the respondents who can perform laparoscopic surgeries are working in university or private hospitals further supports this statement. It is therefore important to plan training programs which can contribute to increasing laparoscopic skills for the untrained urologists. According to the 10-year data from a center providing long-term laparoscopic training in the UK, 69% of participants who prefer the laparoscopic method successfully perform laparoscopic surgeries and these courses are useful in developing laparoscopic skills [10].

Short courses implement basic teaching methods such as the training box and laparoscopic surgical observation, and some courses allow training on the animal model. However, this training is not sufficient for participation in the laparoscopic surgery team. This means that the stepped education model proposed in the literature is not completed [16,17]. After a 3-session and 2-week advanced laparoscopy course with a total of

114 participants consisting of general surgery residents and general surgeons, an increase in the rate of laparoscopic anastomosis was observed and there was no difference between the duration of operation performed by experienced specialists and residents [18]. Asano et al. [19] reported that after a 2-day live surgery course, only 62% of the participants could perform laparoscopic surgeries. Okrainec et al. [20] reported that a 3-day laparoscopic training was insufficient. Laparoscopic surgeries require follow-up and knowledge of correct preoperative and postoperative interventions to be applied when necessary. In our study, the rate of performing laparoscopy in short-term courses of participants was found to be 73%, however, mostly simple laparoscopic cases were performed. Experience in managing complications will provide self-confidence for the surgeon who will begin laparoscopic operations for the first time.

Long-term courses can only be offered in experienced centers. Professional organizations should take an active role in establishing links between these centers and urologists who need courses. A study with general surgery specialists participating in long-term laparoscopy courses revealed that there was a 300% increase in the rate of those who could perform laparoscopic surgeries, pointing out the importance of long course programs in minimally invasive surgery [21]. We have determined that the urologists who did not receive laparoscopy training during their residency mostly preferred attending international long-term courses while those who received laparoscopy training during their residency mostly preferred local long-term courses. Considering the number of urologists who want to attend laparoscopy training, we believe underlining the need for the dissemination of these courses will provide benefit.

The majority of the urologists who participated in our study were eager to perform laparoscopic surgeries. Moreover, none of the respondents who did not receive training or attend courses could perform laparoscopic surgeries while 82.14% of those who did not receive laparoscopy training but later attended courses could. This shows that attending courses helps urologists in starting to perform laparoscopic surgeries.

In laparoscopic urological surgery, reconstructive surgeries require more experience than excisional surgeries. In this study, we classified surgery according to difficulty levels. It was found that the respondents who attended international long-term courses were able to perform more complicated surgeries. A survey with 106 urologists reported a slight increase in laparoscopic nephrectomy, laparoscopic nephroureterectomy, laparoscopic pyeloplasty, and laparoscopic partial nephrectomy skills of urologists after a 5-day laparoscopy program. A lower success rate was observed in difficult surgeries such as pyeloplasty and partial nephrectomy and it was stated that longer courses may be required for such operations [22].

Limitations

The percentage of respondents is low (43.33%), but we believe that the population represents urologists who actively perform laparoscopic surgeries within the country, since the respondents in our study had different amounts of work experience. Additionally, reconstructive surgeries and advanced oncological cases were considered Level-3 and 4 surgeries, however, since a surgeon who is not interested in urologic oncology will not perform Level-4 surgeries, he/she may not appear to be competent in Level-4 surgery, but still perform reconstructive pyeloplasty. Therefore, respondents who can perform Level-3 and 4 surgeries should be considered as able to perform advanced laparoscopic urological surgeries.

Conclusion

The study shows that it is not possible for urologists who do not receive laparoscopy training during residency to start laparoscopic surgeries after short-term training. Also, the trainings held in local and international competent centers will contribute to the learning of laparoscopy. Trainings in the international centers will both be costly and fail to reach large audiences; therefore, competent centers are needed in the country. We believe that the adoption of certain standards by laparoscopic centers, whose numbers are increasing in the country, will allow laparoscopic surgeries to be widely performed.

References

1. Lane BR, Gill IS. 7-Year oncological outcomes after laparoscopic and open partial nephrectomy. J Urol. 2010;183:473–9.
2. McNeill SA, Tolley DA. Review laparoscopy in urology: indications and training. BJU Int. 2002;89:169–73.
3. Shalhav AL, Dabagia MD, Wagner TT, Koch MO, Lingeman JE. Training postgraduate urologists in laparoscopic surgery: The current challenge. J Urol. 2002;167:2135–7.
4. Kaynan AM, Lee KL, Winfield HN. Survey of urological laparoscopic practices in the state of California. J Urol. 2002;167:2380–6.
5. Khan MN, Fayyad T, Cecil TD, Moran BJ. Laparoscopic versus open appendectomy: The risk of postoperative infectious complications. JSLS. 2007;11:363–7.
6. Barnes RW. Surgical handicraft: teaching and learning surgical skills. Am J Surg. 1987;153:422–7.
7. Gonzalez D, Carnahan H, Praamsma M, Dubrowski A. Control of laparoscopic instrument motion in an inanimate bench model: Implications for the training and the evaluation of technical skills. Appl Ergon. 2007;38:123–32.
8. Kroeze SG, Mayer EK, Chopra S, Aggarwal R, Darzi A, Patel A. Assessment of laparoscopic suturing skills of urology residents: a pan-European study. Eur Urol. 2009;56:865–72.
9. Bansal VK, Tamang T, Misra MC, Prakash P, Rajan K, Bhattacharjee HK, et al. suturing skills acquisition: a comparison between laparoscopy exposed and laparoscopy-naive surgeons. JSLS. 2012;16:623–31.
10. Khan MH, Aslam MZ, McNeill A, Tang B, Nabi G. Transfer of Skills From Simulation Lab to Surgical Services: Impact of a Decade Long Laparoscopic Urology Surgical Course. J Surg Educ. 2019;76:591-9.
11. Tunc L, Guven S, Gurbuz C, Gozen AS, Tuncel A, Saracoglu F, et al. Evaluation of applied laparoscopic urology course using validated checklist. JSLS. 2013;17:300-5.
12. Frede T, Erdogru T, Zukosky D, Gulkesen H, Teber D, Rassweiler J. Comparison of training modalities for performing laparoscopic radical prostatectomy: Experience with 1,000 patients. J Urol. 2005;174:673–8.
13. Hruza M, Weiss HO, Pini G, Goezen AS, Schulze M, Teber D, Rassweiler JJ. Complications in 2200 consecutive laparoscopic radical prostatectomies: standardised evaluation and analysis of learning curves. Eur Urol. 2010;58:733–41.
14. Burke LA, Baldwin TT. Workforce training transfer: a study of the effect of relapse prevention training and transfer climate. Hum Resour Manage. 1999;38:227–41.
15. Furriel FT, Laguna MP, Figueiredo AJ, Nunes PT, Rassweiler JJ. Training of European urology residents in laparoscopy: results of a pan-European survey. BJU Int. 2013;112(8):1223-8.
16. Ehdaie B, Tracy C, Reynolds C, Cung B, Thomas K, Floyd T, et al. Evaluation of laparoscopic curricula in American urology residency training. J Endourol. 2011;25:1805-10.
17. Brinkman WM, Tjiam IM, Schout BM, Muijtjens AM, Van Cleynenbreugel B, Koldewijn EL, et al. Results of the European basic laparoscopic urological skills examination. Eur Urol. 2014;65:490-6.
18. Castillo R, Buckel E, León F, Varas J, Alvarado J, Achurra P, Aggarwal R, et al. Effectiveness of learning advanced laparoscopic skills in a brief intensive laparoscopy training program. J Surg Educ. 2015;72:648-53.
19. Asano TK, Soto C, Poulin EC, Mamazza J, Boushey RP. Assessing the impact of a 2-day laparoscopic intestinal workshop. Can J Surg. 2011;54:223–6.
20. Okrainec A, Smith L, Azzie G. Surgical simulation in Africa: the feasibility and impact of a 3-day fundamentals of laparoscopic surgery course. Surg Endosc. 2009;23:2493–8.
21. Dominguez EP, Barrat C, Shaffer L, Gruner R, Whisler D, Taylor P. Minimally invasive surgery adoption into an established surgical practice: impact of a fellowship trained colleague. Surg Endosc. 2013;27:1267–72.
22. Kolla SB, Gamboa AJ, Li R, Santos RT, Gan JM, Shell C, et al. Impact of a laparoscopic renal surgery mini-fellowship program on postgraduate urologist practice patterns at 3-year follow-up. J Urol. 2010;184:2089–93.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):729-733.
DOI: 10.28982/josam.626480

Research article
Araştırma makalesi

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

Evaluation of microorganisms isolated from blood cultures and their susceptibility profiles to antibiotics in five years period

Beş yıllık sürede kan kültürlerinden izole edilen mikroorganizmaların değerlendirilmesi ve antibiyotiklere duyarlılık profilleri

Çiğdem Arabacı [1], Orkide Kutlu [2]

[1] Okmeydanı Training and Research Hospital, Microbiology Laboratory, Istanbul, Turkey
[2] Okmeydanı Training and Research Hospital, Internal Medicine Department, Istanbul, Turkey

ORCID ID of the author(s)
ÇA: 0000-0003-0050-3225
OK: 0000-0002-4402-2231

Corresponding author / Sorumlu yazar:
Orkide Kutlu
Address / Adres: Okmeydanı Eğitim ve Araştırma Hastanesi, Dahiliye Bölümü, İstanbul, Türkiye
e-Mail: orkidekutlu@hotmail.com

Ethics Committee Approval: The study was approved by Okmeydanı Training and Research Hospital ethics committee (Date: 10.9.2019; Number: 1430).
Etik Kurul Onayı: Çalışma Okmeydanı Eğitim ve Araştırma Hastanesi etik kurulu tarafından onaylandı (Tarih: 10.9.2019; Sayı: 1430).

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.

Published: 10/17/2019
Yayın Tarihi: 17.10.2019

Abstract

Aim: In starting antibiotic treatment to know the distribution of infectious agents and the antibiotic resistance rates is vital especially in critically ill patients to prevent disease progression. In this study we aimed to determine the distribution and antimicrobial resistance patterns of blood culture isolates obtained in a tertiary center.

Methods: The microbiological laboratory records between January 2014 and December 2018 were retrospectively reviewed. Each conventional aerobic blood culture bottle per patient with positive results was recorded with the antimicrobial susceptibility profiles of the bacteria isolated. Descriptive statistics (number, percentage, mean and median) were performed. Comparison of descriptive data between groups was performed with cross tables and chi square test. One-way ANOVA test was used to compare the antibiotic resistance rates between spp.

Results: A total of 66004 blood cultures were analyzed in this cross-sectional study. Of the 3882 (21.0%) positive results, 3256 (4.9%) were identified as contamination. The most commonly isolated microorganisms were Coagulase negative staphylococcus, *Escherichia coli, Klebsiella spp., Staphylococcus aureus* and *Acinetobacter spp.* Extended spectrum β-lactamase (ESBL) positivity was determined in 236 (62.4%) isolates of *E.coli,* and 186 (56.8%) isolates of *Klebsiella spp.* Vancomycin resistance showed a significant increase in *Enterococcus spp.* in time. *E.coli* did not show any resistance to imipenem, meropenem, tigecycline or colistin. Methicillin susceptible *Staphylococcus aureus* (MSSA) and methicillin resistant *Staphylococcus aureus* (MRSA) did not show any resistance to vancomycin, teicoplanin, linezolid or daptomycin. In *Enterococcus spp.*, tigecycline resistance was 1.9%, while daptomycin and linezolid resistance were not determined. The most effective resistance agent to *Acinetobacter spp.* and *Pseudomonas spp.* was colistin. Fungal infection was detected in 156 patients. *Candida albicans* and *Candida parapsilosis complex* were the most common isolates.

Conclusion: Antibiotic resistance rates are increasing in all over the world. Rational antibiotic usage may aid the clinicians to overcome this condition. Epidemiological data is important in this regard.

Keywords: Blood culture, Antibiotics susceptibility, Microorganisms

Öz

Amaç: Enfeksiyöz ajanların dağılımını ve antibiyotik direnç oranlarını bilmek, hastalığın ilerlemesini önlemek için antibiyotik tedavisine başlamada hayati öneme sahiptir. Bu çalışmada, Türkiye'de beş yıllık bir dönemde üçüncü basamak merkezimizden elde edilen kan kültürü izolatlarının dağılımını ve antimikrobiyal direnç paternlerini belirlemeyi amaçladık.

Yöntemler: Ocak 2014 - Aralık 2018 arasındaki mikrobiyoloji laboratuvar kayıtları geriye dönük olarak incelendi. Pozitif üreme sonuçları olan hastalar, izole edilen bakterilerin antimikrobiyal duyarlılık profilleri ile kaydedildi. Tanımlayıcı istatistikler (sayı, yüzde, ortalama ve ortanca) yapıldı. Gruplar arasındaki tanımlayıcı verilerin karşılaştırılması çapraz tablolarla ve ki kare testi ile yapıldı. İzolatlar arasındaki antibiyotik direnç oranlarını karşılaştırmak için tek yönlü ANOVA testi kullanıldı.

Bulgular: Bu kesitsel çalışmada toplam 66004 kan kültürü analiz edildi; 3882 (%21,0) pozitif sonuçtan 3256 (%4,9)'sı kontaminasyon olarak tanımlandı. En sık izole edilen mikroorganizmalar, Koagülaz negatif stafilokok, *Escherichiacoli, Klebsiella spp., Staphylococcus aureus* ve *Acinetobacter spp.*olarak belirlendi. Extended spectrum β-lactamase (ESBL) pozitifliği, 236 (% 62,4) *E.coli* izolatı, 186 (%56,8) *Klebsiella spp.*'de saptandı. Vankomisin direnci zamanla *Enterococcus spp.*'de anlamlı bir artış gösterdi. *E.coli,* imipenem, meropenem, tigesiklin veya kolistine karşı herhangi bir direnç göstermedi. Methicillin duyarlı *Staphylococcus aureus* (MSSA) and methicillin dirençli *Staphylococcus aureus* (MRSA), vankomisin, teikoplanin, linezolid veya daptomisine karşı herhangi bir direnç göstermedi. *Enterococcus spp.*'de tigesiklin direnci %1,9 iken daptomisin ve linezolid direnci saptanmadı. Dirençli *Acinetobacter spp.* ve *Pseudomonas spp.* için en etkili ajan kolistin'di. 156 hastada mantar enfeksiyonu saptandı. *Candida albicans ve Candida parapsilosis complex* en sık izolatlardı.

Sonuç: Antibiyotik direnç oranları tüm dünyada artmaktadır. Akılcı antibiyotik kullanımı klinisyenlerin bu durumu aşmalarına yardımcı olabilir. Bu konuda epidemiyolojik veriler önemlidir.

Anahtar kelimeler: Kan kültürü, Antibiyotik duyarlılığı, Mikroorganizmalar

How to cite / Atıf için: Arabacı Ç, Kutlu O. Evaluation of microorganisms isolated from blood cultures and their susceptibility profiles to antibiotics in five years period. J Surg Med. 2019;3(10):729-733.

Introduction

Bloodstream infections are clearly known to cause mortality and critical illnesses and for that reason prompt diagnosis and treatment is essential [1,2]. The etiological agents of bloodstream infections and their antimicrobial resistance rates differ significantly between countries [3]. Selection and timing of antibacterial treatment seriously affect outcomes in blood stream infections and empiric therapy is based on the antimicrobial sensitivity patterns [4]. For that reason, epidemiological data from different countries on different patient groups gain more importance. Blood culture is the gold standard for the diagnosis of bloodstream infections. Delays in diagnosis and treatment of blood stream infections may result in the septic shock and mortality [5].

To know the distribution of infectious agents and the antibiotic resistance rates is vital in starting antibiotic treatment especially in critically ill patients to prevent disease progression. In this study we aimed to determine the distribution and antimicrobial resistance patterns of blood culture isolates obtained in a tertiary center, in five year period, in Turkey.

Materials and methods

This study was performed in Health Sciences University Okmeydanı Education and Research Hospital, Medical Microbiology Department. The microbiological laboratory records between January 2014 and December 2018 were retrospectively reviewed. Each conventional aerobic blood culture bottle per patient with positive results was recorded with the antimicrobial susceptibility profiles of the bacteria isolated.

Blood cultures were assayed on a fully automated blood culture device, BACTEC 9240 (Becton Dickinson, Diagnostic Instrument System, Sparks, USA). The passage of the detected vials in the automated blood culture device to the MacConkey, chocolate and 5% sheep blood agar was performed. Colonies thought to be effective, were identified at the species level by the Phoenix ™ - 100 (Becton Dickinson, Diagnostic Instrument System, Sparks, USA) automated system and antibiotic susceptibilities were studied. Identification and antibiotic susceptibility tests were performed in Phoenix. In evaluation of susceptibilities was performed by Clinical and Laboratory Standards Institute (CLSI) in January 2014-December 2015, and of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) in January 2016- December 2018 [6,7]. Classical methods for identification of fungi and Phoenix ™, Sensititre Yeast One (TREK Diagnostic Systems, USA) kit based on colorimetric method for antifungal susceptibility were used. Due to the high risk of morbidity and mortality in patients with blood stream infections, bacteria with moderate susceptibility were classified as resistant to this antimicrobial agent.

Statistical analysis

Statistical analyses were performed with SPSS 21.0 (IBM Company, Chicago, IL) software. The conformity of the parameters to the normal distribution was evaluated by Kolmogorov-Smirnov test. Descriptive statistics (number, percentage, mean and median) were performed. Comparison of descriptive data between groups was performed with cross tables and chi square test. One-way ANOVA test was used to compare the antibiotic resistance rates between spp. Results with *P*-value <0.05 were considered statistically significant.

Results

In five years period, totally 66004 blood cultures were analyzed and among those, 13882 (21.0%) were having positive results. In detailed analyses of those isolates, 3256 were defined as contamination (mainly coagulase negative staphylococci (CoNS), *Corynebacterium spp., Gemella spp.,* non-pneumococcal alpha hemolytic streptococci, *Micrococcus spp.* etc.). Contamination rate was determined as 4.9%. Reproduction in single blood culture bottle, reproduction of different coagulase negative staphylococci or skin flora elements in the same patient's blood culture bottles obtained at the same time and inconvenience with the clinical features are regarded as contamination [8].

In a total of 10626 reproductions of 3116 patients (1715 female and 1401 male) were examined. Repetitive reproductions of the same patient were excluded. 95% (n=2960) of the reproductions were bacterial and 5% (n=156) were the yeasts. Among patients with bacterial growth, 52.5% were gram positive and 47.5% were gram negative. The mean age of the patients was 56.42 (22.19) years while the median age was 54 (range: 0-109) years. Of the patients, 3007 (96.5%) were hospitalized patients and 109 (3.5%) were outpatients. These patients were admitted to the emergency departments and then transferred to inpatient services.

The distribution of most commonly isolated microorganisms according to years is summarized in Table 1. Although the number of total cultures increased in time, the percentage of positive cultures in years was decreasing. The most commonly obtained microorganism was methicillin resistant coagulase negative staphylococci in all years. *E.coli* and *Klebiella spp.* were increasing in time.

Table 1: The distribution of most commonly isolated microorganisms according to years

	2014	2015	2016	2017	2018	Total
MRSA	22	22	17	32	21	114
MSSA	45	26	40	42	52	205
MRCoNS	180	130	157	110	133	710
MSCoNS	42	32	55	35	37	201
Enterococcus spp.	35	55	56	57	65	268
Escherichia coli	44	90	77	85	81	377
Klebsiella spp.	40	60	74	77	76	327
Acinetobacter spp.	32	61	68	59	81	301
Pseudomonas spp.	20	36	44	25	54	179
Others	36	49	57	76	60	278
Total	496 (5.2%)	561 (4.8%)	645 (4.6%)	598 (4.2%)	660 (3.9%)	2960
Number of blood cultures	9568	11730	13938	14210	16558	66004

MRCoNS: Methicillin Resistant Coagulase negative staphylococci, MSCoNS: Methicillin Susceptible Coagulase negative staphylococci, MRSA: Methicillin Resistant *Staphylococcus aureus*, MSSA: Methicillin susceptible *Staphylococcus aureus*, Others: Beta hemoliytic streptococcus [A, B, F, G], *Streptococcus pneumoniae, Listeria monocytogenes, Brucella spp., Morganella morganii, Serratia spp., Salmonella spp., Enterobacter spp., Proteus spp., Burkholderia cepacia, Stenotrophomonas maltophilia*

Regarding the blood cultures obtained from inpatients, *Acinetobacter*, *Klebsiella*, *Enterococci* and *Pseudomonas spp.* were most commonly isolated from intensive care unit followed by internal medicine wards, while *E.coli* and *S. aureus* were most commonly isolated from internal medicine wards. *Candida spp.* were also most commonly isolated from intensive care unit.

Extended spectrum β-lactamase (ESBL) positivity was determined in 236 (62.4%) isolates of *E.coli*, 186 (56.8%) isolates of *Klebsiella spp.* Distribution of ESBL positivity in time is summarized in Table 2.

Distribution of methicillin resistance in *S.aureus* and coagulase negative *staphylococcus spp*. is summarized in Table

3. Distribution of Vancomycin resistance in *Enterococcus spp.* is summarized in Table 4.

Table 2: Distribution of ESBL positivity in time

	2014	2015	2016	2017	2018	*P*-value
ESBL (+) *E.coli*	39.10%	47.70%	71%	69.40%	75%	0.001
ESBL(+) *Klebsiella spp.*	23%	33.30%	51.30%	79.20%	72.30%	0.001

Table 3: Distribution of MRSA and MRCoNS

	2014	2015	2016	2017	2018	*P*-value
MRSA	48.8%	44.4%	42.5%	43.2%	41.7%	0.105
MRCoNS	81%	80.20%	74%	76%	78%	0.242

Table 4: Distribution of Vancomycin resistance in *Enterococcus spp.* (VRE)

	2014	2015	2016	2017	2018	*P*-value
VRE	5.7 %	6.9 %	8.7 %	9.5 %	9.1 %	0.001

Antibiotic resistance profiles of *E.coli and Klebsiella spp.* were summarized in Table 5, antibiotic resistance profiles of MSSA and MRSA were summarized in Table 6, antibiotic resistance profiles of *Enterococcus spp.* in Table 7 and antibiotic resistance profile of *Pseudomonas* and *Acinetobacter spp.* were summarized in Table 8.

Table 5: Antibiotic resistance profiles of *E.coli* and *Klebsiella spp.* (%)

	E.coli	*Klebsiella spp.*
Ampicillin	81.1	-
Amoxicillin-Clavulanate	70.8	84.7
Piperacillin-Tazobactam	21.3	66.8
Cefazolin	67.3	88.1
Cefuroxime Axetil	75	85.6
Ceftazidime	58.6	80.9
Ceftriaxone	63.9	82.7
Cefepim	65	76.9
Amikasin	2.1	20.4
Gentamycin	27.7	51.9
TMP-SMZ	52.9	76.9
Ciprofloxacin	55.3	71.5
Ertapenem	4.7	57.1
Meropenem	0	42.2
Imipenem	0	41.2
Tigecycline	0	41.9
Colistin	0	28.8

TMP-SMZ: Trimethoprim-sulfamethoxazole

Table 6: Antibiotic resistance profiles of *MSSA* and *MRSA* (%)

	MSSA	MRSA
Erythromycin	11.6	45.2
Clindamycin	4.4	38.1
Tetracycline	7.7	62.1
Rifampicin	20	74.6
Ciprofloxacin	11.9	67.4
Levofloxacin	3.3	56.3
Quinupristin-dalfopristin	0	4.7
Daptomycin	0	0
Vancomycin	0	0
Teicoplanin	0	0
Linezolid	0	0
Tigecycline	0.6	16.9
TM*P*-SMZ	2.8	11.1

Table 7: Antibiotic resistance profile of *Enterococcus spp.* (%)

	Enterococcus spp.
Tigecycline	1.9
Vancomycin	9.6
Teicoplanin	9.6
Ampicillin	39.5
Daptomycin	0
Linezolid	0
Gentamycin (high level)	45.8
Streptomycin (high level)	62.1

Table 8: Antibiotic resistance profile of *Pseudomonas spp.* and *Acinetobacter spp.* (%)

	Pseudomonas spp.	*Acinetobacter spp.*
Imipenem	45	94.9
Meropenem	43.4	94.9
Piperacillin-Tazobactam	37.9	93.2
Ceftazidime	40.7	-
Ciprofloxacin	36.5	94.9
Levofloxacin	26.1	93.3
Colistin	2	3.4
TMP-SMZ	-	75

The number of fungal infections reproduced in the blood cultures of patients was 156 in five years. Among those, 36.5% (n=57) were *C.albians* and 63.5% (n=99) were non-albicans yeasts. The frequency of non-albicans yeasts, *C.parapsilosis complex*, *C.tropicalis*, *C.glabrata* and others (*C.keyfr*, *C.krusei*, *C.lusitaniae*, *C.dubliniensis etc.*) was 34%, 10.3%, 10.3% and 8.9%, respectively. Resistance to echinocandins was detected in one *C.parapsilosis* complex strain and Fluconazole resistance was detected in eight *C.parapsilosis* complex, two *C.albicans* and two naturally resistant *C.krusei* strains. The MIC value in amphotericin B (0.25 g/ml -1 µg/ml) was the highest in four *C.krusei, two C. albicans, two C.parapsilosis complex, one C.kefyr* and one *Trichosporon asahii.*

Discussion

In this study we reported the five years blood culture results with the susceptibility patterns of a tertiary center in Turkey. Culture positivity was 21.0% in this period of time. The five most commonly isolated microorganisms were coagulase negative staphylococcus, *E coli, Klebsiella spp., S aureus* and *Acinetobacter spp.* There was a significant increase in time in ESBL positivity in *E. coli* and *Klebsiella spp.* methicillin resistance did not increase significantly in time in *S. aureus* or coagulase negative staphylococcus. Vancomycin resistance showed a significant increase in *Enterococcus spp.* in time. *E.coli* did not show any resistance to imipenem, meropenem, tigecycline or colistin. MSSA and MRSA did not show any resistance to vancomycin, teicoplanin, linezolid or daptomycin. In *Enterococcus spp.*, tigecycline resistance was 1.9%, while Daptomycin, Linezolid resistance were not determined. *Acinetobacter spp.* was highly resistant to many antibiotics. The most effective agent for *Acinetobacter spp.* and *Pseudomonas spp.* was colistin.

Social, economical and environmental factors may affect the distribution of pathogens isolated from blood stream infections [9]. Culture positivity was 21.0%. The positivity rate was 16.1% when isolates considered to be contaminated were removed. In previous literature culture positivity was ranging between 12-50%. Our results were compatible with the previous data. Since our hospital is a tertiary center and the data was obtained from all of the departments of hospital, this data is crucial [10,11].When we look at the frequency of contamination detected in blood culture samples, this rate was 8.7% in the study of Yılmaz et al. [12] and 10.5% in the study of Sevim et al. [13]. On the other hand, Bentley et al. [14] found the rate of contamination as 4.74%. In our study, this rate was found to be 4.9%. Ideally, the contaminated blood culture rate should not exceed 2-3% [15]; however the rate of contamination in our hospital was higher. As a result, problems related to blood collection techniques, education level of the personnel taking blood, the place or region where the culture is taken are among the reasons that should be considered in the first place.

In this study, the most commonly isolated microorganisms were coagulase negative staphylococcus, *Klebsiella spp., S aureus, and E coli*. Similarly, in a study of Tian et al. *E. coli, S. aureus* and *K. pneumoniae* were reported as the most common pathogens in bloodstream infections in China [16]. Banik et al. [17] reported the contamination rate as 1.63% in 1895 blood specimens. They also reported the most common organisms as *S aureus*, Coagulase negative staphylococcus, and *Acinetobacter spp*.

ESBL production is an important resistance mechanism for bacteria causing a global health burden. It is an important cause of poor outcomes and increased hospital expenses [18,19].

Fennell et al. [20] reported that there was an increase in numbers of ESBL-producing *E. coli* isolated from urine and blood cultures between 2004 and 2008. In Ireland, in a surveillance performed with blood culture isolates, an increase in the prevalence of ESBL in *E. coli* has been reported [21]. In this study, we determined that ESBL positive *E.coli* was still highly susceptive to imipenem, meropenem, tigecycline and colistin but the same condition was not the case for *Klebsiella spp*. Carbapenem-resistance is one of the main problems in *K. pneumoniae. The rate of* carbapenem-resistant *K. pneumoniae* isolates was reported to be over 50%, which is a very serious condition [22]. In our country, ertapenem resistance in *K. pneumoniae* isolates was reported as 43% while imipenem/meropenem resistance was reported as 38% [23]. Due to the rapidincrease of carbapenem-resistance, colistin has been defined as the only treatment choice in resistant enteric bacteria [24]. In a recent study, Rojas et al. [25] reported the colistin resistance as 13% in 246 patients infected with *K. pneumonia.* Colistin resistance was also determined to be associated with high mortality. In our study, we found carbapenem resistance as 40-50% and colistin resistance as 28.8%. This high resistance rates significantly reduce the chance of treatment in *Klebsiella* infections.

We did not determine an increase in Methicillin resistance in *S.aureus* or in coagulase negative staphylococcus. Methicillin resistance is also a global health problem increasing morbidity and mortality and reaching 70% in *S.aureus* isolates in some southern countries [26,27]. We also determined that approximately half of *S. aureus* isolates and more than three fourth of coagulase negative staphylococcus isolates were Methicillin resistant. In a recent study performed on pediatric and adolescent patients, in a tertiary referral center, the most frequently identified microorganisms causing bacteremia were *S epidermidis* (26.1%), and *S aureus* (14.9%). They defined the Methicillin resistance in 60.3% of *S aureus* isolates [28]. As expected, MRSA isolates were more resistant to many antimicrobial agents than MSSA isolates. However, MRSA was completely susceptible to Vancomycin, teicoplanin, linezolid and daptomycin but was having a resistance rate of 4.7% to Quinupristin-dalfopristin. Vancomycin, linezolid and daptomycin are the first line recommended agents in MRSA treatment; which is also compatible with our results. Teicoplanin is another alternative in MRSA cases [29,30].

Enterococcus spp. are also an important cause of blood stream infections. In resistant cases the best alternative are the daptomycin and linezolid. Tigecycline resistance was also very low (1.9%) in *Enterococcus spp*. The number of vancomycin resistance in *Enterococcus spp*. was also increasing significantly in time. VRE were also highly resistant to high level gentamycin or streptomycin. In a recent study daptomycin treatment was reported to be associated with a higher rate of clinical failure as compared with linezolid treatment [31].

Another important finding of this study was also the high antibiotic resistance rates of *Acinetobacter spp*. This was also compatible with the previous literature [32]. In a study of El Mekes et al. [33], the most commonly isolated multi-drug resistant bacteria in the ICU were *Acinetobacter baumannii*. Multi-drug resistance in *Acinetobacter spp*. is also an imperative issue in hospitals.

Unfortunately, Candida species are increasingly causing hospital-acquired infections, which can lead to serious mortality, especially in immunocompromised patients. The most common *Candida species* in the world are *C.albicans* in the USA, Northern and Central Europe; while it is reported as non-albicans *Candida* in Asia, Southern Europe and South America [34]. In a study conducted in South Korea [35], *C.albicans* was found to be 38%, *C.parapsilosis* 26%, *C.tropicalis* 20% while in a study of Oztürk et al. [36], the rates of these fungi were reported as 53%, 30%, 5.5%, respectively. In our study, *C. albicans, C. parapsilosis complex* and *C. tropicalis* were the first three candida species in accordance with the previous data.

Varying proportions (0-20%) of amphotericin B resistance have been reported in previous literature [37-39]. Aydın et al. [40] reported *C.kefyr* and *C.lusitaniae* strains having MIC values >1 μg/ml for amphotericin B.

In our study, the MIC value in Amphotericin B was between 0.25 μg / ml -1 μg / ml and the highest MIC values were found in 4 *C. krusei*, 2 *C.albicans*, 2 *C.parapsilosis complex*, 1 *C.kefyr* and 1 *Trichosporonasahii*. Oztürk et al. [36] did not determine Fluconazole resistance in non-albicans *Candida species* other than intrinsic resistant *C. krusei*, whereas resistance was observed in 6 (32%) of *C.albicans* isolates. Aydın et al. [40] did not detect Fluconazole resistance except *C. glabrata* strains. In a study of Karabicak et al. [41], Fluconazole resistance rate was found to be 3.5% in *Candida species*. In our study, Fluconazole resistance was 6.4% for all candida species.

Echinocandin resistance is quite variable among *Candida* isolates. Diekema et al. [42] found micafungin resistance as 0.8% and Etiz et al. [43] found caspofungin resistance, anechinocandin derivative, as 11%. In our study, we detected echinocandin resistance in only one *Candida parapsylosis complex* isolate. This value was significantly lower than the data in the previous studies. Perhaps it may be due to the lack of intensive use of echinocandin in our hospital.

Limitations

The main strength of this study was the high number of blood cultures isolated. There are also some limitations of this study that should be mentioned. First, this is the report of a single center. Secondly, the treatment outcomes and antibiotic responses of patients were not analyzed since the number of blood cultures analyzed was very high. Lastly, chronic disease or conditions predisposing these infections were not recorded and analyzed in the study, which may be the topic of another study.

Conclusion

For rational antibiotic usage, epidemiological data is important. All tertiary centers should know the distribution of microorganisms and their susceptibility patterns in detail, in initiating treatment promptly to improve outcomes.

References

1. Kim HJ, Lee NY, Kim S, Shin JH, Kim MN, Kim EJ, et al. Characteristics of microorganisms isolated from blood cultures at Nine University Hospitals in Korea during 2009. Korean J Clin Microbiol. 2011;14:48–54.
2. Yiş R. Evaluation of blood cultures in a children's hospital located in Southeastern Anatolia. Turk Pediatri Ars. 2015 Jun 1;50(2):102-7.
3. Dat VQ, Vu HN, Nguyen The H, Nguyen HT, Hoang LB, Vu Tien Viet D, et al. Bacterial bloodstream infections in a tertiary infectious diseases hospital in Northern Vietnam: aetiology, drug resistance, and treatment outcome. Wertheim HFLBMC Infect Dis. 2017 Jul 12;17(1):493.

4. Deen J, von Seidlein L, Andersen F, et al. Community-acquired bacterial bloodstream infections in developing countries in south and southeast Asia: a systematic review. Lancet Infect Dis. 2012;12:480-7.
5. Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006 Jun;34(6):1589-96.
6. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. Twenty-fourth informational supplement update. CLSI document M100-S24. Clinical and Laboratory Standards Institute, Wayne, PA (2014).
7. EUCAST. EUCAST Clinical Breakpoint TableVersion 6.0, Valid From 2016-01-01. Basel: EUCAST, 2016. http://www.eucast.org/clinical_breakpoints/
8. Forbes BA, Sahm DF, Weissfeld AS. Bloodstream infectious. Bailey and Scott's Diagnostic Microbiology. 12th ed. St. Louis: Mosby Elsevier, 2012:778-97.
9. Diekema DJ, Pfaller MA, Schmitz FJ, Smayevsky J, Bell J, Jones RN, et al. Survey of infections due to Staphylococcus species: frequency of occurrence and antimicrobial susceptibility of isolates collected in the United States, Canada, Latin America, Europe, and the Western Pacific region for the SENTRY Antimicrobial Surveillance Program, 1997-1999. Clin Infect Dis. 2001 May 15;32 Suppl 2:S114-32.
10. Wattal C, Raveendran R, Goel N, Oberoi JK, Rao BK. Ecology of blood stream infection and antibiotic resistance in intensive care unit at a tertiary care hospital in North India. Braz J Infect Dis. 2014 May-Jun;18(3):245-51.
11. Mehdinejad M, Khosravi AD, Morvaridi A. Study of prevalence and antimicrobial susceptibility pattern of bacteria isolated from blood cultures. J Biol Sci. 2009;9:249–53.
12. Yılmaz S, Gümral R, Güney M, Bedir O, Üsküdar Güçlü A, Duyan S, et al. İki yıllık dönemde kankültürlerinden izole edilen mikroorganizmalar ve antibiyotik duyarlılıkların değerlendirilmesi. Gülhane Tıp Derg. 2013;55:247-52.
13. Sevim S, Öztürk Ş, Coşkuner A, Özgenç O, Avcı M. BACTEC kan kültür sistemi ile izole edilen mikroorganizmaların değerlendirilmesi. Turkish Journal of Infection. 2007;21(3):135-40.
14. Bentley J, Thakore S, L Muir, Baird A, Lee J. A change of culture: reducing blood culture contamination rates in an Emergency Department BMJ Quality Improvement Reports 2016;5:u206760.w275.
15. Sucu N, Çaylan R, Aydın K, Yılmaz G, Aktoz Boz G, Köksal İ. Karadeniz Teknik Üniversitesi Tıp Fakültesi Hastanesinde kan kültürlerinin prospektif olarak değerlendirilmesi. Mikrobiyol Bült. 2005;39:455-64.
16. Tian L, Sun Z, Zhang Z. Antimicrobial resistance of pathogens causing nosocomial bloodstream infection in Hubei Province, China, from 2014 to 2016: a multicenter retrospective study. BMC Public Health. 2018 Sep 15;18(1):1121.
17. Banik A, Bhat SH, Kumar A, Palit A, Snehaa K. Bloodstream infections and trends of antimicrobial sensitivity patterns at Port Blair. J Lab Physicians. 2018 Jul-Sep;10(3):332-7.
18. Lee SY, Kotapati S, Kuti JL, Nightingale CH, Nicolau DP. Impact of extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella species on clinical outcomes and hospital costs: a matched cohort study. Infect Control Hosp Epidemiol. 2006;27:1226–32.
19. Stewardson A, Fankhauser C, De Angelis G, Rohner P, Safran E, Schrenzel J, et al. Burden of bloodstream infection caused by extended-spectrum β-lactamase-producing enterobacteriaceae determined using multistate modeling at a Swiss University Hospital and a nationwide predictive model. Infect Control Hosp Epidemiol. 2013 Feb;34(2):133-43.
20. Fennell J, Vellinga A, Hanahoe B, Morris D, Boyle F, Higgins F, et al. Increasing prevalence of ESBL production among Irish clinical Enterobacteriaceae from 2004 to 2008: An observational study. BMC Infect Dis. 2012 May 15;12:116.
21. Health Protection Surveillance Centre Annual Report 2007. http://www.hpsc.ie/hpsc/AboutHPSC/AnnualReports/File,3377,en.pdf
22. World Health Organization. Antimicrobial resistance global report on surveillance. 2014. https://www.who.int/drugresistance/documents/surveillancereport/en/(Date of access: December 2018).
23. World Health Organization. Central Asian and eastern European surveillance of antimicrobial resistance (CAESAR), Annual report. 2018 http://www.euro.who.int/en/healthtopics/diseaseprevention/antimicrobial-resistance/publications/2017/centralasian-and-eastern-european-surveillance-ofantimicrobial-resistanceannual-report 2017-2018.
24. Neuner EA, Yeh JY, Hall GS, Sekeres J, Endimiani A, Bonomo RA, et al. Treatment and outcomes in carbapenem-resistant Klebsiellapneumoniae bloodstream infections. Diagn Microbiol Infect Dis. 2011;69(4):357-62.
25. Rojas LJ, Salim M, Cober E, Richter SS, Perez F, Salata RA, et al. Colistin resistance in carbapenem-resistant Klebsiella pneumoniae: Laboratory detection and impact on mortality. Clin Infect Dis. 2017;64(6):711-8.
26. Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, et al. Clinical practice guidelines by the infectious diseases society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children: executive summary. Clin Infect Dis. 2011 Feb 1;52(3):285-92.
27. 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 Oct 14;15(41):19688.
28. Stover KR, Morrison A, Collier T, Schneider E, Wagner JL, Capino AC, et al. Epidemiology and Risk Factors for Bacteremia in Pediatric and Adolescent Patients. J Pharm Pract. 2019 Aug 26:897190019868056.
29. Holland TL, Arnold C, Fowler VG Jr. Clinical management of Staphylococcus aureus bacteremia: a review. JAMA. 2014 Oct 1;312(13):1330-41.
30. Holubar M, Meng L, Deresinski S. Bacteremia due to Methicillin-Resistant Staphylococcus aureus: New Therapeutic Approaches. Infect Dis Clin North Am. 2016 Jun;30(2):491-507.
31. Narayanan N, Rai R, Vaidya P, Desai A, Bhowmick T, Weinstein MP. Comparison of linezolid and daptomycin for the treatment of vancomycin-resistant enterococcal bacteremia. Ther Adv Infect Dis. 2019 Feb 13;6:2049936119828964.
32. World Health Organization WHO publishes list of bacteria for which new antibiotics are urgently needed. (2017) Available from http://www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/en/ Accessed 1st Jan 2018
33. El Mekes A, Zahlane K, Ait Said L, Tadlaoui Ouafi A, Barakate M. The clinical and epidemiological risk factors of infections due to multi-drug resistant bacteria in an adult intensive care unit of University Hospital Center in Marrakesh-Morocco. J Infect Public Health. 2019 Sep 16.
34. Falagas ME, Roussos N, Vardakas KZ. Relative frequency of albicans and the various non-albicans Candida spp among candidemia isolates from inpatients in various parts of the world: a systematic review. Int J Infect Dis. 2010;14(11):e954-66.
35. Jung SI, Shin JH, Song JH, et al. Korean Study Group for Candidemia. Multicenter surveillance of species distribution and antifungal susceptibilities of Candida bloodstream isolates in South Korea. Med Mycol. 2010;48(4):669-74.
36. Öztürk T, Özseven AG, Sesli Çetin E, Kaya S. Kan kültürlerinden izole edilen Candida suşlarının tiplendirilmesi ve antifungal duyarlılıklarının araştırılması. Kocatepe Tıp Derg. 2013;14(1):17-22.
37. Fındık D, Tuncer İ, Arslan U. Candida Albicans Türü Maya Mantarlarında Antifungal İlaç Direnci. Serbest bildiri, P07-02. XXIX. Türk Mikrobiyoloji Kongresi, Antalya 8-13 Ekim 2000.
38. Zer Y, Balcı İ. Yoğun Bakım Ünitesindeki Hastalardan izole Edilen Candida Suşlarının İdentifikasyonu ve Antifungal Duyarlılıkları. Türk Mikrobiyol Cem Derg. 2002;32:230-4.
39. Cheng MF, Yu KW, Tang RB, Fan YH, Yang YL, Hsieh KS, et al. Distribution and Antifungal Susceptibility of Candida Species Causing Candidemia from 1996 to 1999. Diagn Microbiol Infect Dis. 2004;48:33-7.
40. Aydin F, Bayramoglu G, Guler NC, Kaklikkaya N, Tosun I. Bloodstream Yeast Infections in a University Hospital in Northeast Turkey: A 4-Year Survey. Med Mycol. 2011;49(3):316-9.
41. Karabıçak N, Alem N. Türlerinin Triazol Antifungal Duyarlılık Profilleri: Antifungal Direncin Belirlenmesinde Yeni CLSI Türe Özgü Klinik Direnç Sınır Değerleri ve Epidemiyolojik Eşik Değerlerinin Uygulanması. Mikrobiyol Bul. 2016;50(1):122-32.
42. Diekema DJ, Messer SA, Boyken LB, Hollis RJ, Kroeger J, Tendolkar S, et al. In vitro activity of seven systemically active antifungal agents against a large global collection of rare Candida species as determined by CLSI broth microdilution methods. J Clin Microbiol. 2009;47(10):3170-7.
43. Etiz P, Kibar F, Ekenoğlu Y, Yaman A. Kan kültürlerinden izole edilen Candida türlerinin dağılımının ve antifungal duyarlılıklarının retrospektif olarak değerlendirilmesi. ANKEM Derg. 2015;29(3):105-13.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):734-739.
DOI: 10.28982/josam.622377

Research article
Araştırma makalesi

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

Comparison of erythrocyte distribution width, mean platelet volume and platelet distribution width in patients with obstructive sleep apnea syndrome

Obstrüktif uyku apne sendromlu hastalarda eritrosit dağılım genişliği, ortalama trombosit hacmi ve trombosit dağılım aralığı karşılaştırılması

Hakan Çelikhisar [1], Gülay Daşdemir İlkhan [2]

[1] Izmir Metropolitan Municipality Hospital, Chest Diseases Clinic, Izmir, Turkey
[2] Okmeydanı Training and Research Hospital, Department of Chest Diseases, Istanbul, Turkey

ORCID ID of the author(s)
HC: 0000-0002-0109-3208
GDI: 0000-0001-6453-3867

Corresponding author / Sorumlu yazar:
Hakan Çelikhisar
Address / Adres: Gaziler Cad. No: 315, 35110, İzmir, Turkiye
e-Mail: hcelikhisar@hotmail.com

Ethics Committee Approval: The study was approved by Bezmialem Vakıf University, Non-Interventional Research Ethics Committee (Date: 05.02.2019, No: 54022451-050.05.04-1965).
Etik Kurul Onayı: Çalışma, Bezmialem Vakıf Üniversitesi, Girişimsel Olmayan Araştırmalar Etik Kurulu tarafından onaylandı (Tarih: 05.02.2019, Sayı: 54022451-050.05.04-1965).

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.

Published: 10/21/2019
Yayın Tarihi: 21.10.2019

Abstract

Aim: Reliable markers are needed to evaluate the response of chronic inflammation in obstructive sleep apnea syndrome (OSAS) to positive airway pressure (PAP) treatment. In this study, we aimed to investigate the long-term effects of PAP treatment on hemogram parameters and its relationship with inflammation and severity of disease in OSAS patients.

Methods: Based on polysomnography (PSG) results, 61 (35.1%) participants and 113 OSAS patients (64.9%) were included in the control and study groups, respectively. Among these patients, 31.6% had moderate and 33.3% had severe OSAS. MPV, PDW, RDW, hemoglobin, hemotocrit, platelet values were evaluated and compared between the groups at six and twelve-month intervals in this prospective cohort study.

Results: All participants (n=174) were males aged between 33-62 years. Hemoglobin, hematocrit and MPV values of the study group were significantly higher at the baseline (P=0.008, P=0.007, P=0.004, respectively) and had decreased significantly by the 6th and 12th months in both groups P=0.004, P=0.003, P=0.004, respectively).

Conclusion: All participants were chosen from males to exclude hormonal effects on hemogram parameters, which also turned out to be a limitation of this study. Our study showed a correlation between MPV, RDW, PDW, hemoglobin and hematocrit values and OSAS severity. MPV, RDW, hemoglobin, hematocrit and platelet may be considered inexpensive biomarkers easily obtained from blood tests which make it useful in determining the severity of OSAS and prioritizing patients for PAP therapy.

Keywords: Obstructive sleep apnea syndrome, Red cell distribution width, Mean platelet volume, Platelet distribution width

Öz

Amaç: Obstrüktif uyku apne sendromunda (OUAS) intermitant hipoksiye bağlı gelişen kronik inflamasyonun PAP tedavisine yanıtını değerlendirmede kullanılacak güvenilir belirteçlere ihtiyaç vardır. Bu çalışmada, pozitif havayolu basıncı tedavisinin uzun dönem sonuçlarının hemogram parametreleri üzerine etkisini ve OUAS'lı hastalarda inflamasyon ve hastalığın ciddiyeti ile ilişkisini araştırmayı amaçladık.

Yöntemler: Çalışma prospektif kohort tipi çalışma olarak planlandı. Polisomnografi (PSG) sonuçlarına göre OUAS saptanmayan 61 katılımcı (%35.1) kontrol grubu olarak alındı. OUAS saptanan 113 hasta (%64,9) çalışma grubu olarak alındı. Çalışma grubunun (%31,6)'sı orta OUAS, 58'i (%33,3) şiddetli OUAS idi. Hastaların MPV, PDW, RDW, hemoglobin, hemotokrit, trombosit değerleri değerlendirildi ve altı ve on iki ay arayla karşılaştırıldı.

Bulgular: Yaşları 33 ile 62 arasında değişen, toplam 174 hasta çalışmaya alındı. Başlangıçta hemoglobin, hematokrit ve MPV değerleri çalışma grubunda kontrol grubuna göre anlamlı derecede yüksek (sırasıyla P=0,008, P=0,007, P=0,004), her iki grupta da 6 ve 12 aydaki düşüşler istatistiksel olarak anlamlıydı (sırasıyla P=0,004, P=0,003, P=0,004).

Sonuç: Tüm katılımcıların erkek olması hemogram parametrelerine hormonal etkilerin dışlanması nedeni ile idi. Ancak çalışmaya sadece erkek katılımcıların dahil edilmesi aynı zamanda bu çalışmanın limitasyonu olabilir. Çalışmamız MPV, RDW, PDW ve hemoglobin, hematokrit değerleri ve OUAS şiddeti arasında bir ilişki olduğunu göstermiştir. MPV, RDW, hemoglobin, hematokrit, trombosit, PAP tedavisini değerlendirmeyi bekleyen OUAS hastalarını önceliklendirmede faydalı kılan basit, ucuz bir kan biyobelirteçine dönüşebilir.

Anahtar kelimeler: Obstrüktif uyku apne sendromu, Eritrosit dağılım genişliği, Ortalama trombosit hacmi, Trombosit dağılım aralığı

How to cite / Atıf için: Çelikhisar H, İlkhan GD. Comparison of erythrocyte distribution width, mean platelet volume and platelet distribution width in patients with obstructive sleep apnea syndrome. J Surg Med. 2019;3(10):734-739.

Introduction

Obstructive sleep apnea syndrome (OSAS), which is the most common respiratory sleep disorder, is characterized by recurrent collapse of the upper airway during sleep, nocturnal hypoxemia, and sleep interruption [1]. OSAS progresses with inflammation and airway remodeling and is associated with systemic inflammation [2]. Systemic inflammation is also strongly related with various metabolic and cardiovascular diseases such as peripheral vascular disease, coronary artery disease, hypertension, heart failure, cardiac arrhythmias, and diabetes mellitus [2,3]. Red cell distribution width (RDW), platelet activation and inflammation are connected with OSAS pathogenesis. There are studies indicating that erythrocyte distribution width and platelet activation increase in cardiovascular events. Mean platelet volume (MPV) and Platelet distribution width (PDW) are indicators of platelet activation [3,4].

OSAS increases the risk of cardiovascular and metabolic diseases independent of weight [4]. Recently, the autonomic nervous system changes caused by recurrent respiratory events and arousals, systemic inflammatory changes caused by hypoxia attacks and sleep deprivation were researched and different results were obtained [5].

Inflammation is a reaction caused by harmful agents in the tissue. In OSAS, asphyxia, increased intrathoracic negative pressure, hypoxia-reoxygenation, ischemia-reperfusion, hypercapnia, acidosis, apnea, and arousal-induced autonomic nervous system activation are effective in the development of local and systemic inflammation [6]. Endothelial damage, increased inflammatory mediators, increased sympathetic activity and hypoxemia are the leading factors in the development of cardiovascular events frequently seen in OSAS [7]. The formation of hypoxia-induced free radicals is associated with subsequent oxidative stress and hypercapnia, which causes endothelial function loss by local, neural reflex mechanisms, paving the way for atherosclerosis. In patients with apnea, oxidative stress causes subclinical atherosclerosis without any cardiovascular disease, which may increase cardiovascular morbidity [8]. If treatment is begun after the detection of OSAS, it becomes less challenging to control a series of systemic and vascular diseases with severe morbidity such as hypertension, arrhythmia, and atherosclerosis [10,11]. Inflammation plays a key role in endothelial dysfunction and atherosclerotic vascular disease. Platelets are related to inflammation, thrombosis and atherogenesis [9,10] in the following way: Active platelets stimulate leukocyte activation by forming aggregates through physical interaction with leukocytes. These platelet-leukocyte complexes are considered as markers in platelet activating conditions such as stable coronary artery disease, unstable atherosclerosis, and vascular disease [11].

To better understand the pathophysiology of OSAS, recent studies have been conducted to evaluate the course of hematological parameters, especially MPV, PDW and RDW. However, the relationship between these parameters and severity of OSAS remains controversial. The aim of this study was to evaluate the relationship between hematological parameters, disease severity and response to PAP treatment in OSAS.

Materials and methods

Patients who were diagnosed with moderate and severe OSAS by polysomnography (PSG) between January 2017 and December 2018 in Izmir Eşrefpaşa Municipality Hospital sleep laboratory and treated with PAP were included in this prospective cohort study. Patients with other sleep disorders, anemia, polycythemia and other hematological diseases, any malignities, chronic liver-kidney disease, heart failure, ischemic heart disease, peripheral vascular disease, those receiving anticoagulant medications, patients with CRP>10 and female patients were excluded from the study. Only males were included in this study to exclude the variability of hormonal effects on hemogram parameters. According to studies, 17-beta estradiol inhibits erythropoietin synthesis caused by hypoxia in the kidneys and testosterone has a stimulating effect on erythropoiesis, the mechanism of which is unknown [12]. Individuals with normal PSG results and no known diseases were included in the control group.

The demographic and clinical characteristics of each participant, i.e., age, weight, height, smoking, and medical history, were recorded. All participants were followed-up at night by a trained sleep technician in our sleep center with a PSG device, obtaining a PSG record of at least 6 hours. PSG was performed in accordance with the American Academy of Sleep Diseases Classification criteria [1]. Based on PSG results, apnea hypopnea index (AHI) <5 was considered normal and AHI ≥5 was classified as OSAS. Then the OSAS group was divided into three groups according to the degree of disease. Those with AHI scores of 5-15 were classified as mild OSAS, 15-30 as moderate OSAS and AHI score >30 as severe OSAS. Patients with mild OSAS were excluded because they were not indicated to receive PAP treatment.

Blood was collected into hemogram tubes for routine complete blood counts. Hemogram parameters were measured with an automated hematology analyzer (Abbott Cell-Dyn 3700 Hematology Analyzer, Abbott Diagnostics, USA). All test results were recorded. Baseline MPV, PDW, RDW, hemoglobin, hematocrit, platelet values of the three groups were recorded and compared.

One hundred thirteen patients with moderate and severe OSAS underwent PSG for the second time and positive airway pressure (PAP) titration was performed. MPV, PDW, RDW, hemoglobin, hematocrit, platelet counts were obtained in the 6^{th} and 12^{th} months when 113 moderate and severe OSAS patients receiving PAP treatment were invited for follow-up visits. Patients under PAP treatment were evaluated for compliance based on PAP software data. They were considered compliant with more than 4 hours of use per night for at least 4 days a week [13].

Statistical analysis

IBM SPSS Statistics v22 (SPSS IBM, Turkey) were used. Demographic definitions of individuals were presented as Frequency (n) and Percent (%). Kolmogorov-Smirnov test was performed to determine the normality of the data, which showed that not all variables were normally distributed ($P<0.05$). For non-normal distribution, non-parametric tests were used to evaluate the differences between the groups. Chi-Square test was used to determine whether obstructive sleep apnea syndrome

(OSAS) severity differed with demographic characteristics such as age and smoking status. Kruskal-Wallis test was used to compare the initial hemogram results of patients with moderate and severe OSAS. Friedman test was performed to evaluate hemogram values at baseline, 6th and 12th months moderate and severe OSAS patients. Spearman's Rho Correlation Coefficient was utilized to evaluate the relationship between red cell distribution width, apnea-hypopnea index, minimum oxygen saturation, average oxygen saturation and mean desaturation index.

Results

The study was conducted on 174 male patients aged between 33 to 62 years. 61 participants (35.1%) constituted the control group. 55 patients (31.6%) with moderate OSAS and 58 patiens (33.3%) with severe OSAS were included in the study group. The mean age of all patients was 44.6 (6.5) years. Mean apnea-hypopnea index (AHI) of patients with moderate and severe OSAS and all OSAS patients combined were 21.00, 50.90 and 35.4, respectively. The mean body mass index (BMI) of the cases was 31.4 (3.5). 74 (42.5%) patients had never smoked, 70 (40.2%) were smoking and 30 (17.3%) were ex-smokers.

There was no statistically significant difference with respect to age and smoking rates between moderate, severe OSAS and non-OSAS (P=0.076) participants. There was a significant difference between the BMI rates (P<0.001). However, no statistically significant BMI change was observed in the moderate and severe OSAS groups after PAP treatment (P=0.741). Demographic and clinical characteristics of moderate and severe OSAS and control groups are shown in Table 1.

The comparison of baseline Hb, Htc, PLT, MPV, PDW and RDW values yielded a statistically significant difference among all three groups (P<0.05). Initial hemogram values and multiple comparison tests of the patients are shown in tables 2 and 3. The hematological parameters of moderate OSAS patients under treatment are shown in Tables 4 and 5. Baseline, 6th and 12th month-RDW values of moderate OSAS patients remained similar (P=0.473). All other hemogram values were significantly different in at least two measurements. The hemogram values of severe OSAS patients under treatment are shown in Tables 6 and 7.

In severe OSAS patients, the only statistically non-significant overall change from baseline until the 6th and 12th months occurred in PDW values (P=0.101). All other hemogram values differed significantly. In addition, the multivariate analysis revealed that RDW values between baseline and at the 6th month were similar (P=0.971), and all other changes were significant.

Table 1: Comparison of demographic and clinical characteristics of the groups

	OSAS None (n=65)	Moderate OSAS (n= 55)	Severe OSAS (n=58)	*P*-value
Age	45.6 (7.6)	44.5 (1.4)	43.7 (5.3)	0.076
BMI	29.2 (2.5)	31.8 (1.7)	33.8 (3.1)	<0.001
Cigarette				
Never smoked	29 (16.7%)	22 (29.7%)	23 (13.2%)	0.240
Ex smoker	11 (6.3%)	11 (36.7%)	8 (4.6)	
Smoker	21 (12.1%)	22 (31.4%)	27 (15.5%)	

OSAS: Obstructive Sleep Apnea Syndrome, BMI: Body mass index

Table 2: Kruskal Wallis test results for initial hemogram values

Variant	OSAS Classification	n	Mean Average (SD)	Median	Test Value	*P*-value
Hemoglobin	Control group	61	12.16 (1.282)	12.20	110.426	0.008*
	Moderate OSAS	55	16.03 (1.305)	16.10		
	Severe OSAS	58	16.75 (1.508)	16.80		
Hematocrit	Control group	61	36.36 (5.614)	37.10	104.374	0.007*
	Moderate OSAS	55	47.54 (6.953)	47.20		
	Severe OSAS	58	136.65(663.303)	50.75		
Platelet	Control group	61			62.704	0.004*
	Moderate OSAS	55				
	Severe OSAS	58				
MPV	Control group	61	8.31 (1.134)	8.20		
	Moderate OSAS	55	11.65 (1.272)	11.30	109.714	0.007*
	Severe OSAS	58	12.78 (1.647)	12.55		
PDW	Control group	61	13.94 (2.231)	13.20		
	Moderate OSAS	55	17.61 (3.317)	16.50	53.694	0.008*
	Severe OSAS	58	15.12 (9.157)	13.15		
RDW	Control group	61	13.24 (1.285)	13.20		
	Moderate OSAS	55	14.17 (1.626)	13.50	11.006	0.004*
	Severe OSAS	58	13.77 (1.626)	14.20		

Kruskal Wallis Test, *: Statistically significant (P<0.05), SD: Standard Deviation, MPV: Mean platelet volume, PDW: Platelet distribution width, RDW: Red cell distribution width

Table 3: Multiple comparison test results for initial hemogram values

Variant	Multiple groups	Test Value (SD)	*P*-value
Hemoglobin	Control-Mod. OSAS	-73.381 (9.360)	0.007*
	Control-Svr. OSAS	-91.431 (9.231)	0.005*
	Mod.OSAS-Svr. OSAS	-18.050 (9.474)	0.170
Hematocrit	Control-Mod. OSAS	-75.048 (9.364)	0.004*
	Control-Svr. OSAS	-86.777 (9.236)	0.006*
	Mod.OSAS-Svr. OSAS	-11.729 9.479)	0.648
Platelet	Control-Mod. OSAS	-64.187 (9.352)	0.003*
	Control-Svr. OSAS	1.506 (9.224)	0.99
	Mod.OSAS-Svr. OSAS	65.693 (9.466)	0.002*
MPV	Control-Mod. OSAS	-68.462 (9.357)	0.004*
	Control-Svr. OSAS	-93.120 (9.226)	0.006*
	Mod.OSAS-Svr. OSAS	-24.658 (9.471)	0.028*
PDW	Control-Mod. OSAS	-57.283 (9.351)	0.003*
	Control-Svr. OSAS	5.361 (9.223)	0.97
	Mod.OSAS-Svr. OSAS	62.645 (9.465)	0.001*
RDW	Control-Mod. OSAS	-30.704 (9.334)	0.007*
	Control-Svr. OSAS	-18.023 (9.326)	0.151
	Mod.OSAS-Svr. OSAS	12.681 (9.447)	0.539

*: Statistically significant (P<0.05) MPV: Mean platelet volume, PDW: Platelet distribution width, RDW: Red cell distribution width, Mod: Moderate, Svr: Severe

Table 4: Friedman test results for hemogram values in moderate OSAS patient group

Variable	Time	Mean	*P*-value
Hemoglobin	Baseline	16.03	0.004*
	6th month	13.70	
	12th month	12.85	
Hematocrit	Baseline	47.54	0.003*
	6th month	42.14	
	12th month	39.09	
Platelet	Baseline	339818	0.005*
	6th month	279090	
	12th month	228818	
MPV	Baseline	11.65	0.004*
	6th month	7.39	
	12th month	6.54	
PDW	Baseline	17.61	0.006*
	6th month	16.41	
	12th month	16.07	
RDW	Baseline	14.17	0.473
	6th month	14.33	
	12th month	14.21	

*: Statistically significant (P<0.05), MPV: Mean platelet volume, PDW: Platelet distribution width, RDW: Red cell distribution width

Table 5: Multiple comparison test results for hemogram values in the moderate OSAS group

Variable	Multiple groups	Test Value	*P*-value
Hemoglobin	Baseline- 6th month	1.018	0.008*
	Baseline- 12th month	1.982	0.007*
	6th month-12th month	0.964	0.005*
Hematocrit	Baseline-6th month	1.000	0.006*
	Baseline-12th month	1.945	0.007*
	6th month-12th month	0.945	0.005*
Platelet	Baseline-6th month	0.909	0.008*
	Baseline-12th month	1.764	0.004*
	6th month-12th month	0.855	0.003*
MPV	Baseline-6th month	0.964	0.007*
	Baseline-12th month	1.982	0.004*
	6th month-12th month	1.018	0.008*
PDW	Baseline-6th month	0.473	0.040*
	Baseline-12th month	0.727	0.005*
	6th month-12th month	0.255	0.546

*: Statistically significant (P<0.05) MPV: Mean platelet volume, PDW: Platelet distribution width.

Table 6: Friedman test results for hemogram values in severe OSAS patients

Variable	Time	Mean (SD)	Test Value	*P*-value
Hemoglobin	Baseline	16.75 (2.95)	102.448	0.004*
	6th month	13.61 (1.98)		
	12th month	12.71 (1.07)		
Hematocrit	Baseline	49.58 (2.95)	100.652	0.006*
	6th month	42.97 (1.96)		
	12th month	39.58 (1.09)		
Platelet	Baseline	248224 (1.34)	48.517	0.007*
	6th month	283965 (2.02)		
	12th month	312120 (2.64)		
MPV	Baseline	12.78 (2.97)	110.103	
	6th month	7.62 (2.02)		0.008*
	12th month	6.21 (1.02)		
PDW	Baseline	15.12 (1.81)	4.586	
	6th month	14.54 (2.21)		0.101
	12th month	13.99 (1.98)		
RDW	Baseline	13.77 (2.28)	15.799	
	6th month	13.35 (2.13)		0.009*
	12th month	13.09 (1.59)		

*: Statistically significant (P<0.05), MN Mean: Mean of Row Numbers, MPV: Mean platelet volume, PDW: Platelet distribution width, RDW: Red cell distribution width

Table 7: Multiple comparison test results for hemogram values in severe OSAS patient group

Variant	Multiple groups	Test value	*P*-value
Hemoglobin	Baseline-6th month	0.914	0.008*
	Baseline-12th month	1.879	0.007*
	6th month-12th month	0.966	0.009*
Hematocrit	Baseline-6th month	0.862	0.008*
	Baseline-12th month	1.853	0.007*
	6th month-12th month	0.991	0.009*
Platelet	Baseline-6th month	-0.672	0.005*
	Baseline-12th month	-1.293	0.004*
	6th month-12th month	-0.621	0.007*
MPV	Baseline-6th month	1.000	0.06*
	Baseline-12th month	1.948	0.005*
	6th month-12th month	0.948	0.008*
RDW	Baseline-6th month	0.155	0.971
	Baseline-12th month	0.698	0.007*
	6th month-12th month	0.543	0.009*

*: Statistically significant, MPV: Mean platelet volume, PDW: Platelet distribution width

The hemogram values of moderate and severe OSAS patients under treatment are presented in Tables 8 and 9. There was no statistically significant difference in platelet and PDW values between baseline and post-treatment hemogram results in patients with moderate and severe OSAS (P=0.334, P=0.089, respectively). All other hemogram values (Hb, Htc, MPV, RDW) were statistically different between at least two measurements. In the multiple comparison test analysis performed to compare the variables at baseline and 6th month of PAP therapy between moderate and severe OSAS groups, the only non-significant result was detected in RDW values (P=0.994). All other hemogram values were significantly different between baseline, 6th and 12th month measurements.

Table 10 presents the analysis performed to determine the correlation between RDW, apnea hypopnea index (AHI) of moderate and severe OSAS patients under treatment, minimum oxygen saturation, average oxygen saturation and ODI (Oxygen desaturation index). A positive and statistically significant correlation was found between baseline and 6th month RDW values, and 6th month and 12th month RDW values (Rho = 0.427, P<0.01). A negative statistically significant correlation of 15.5% was found to exist between 12th month RDW and ODI (Rho=-0.155, P<0.05). AHI was seen to negatively correlate with minimum O_2 saturation and mean O_2 saturation, and strongly positively correlate with ODI by 94.7%. Finally, mean O_2 saturation was found to significantly negatively correlate with ODI (Rho=-0.539, P<0.01).

Table 8: Friedman test results for hemogram values in moderate and severe OSAS patient groups

Variable	Time	Mean (SD)	Test Value	*P*-value
Hemoglobin	Baseline	16.40 (2.96)	211.218	0.008*
	6th month	13.65 (2.00)		
	12th month	12.78 (1.04)		
Hematocrit	Baseline	48.54 (2.96)	204.520	0.007*
	6th month	42.97 (1.99)		
	12th month	39.58 (1.06)		
Platelet	Baseline	248224 (2.09)	2.195	0.334
	6th month	283965 (2.02)		
	12th month	312120 (1.89)		
MPV	Baseline	12.78 (2.98)	218.071	
	6th month	7.62 (2.02)		0.006*
	12th month	6.21 (1.02)		
PDW	Baseline	15.12 (2.10)	4.832	
	6th month	14.54 (2.07)		0.089
	12th month	13.99 (1.87)		
RDW	Baseline	13.77 (2.10)	8.783	
	6th month	13.35 (2.13)		0.012*
	12th month	13.09		

*: Statistically significant (P<0.05), MPV: Mean platelet volume, PDW: Platelet distribution width, RDW: Red cell distribution width

Table 9: Multiple comparison test results for hemogram values in moderate and severe OSAS patient groups

Variable	Multiple groups	Test value	*P*-value
Hemoglobin	Baseline-6th month	0.965	0.008*
	Baseline-12th month	1.929	0.006*
	6th month-12th month	0.965	0.009*
Hematocrit	Baseline-6th month	0.969	0.007*
	Baseline-12th month	1.898	0.005*
	6th month-12th month	0.929	0.009*
MPV	Baseline-6th month	0.982	0.008*
	Baseline-12th month	1.965	0.006*
	6th month-12th month	0.982	0.009*
RDW	Baseline-6th month	-0.031	0.994
	Baseline-12th month	0.323	0.046*
	6th month-12th month	0.354	0.023*

*: Statistically significant (P<0.05), MPV: Mean platelet volume, RDW: Erythrocyte distribution width

Table 10: Correlation analysis results to determine the correlation between the variants

	RDW at the 6th month	RDW at the 12th month	Minimum O_2 saturation	Apnea-hypopnea index	Mean O_2 saturation	ODI
RDW Baseline	0.458** (P<0.01)	0.138 0.069	0.1 0.191	-0.067 0.377	-0.108 0.156	0.098 0.200
RDW 6th month		0.427** (P<0.01)	-0.085 0.264	0.056 0.460	-0.043 0.569	-0.111 0.144
RDW 12th month			-0.123 0.105	0.021 0.783	0.184 0.015	-0.155 0.042
Apnea-hypopnea index				-0.684** (P<0.01)	-0.510** (P<0.01)	0.947** (P<0.01)
Minimum O_2 Saturation					0.526** (P<0.01)	-0.719** (P<0.01)
Mean O_2 Saturation						-0.539** (P<0.01)

**: Statistically significant (P<0.01) , RDW: Red cell distribution width, ODI: Oxygen desaturation index

Discussion

In this study, we aimed to investigate the relationship between severity and MPV, PDW, RDW, Hb, and platelet count. The secondary aim was to investigate the effects of inflammation in OSAS and its response to PAP treatment. MPV, PDW and RDW were considered as markers of inflammation.

New indices related to erythrocytes and platelet counts were investigated and their relationship with MPV, PDW and RDW gained importance [14]. Platelet size measured by MPV is the best-known platelet indice and a sign of platelet activity and aggregation. Another sign would be the platelet distribution width (PDW), which is obtained from direct flow cytometric measurements of platelet cell volume. RDW is a dimensional measure of variability of circulating erythrocytes. Impaired eryhtropoiesis and increased eryhtrocyte destruction lead to greater heterogeneity and subsequentially, higer RDW. These parameters are useful clinical markers of various cardiovascular and thrombotic diseases [15].

In our study, MPV, an indicator of platelet activation, was significantly higher in patients with both moderate and severe OSAS at baseline compared to the control group.

Decreases in MPV values at the 6th and 12th months compared to baseline values after PAP treatment were statistically significant in both groups and the decrease in MPV correlated with AHI and desaturation index.

In a previous study, a relationship was found between MPV and cardiovascular disease risk and prognosis [16]. PAP is known to reduce cardiovascular risks by reducing ambulatory blood pressure and arterial stiffness while increasing the sensitivity of arterial baroreflex [17]. In addition, PAP reduces systemic inflammation, airway obstruction and hypoxia, and decreases levels of OSAS-mediated inflammatory mediators [18]. Similar to our results, it was found that a 6-month-long PAP treatment significantly reduced MPV values in patients with severe OSAS [19,20]. Decreased MPV can be explained by reduced hypoxia and inflammation.

Günbatar at al. [21] investigated the relationship between OSAS and MPV values and found that MPV values were similar in OSAS and control groups. However, subjective tests were applied to control group patients and polysomnography (PSG) was not performed. One of the major differences of our study was that the control group was selected from patients with AHI <5 based on the results of PSG examination.

Increased inflammatory markers causing inflammation have been reported in OSAS patients [22]. This situation is one of the presumed links between OSAS and increased cardiovascular morbidity. Inflammation is strongly associated with pro-inflammatory cytokine production, ineffective erythropoiesis, tumor necrosis factor alpha, interleukin 6, which renders bone marrow erythroid progenitors susceptible to erythropoiesis, prevents erythrocyte maturation and promotes anisocytosis [23]. Other mechanisms responsible for increased thrombotic risk in OSAS patients, which should not be ignored, are obesity and concurrently reduced exercise capacity [24].

In our study, no statistically significant difference was found in the BMI values of patients before and after treatment. The fact that BMI values do not affect the results of the study is valuable. RDW is hypothesized to change in coronary artery diseases, in which erythropoiesis is disrupted due to chronic inflammation or increased due to erythropoietin production [25].

In our study, RDW values were significantly higher in patients with moderate OSAS compared to controls at baseline, but the decrease in RDW at 6th and 12th months of treatment was not significant. In the severe OSAS group, the initial RDW values were non-significantly higher than the control group and there was a significant decrease in RDW between the 6th and 12th months.

There is no consensus in the literature about the RDW expression in OSAS. Some authors have shown that RDW values are higher in OSAS patients than controls [25,26], while other studies have reported that the RDW values of OSAS patients, indiviuals with simple snoring and control group were similar. Similar to our study, there are studies reporting that patients with OSAS have higher RDW values than controls, but there is no correlation between OSAS severity and RDW [26]. In our study, RDW was significantly increased regardless of the severity of OSAS, but it was associated with OSAS severity after PAP treatment and there was a more significant decrease in RDW value in the second six-month period. The precise mechanism of these results is unclear; however, this may be related to the presence of chronic inflammation In fact, chronic inflammation increases RDW by increasing the deformability of the red blood cell membrane and changes erythropoiesis [27]. In this sense, the strongest correlation of 94.7% existed between AHI and ODI values. Finally, there is a statistically significant negative relationship between the average O_2 saturation and ODI.

In our study, PDW values were significantly higher in patients with moderate OSAS compared to controls at baseline and a significant decrease in PDW was observed when the baseline and 6th month and baseline and 12th month measurements of treatment were compared. In the severe OSAS group, the initial PDW values were non-significantly higher than the control group, and there was no statistically significant difference between the 6th and 12th month measurement values. Our results regarding the tendency of MPV and PDW to increase with OSAS severity can be explained by increased platelet activation [28]. MPV is the best known of platelet parameters, whereas PDW is less documented and derived from direct flow cytometric measurements of platelet cell volume. Interestingly, there is no data and acceptance to show cut-off values for MPV and PDW and to diagnose increased platelet activation in patients with OSAS.

Bülbül and collegues [29] suggested that the optimal PDW value that differentiates non-apneic controls from patients with OSAS is 16.62. However, a consensus is yet to be reached. Due to the quantitative nature of PDW in the assessment of platelet size and volume, its use remains limited [28,29].

Initially, Hb and Htc values were significantly higher in patients with moderate and severe OSAS compared to the control group, and the decrease in values at 6 and 12 months after treatment was statistically significant. Platelet values were higher in both moderate and severe groups than that of the control group, but statistically significant only in the moderate group and the decreases at 6 and 12 months after PAP treatment were significant in both groups.

Chronic intermittent hypoxia with an increase in hematological parameters causes an increase in erythropoietin expression, which induces erythropoiesis [28].

Correction of respiratory events with PAP and associated hypoxia and inflammation may result in decreased RDW, hemoglobin, and hematocrit as in our study. These findings contradict the expected increase in RDW following a decrease in hemoglobin. Therefore, RDW may be affected by PAP regardless of hemoglobin levels due to the beneficial effects of PAP on hypoxia, which may reduce RDW.

Significant decrease in MPV, hemoglobin and hematocrit levels in both OSAS groups after PAP treatment in OSAS is consistent with similar studies [29,30]. In our study, there was no statistically significant difference between the baseline and post-treatment platelet and PDW values, in which patients with moderate and severe OSAS were evaluated together. This can be attributed to the decrease in mean values of platelets and PDW in the severe OSAS group. In all other hemogram values (Hb, Htc, MPV, RDW), a statistically significant difference was found between at least two

measurements when the control group and the medium-severe group were compared.

In the multiple comparison test analysis of the variables with statistically significant differences in the moderate-severe OSAS group, no statistically significant difference was found between the initial and 6th month-RDW values. All other hemogram values were statistically different between baseline, 6th and 12th month measurements. Our study demonstrated the importance of hematological assessment as a complementary tool for diagnosis and response to treatment in OSAS patients.

Limitations

The inclusion of only the male patients in the study is the limitation of our study. The findings of this study must be evaluated in light of this limitation.

Conclusion

RDW and PDW values can be used as indicators of OSAS severity. They are easy and inexpensive tools to assess OSAS patients initially and after PAP treatment in laboratories with long waiting lists.

References

1. Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. Chest. 2014 Nov;146(5):1387-94.
2. Waters KA, Mast BT, Vella S, De la Eva R, O'brien LM, Bailey S, et al. Structural equation modeling of sleep apnea, inflammation, and metabolic dysfunction in children. J Sleep Res. 2007;16(4):388-95.
3. Rahangdale S, Yeh SY, Novack V, Stevenson K, Barnard MR, Furman MI, et al. The influence of intermittent hypoxemia on platelet activation in obese patients with obstructive sleep apnea. J Clin Sleep Med. 2011;7(02):172-8.
4. Drager LF, Togeiro SM, Polotsky VY, Lorenzi-Filho G. Obstructive sleep apnea: a cardiometabolic risk in obesity and the metabolic syndrome. J Am Coll Cardiol. 2013;62(7):569-76.
5. Leung RS, Douglas Bradley T. Sleep apnea and cardiovascular disease. Circulation. 2001;164(12):2147-65.
6. Ardiç S. Obstrüktif Uyku Apne Sendromu ve İnflamasyon. J Int Med Sci. 2007;3(26):61-8.
7. Kondo Y, Kuwahira I, Shimizu M, Nagai A, Iwamoto T, Kato S, et al. Significant relationship between platelet activation and apnea-hypopnea index in patients with obstructive sleep apnea syndrome. Tokai J Exp Clin Med. 2011;36(3):79-83.
8. Mandal S, Kent BDJJotd. Obstructive sleep apnoea and coronary artery disease. J Thorac Dis. 2018;10(Suppl 34):S4212.
9. Gabryelska A, Łukasik ZM, Makowska JS, Białasiewicz P. Obstructive sleep apnea: from intermittent hypoxia to cardiovascular complications via blood platelets. Front Neurol. 2018;9.
10. Langer HF, Gawaz M. Platelet-vessel wall interactions in atherosclerotic disease. Thromb Haemost. 2008 Mar;99(3):480-6.
11. Nena E, Papanas N, Steiropoulos P, Zikidou P, Zarogoulidis P, Pita E, et al. Mean platelet volume and platelet distribution width in non-diabetic subjects with obstructive sleep apnoea syndrome: new indices of severity? Platelets. 2012;23(6):447-54.
12. Coviello AD, Kaplan B, Lakshman KM, Chen T, Singh AB, Bhasin S. Effects of graded doses of testosterone on erythropoiesis in healthy young and older men. J Clin Endocrinol Metab. 2008 Mar;93(3):914-9.
13. Hiensch R, Nandedkar DS, Feinsilver SH. Optimizing CPAP Treatment for Obstructive Sleep Apnea. Curr Sleep Medicine Rep. 2016;2(2):120-5.
14. Wiwanitkit V. Plateletcrit, mean platelet volume, platelet distribution width: its expected values and correlation with parallel red blood cell parameters. Clinical and applied thrombosis/hemostasis: Official journal of the International Academy of Clinical and Applied Thrombosis/Hemostasis. Cardiology. 2004;10(2):175-8.
15. Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianou I. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. Hippokratia. 2010;14(1):28.
16. Yokoe T, Minoguchi K, Matsuo H, Oda N, Minoguchi H, Yoshino G, et al. Elevated levels of C-reactive protein and interleukin-6 in patients with obstructive sleep apnea syndrome are decreased by nasal continuous positive airway pressure. Circulation. 2003;107(8):1129-34.
17. Ciccone M, Scicchitano P, Zito A, Cortese F, Boninfante B, Falcone V, et al. Correlation between inflammatory markers of atherosclerosis and carotid intima-media thickness in obstructive sleep apnea. Molecules. 2014;19(2):1651-62.
18. Karamanli H, Ozol D, Ugur KS, Yildirim Z, Armutcu F, Bozkurt B, et al. Influence of CPAP treatment on airway and systemic inflammation in OSAS patients. Sleep Breath. 2014;18(2):251-6.
19. Varol E, Ozturk O, Yucel H, Gonca T, Has M, Dogan A, et al. The effects of continuous positive airway pressure therapy on mean platelet volume in patients with obstructive sleep apnea. Platelets. 2011;22(7):552-6.
20. Sökücü SN, Özdemir C, Dalar L, Karasulu L, Aydın Ş, Altın S. Complete blood count alterations after six months of continuous positive airway pressure treatment in patients with severe obstructive sleep apnea. J Clin Sleep Med. 2014;10(08):873-8.
21. Gunbatar H, Sertogullarindan B, Ekin S, Akdag S, Arisoy A, Sayhan H, et al. The correlation between red blood cell distribution width levels with the severity of obstructive sleep apnea and carotid intima media thickness. Med Sci Monit. 2014;20:2199.
22. Akgül E, Engin M, Özyazıcıoğlu A. Effects of mean platelet volume and platelet counts on peripheral biodegradable stent restenosis. J Surg Med. 2019;3(9):663-5.
23. Lattimore J-DL, Celermajer DS, Wilcox I. Obstructive sleep apnea and cardiovascular disease. J Am Coll Cardiol. 2003;41(9):1429-37.
24. Macdougall IC, Cooper AJNDT. The inflammatory response and epoetin sensitivity. Nephrol Dial Transplant. 2002;17(90001):48-52.
25. İslamoğlu Z, Demirbaş A. Mean platelet volume and platelet distribution width levels in discoid lupus erythematosus patients: A case-control study. J Surg Med. 2019; 3(8): 561-563.
26. Sleep related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. Sleep. 1999;22:667-89.
27. Ozsu S, Abul Y, Gulsoy A, Bulbul Y, Yaman S, Ozlu T. Red cell distribution width in patients with obstructive sleep apnea syndrome. Lung. 2012;190(3):319-26.
28. Schofield CJ, Ratcliffe P. Oxygen sensing by HIF hydroxylases. Mol. Cell. Biol. 2004;5(5):343.
29. Bülbül Y, Aydın EÖ, Örem A. Platelet indices in obstructive sleep apnea: the role of mean platelet volume, platelet distribution width and plateletcrit. Tuberk Toraks. 2016;64(3):206-10.
30. Feliciano A, Linhas R, Marçôa R, Cysneiros A, Martinho C, Reis R, et al. Hematological evaluation in males with obstructive sleep apnea before and after positive airway pressure. Rev Port Pneumol. 2017;23(2):71-8.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):740-745.
DOI: 10.28982/josam.630645

Research article
Araştırma makalesi

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

A comparative evaluation of bilateral hippocampus and amygdala volumes with ADC values in pediatric primary idiopathic partial epilepsy patients

Pediatrik yaş grubu primer idiyopatik parsiyel epilepsi hastalarında bilateral hipokampus ve amigdala volümlerinin ADC değerleri ile karşılaştırmalı değerlendirilmesi

İsmail Taşkent [1], Gürkan Danışan [1], Hanefi Yıldırım [2]

[1] Mus State Hospital, Radiology Unit, Mus, Turkey
[2] Department of Radiology, Faculty of Medicine, Firat University, Elazig, Turkey

ORCID ID of the author(s)
İT: 0000-0001-6278-7863
GD: 0000-0003-2052-0006
HY: 0000-0002-6204-6392

Abstract

Aim: Approximately 70% of temporal seizures are hippocampal seizures, which are often concomitant with amygdala seizures. Seizures occurring in this region are usually complex partial. The aim of this study was to determine whether there was a significant change in hippocampus and amygdala volumes in idiopathic partial epilepsy patients without pathology on routine cranial MRI and to compare the hippocampus and amygdala ADC values with the control group.

Methods: In this case-control study, 27 patients aged between 1-18 years, who were admitted to our hospital between the years of 2014 and 2017 and diagnosed with idiopathic partial epilepsy based on EEG and clinical findings were compared with 20 children in the control group, which consisted of twenty children of similar ages who were referred to our hospital with nonspecific complaints such as headache and dizziness and who underwent cranial MRI. Children with histories of any congenital diseases, acquired neurodegenerative diseases, intracranial infections, intracranial masses, and those who were perinatally affected were not included in the study. Drawings, volumetric measurements, and ADC calculations were performed by two separate evaluators (one neuroradiology and one radiology research assistant).

Results: Hippocampus and amygdala volumes of the study group were decreased compared to the control group, but the results were significant only for the left hippocampus. Although ADC values of the study group were increased, the findings were statistically significant only for the left amygdala.

Conclusion: In our study, we found that the hippocampus and amygdala volumes of patients diagnosed with idiopathic partial epilepsy were decreased ipsilateral to the seizure focus, and the ADC values of the ipsilateral amygdala were increased.

Keywords: Idiopathic partial epilepsy, Hippocampus, Amygdala, Pediatric, ADC

Öz

Amaç: Temporal nöbetlerin yaklaşık %70'i hipokampal nöbetlerdir ve genellikle amigdala nöbetleri ile birliktedir. Bu bölgede meydana gelen nöbetler genellikle kompleks parsiyel nöbetlerdir.Çalışmamızın amacı, rutin kraniyal MRG'de patolojisi olmayan 0-18 yaş arasındaki idiyopatik parsiyel epilepsi hastalarında hipokampus ve amigdala hacminde anlamlı bir değişiklik olup olmadığını belirlemek ve hastaların hipokampüs ile amigdala ADC değerlerini kontrol grubu ile karşılaştımalı olarak değerlendirmektir.

Yöntemler: Yapılan olgu-kontrol çalışmasında 2014 ve 2017 yılları arasında hastanemize başvuran, 1-18 yaş arasında olup, EEG ve klinik bulgularıyla idiyopatik parsiyel epilepsi tanısı alan 27 hasta ile 20 kontrol grubu karşılaştırıldı. Kontrol grubu olarak, benzer yaşlarda olup hastanemize baş ağrısı ve baş dönmesi gibi nonspesifik şikâyetlerle başvuran ve kraniyal MRG çekilen 20 çocuk değerlendirildi. Çalışma ve kontrol grubunda bilinen konjenital hastalık öyküsü olan, edinsel nörodejeneratif hastalık geçiren, intrakraniyal enfeksiyon ya da perinatal etkilenme öyküsü bulunan ve intrakraniyal kitlesi olan çocuklar çalışmaya dâhil edilmemiştir Çizimler, volümetrik ölçümler ve ADC ölçümleri iki ayrı değerlendirici tarafından yapıldılar (Biri nöroradyolog, diğeri radyoloji araştırma görevlisi).

Bulgular: Kontrol grubu ile karşılaştırıldığında, çalışma grubunda hipokampüs ve amigdala volümlerinde azalma izlenmekle beraber sonuçlar sadece sol hipokampüs için anlamlıydı. ADC değerlerinin karşılaştırılmasında çalışma grubunun ADC değerleri kontrol grubuna kıyasla artmış olmakla birlikte bulgular sadece sol amigdala için istatistiksel olarak anlamlıydı.

Sonuç: Çalışmamızda, idiyopatik parsiyel epilepsi tanısı alanlarda, hipokampus ve amigdala volümlerinin, nöbet odağına bağlı olarak ipsilateral azalmış olduğunu bulduk. Aynı zamanda, ipsilateral amigdalada ADC değerlerinde artış olduğunu bulduk.

Anahtar kelimeler: İdiyopatik parsiyel epilepsi, Hipokampüs, Amigdala, Pediyatrik, ADC

Corresponding author / Sorumlu yazar:
İsmail Taşkent
Address / Adres: Muş Devlet Hastanesi, Radyoloji Birimi, Muş, Türkiye
e-Mail: dr.taskent@gmail.com

Ethics Committee Approval: Approval was obtained from Fırat University Non-Interventional Research Ethics Committee (22.02.2016/132621).
Etik Kurul Onayı: Fırat Üniversitesi Girişimsel Olmayan Araştırmalar Etik Kurulundan onay alınmıştır (22.02.2016/132621).

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.

Published: 10/21/2019
Yayın Tarihi: 21.10.2019

How to cite / Atıf için: Taşkent İ, Danışan G, Yıldırım H. A comparative evaluation of bilateral hippocampus and amygdala volumes with ADC values in pediatric primary idiopathic partial epilepsy patients. J Surg Med. 2019;3(10):740-745.

Introduction

Idiopathic partial epilepsies (IPE) are thought to be hereditary, childhood epilepsy syndromes characterized by focal epilepsy seizures. IPEs are common and account for approximately %20 of epilepsies which begin between 2-13 years of age and %50 of all partial epilepsies. Electroencephalogram (EEG) shows epileptiform activities with special morphology that become evident with sleep. Cranial imaging and other ancillary studies do not reveal any anatomic lesions and seizures tend to end spontaneously after a certain age [1].

Limbic system is the border area where psychiatry and neurology intersect. Temporolimbic system is considered to consist of two main parts, namely, medial limbic and lateral limbic circuits. Medial circuits include the hypothalamus, anterior thalamic nucleus, cingulate gyrus, hippocampus, and related pathways; are associated with reticular formation, and manage learning, memory, and attention control functions. Lateral (or basolateral) circuits include the amygdala, dorsomedial thalamic nucleus, orbitofrontal cortex and the insula [2].

Approximately %70 of temporal seizures are hippocampal seizures and are often concomitant with amygdala seizures. Seizures occurring in this region are usually complex partial. Oral and alimentary automatisms such as chewing, licking, swallowing may follow the seizures. The spread of discharge may induce seizures to turn into generalized tonic-clonic convulsions. Focal lateralized or bilateral 4-6 Hz. sharp waves may be seen in ictal EEG [3].

It is pointed out that amygdala may be an important structure in triggering fear response. Ictal fear in temporal lobe epilepsy (TLE) is reportedly associated with volume reduction in the amygdala [4]. In some TLE patients, fear attacks disappear after temporal lobectomy with amygdala removal [5]. TLE patients who underwent right temporal lobectomy have been shown to exhibit less emotional signs than right TLE patients [6].

The aim of our study was to determine whether there was a significant change in the hippocampus and amygdala volumes in idiopathic partial epilepsy patients between 0-18 years of age who had no pathology in routine cranial magnetic resonance imaging (MRI), and to comparatively evaluate the patients' hippocampus and amygdala apparent diffusion coefficient (ADC) values.

Materials and methods

Three dimensional MRIs, obtained according to predetermined epilepsy protocols in our department, belonging to patients aged 0-18 years who had preliminary diagnoses of epilepsy were retrospectively evaluated. Twenty-seven patients who had partial seizures but had no pathology on cranial MRI were included in the study. Children with a history of congenital disease, neurodegenerative disease, intracranial infection or perinatal involvement, and an intracranial mass were not excluded.

The control group consisted of twenty children within the same gender and age group as the study group patients, who had nonspecific complaints such as headache or dizziness, whose MRIs were obtained with suspicion of intracranial pathology and reported normal. Just as in the study group, children with intracranial masses, acquired or congenital diseases, and a history of intracranial infections were excluded. There were no findings suggestive of epilepsy in the history and examination of the children.

Age, gender, and EEG findings of all participants were determined from the medical records. Patients were classified as having temporal and non-temporal localizations according to EEG findings. All occipital, frontal, and parietal discharges were considered non-temporal. Right or left hemispheric localizations of all epileptic discharges were also determined.

Brain MRI examinations of the patients were performed using a 1.5 Tesla (Philips, Ingenia, Netherlands) MRI device using a standard head coil. In our clinic, 3-dimensional T1-sagittal turbo field echo (TFE), 3-dimensional turbo spin echo (TSE), fluid attenuated inversion recovery (FLAIR), T2-axial fast field echo (FFE) and turbo spin echo were performed routinely to pediatric epilepsy patients to obtain T2-sagittal, axial and coronal diffusion echo planar image (EPI) sequences. The following parameters are used to obtain 3D T1 sagittal images:

Volumetric measurements

Volumetric examinations of the amygdala and hippocampus regions of each patient were performed via 3D T1-sagittal TFE reformat images. The boundaries were drawn with the help of the workstation (General Electric Medical System, Advantage Windows, v4.6). Measurements defined by Watson et al. [7] were taken into consideration in drawing the hippocampus borders. The distinction between the anterior border of the hippocampus and the amygdala was made by alveus and uncal recesses. The borders were distinguished by the visualization of the choroid plexus superiorly, temporal horn in externally, perimesencephalic cisterna medially, fornix crus posteriorly and subiculum inferiorly. The study of Atmaca et al. [8] was referred to in determining the amygdala boundaries. The trace for drawing the boundaries began from where the mammillary bodies first appeared. The upper and lateral margins were formed by the white matter of the temporal lobe. The white matter of the parahippocampal gyrus formed the lower boundary. The anterior border was drawn from where the gray matter of the amygdala was no longer distinguishable from the rest of the temporal lobe. Drawings were made by two separate evaluators (one neuroradiology and one radiology research assistant).

After the hippocampus and amygdala boundaries were determined, volume was calculated with the help of the workstation and data were recorded in cubic centimeters. The measurements were made primarily by hand on the coronal plane and checked on the axial and sagittal planes (Figure 1-5).

ADC measurements

Diffusion-weighted images were obtained via single shot echo planar imaging vertical to the hippocampus in the coronal plane. Technical parameters used to obtain these images are as follows: Time of repetition (TR)=4284 ms, time of echo (TE)=91 ms, section thickness: 5mm, matrix size=152–102, number of signal averaging (NSA)=1, field of view (FOV)=23cm-23cm, sectional gap=1 mm, B value=1000 s/mm^2.

Images were evaluated with the Stejskal Tanner method using a workstation (Philips IntelliSpace Portal, R5.1.7 software)

[9]. Bilateral hippocampus and amygdala were determined in coronal plane and ADC measurements were performed. The hippocampus was measured from the head, corpus and tail, after which arithmetic mean was obtained. The mean region of interest (ROI) was 15 mm^2. The neighboring structures and cerebrospinal fluid were avoided during the measurements, and the hippocampus and amygdala were kept within ROI as much as possible. Thus, false values that may occur due to partial volume were prevented (Figure 6, 7).

Figures and Legends

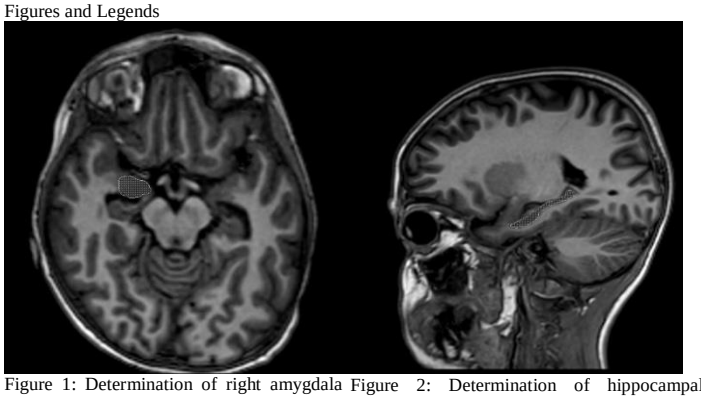

Figure 1: Determination of right amygdala border in axial plane

Figure 2: Determination of hippocampal border in sagittal plane

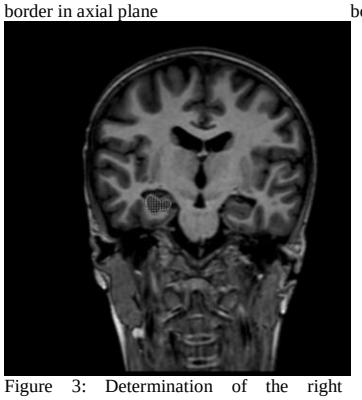

Figure 3: Determination of the right amygdala border in the coronal plane

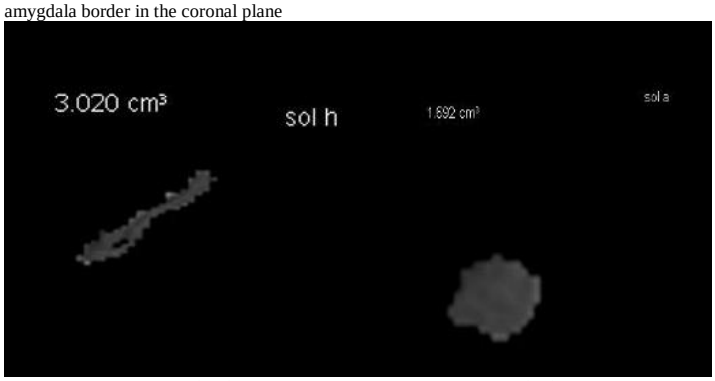

Figure 4: Calculation of left hippocampal volume

Figure 5: Calculation of left amygdala volume

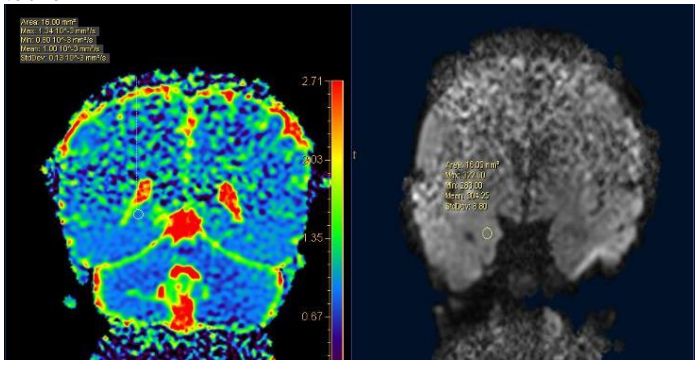

Figure 6: ADC image of posterior section of right hippocampus

Figure 7: Diffusion MR image of right amygdala

Statistical analysis

Data were expressed as mean (standard deviation). Independent sample t test was used to analyze the differences between the control and study groups. Spearman correlation test was used to determine the correlation between right and left values within each group. Statistical analysis was performed using SPSS (SPSS 20.0 for Windows) 20.0 package program. $P<0.05$ was considered statistically significant.

Amygdala and hippocampus volumes are known to vary in relation to intracranial volume. Therefore, to eliminate the effect of intracranial volume difference, the previously reported correction method was applied to amygdala and hippocampus volumes obtained with volumetric MRI [10]. Correction is reportedly more sensitive in demonstrating bilateral hippocampal sclerosis [11]. Likewise, bilateral changes in amygdala volumes may be evaluated more accurately after correction. According to this correction method, brain limits were determined visually in each section in brain volume calculation. The volume data, obtained from the manual drawing from the serial sections with determined boundaries, was recorded in cubic centimeters. The following formula was used to calculate the corrected volume:

$$\text{Adjusted volume} = \frac{\text{Mean cerebral volume of control subjects x hippocampus volume}}{\text{Cerebral volume of the patient}}$$

Results

Among 27 patients with idiopathic partial epilepsy, 18 (66%) were male and 9 (33%) were female, with a male / female ratio of 2. The control group comprised 12 (60%) males and 8 (40%) females. The ages of the patients in both groups ranged from 1 to 18 years. There was no statistically significant difference between the study and control groups in terms of mean age and gender distribution. EEG showed right, left, and non-temporal discharge in right and left hemispheres in 7 (25.9%), 10 (37%), 4 (14.8%) and 6 (22.2%) patients, respectively. The cerebral volumes of the control and study groups were similar. The male and female patients were alike in terms of amygdala, hippocampus and cerebral volumes, as well as age.

The hippocampus and amygdala ADC values of the study group patients were higher, but a significant difference was found between the left amygdala values only ($P=0.024$, Table 1). While bilateral hippocampus and left amygdala volumes of the study group were lower than that of the control group, the right amygdala volume was higher. These results were not statistically significant. The same results were obtained with corrected volumes as well (Table 2).

In the comparison of left hemisphere-induced epilepsy group, left hippocampus volume was significantly ($P=0.015$) and the left amygdala volume was non-significantly decreased in the study group ($P=0.374$, Table 3). The hippocampus and amygdala ADC values on the left side were higher than the control group and the difference was significant for the amygdala ($P=0.018$) and not for the hippocampus (Table 4).

The left hippocampus volume of patients with left temporal lobe-induced epilepsy was significantly ($P=0.037$) and the left amygdala volume was non-significantly ($P=0.522$) decreased in the study group (Table 5). The hippocampus and amygdala ADC values on the left side were higher than the control group and the difference was significant for the amygdala ($P=0.027$) and not for the hippocampus (Table 6).

Table 1: Comparison of hippocampus and amygdala ADC values between the study and control groups

	Right hippocampus mean (SD)	Left hippocampus mean (SD)	Right amygdala mean (SD)	Left amygdala mean (SD)
Study group (n=27)	0.882 (0.485)	0.898 (0.430)	0.852 (0.598)	0.853 (0.436)
Control group (n=20)	0.864 (0.482)	0.883 (0.627)	0.828 (0.549)	0.823 (0.441)
P-value	0.226	0.344	0.163	0.024

Table 2: Comparison of study and control groups in terms of adjusted hippocampus and amygdala volumes

	Right hippocampus mean (SD)	Left hippocampus mean (SD)	Right amygdala mean (SD)	Left amygdala mean (SD)
Study group (n=27)	2.408 (0.229)	2.356 (0.348)	1.174 (0.210)	1.078 (0.273)
Control group (n=20)	2.471 (0.300)	2.482 (0.281)	1.145 (0.179)	1.109 (0.158)
P-value	0.417	0.191	0.618	0.644

Table 3: Comparison of left hippocampus and left amygdala volumes in patients with left hemisphere-induced epilepsy

	Left hippocampus mean (SD)	Left amygdala mean (SD)
Study group (n=16)	2.173 (0.393)	1.034 (0.303)
Control group (n=20)	2.471 (0.302)	1.106 (0.169)
P-value	0.015	0.374

Table 4: Comparison of left hippocampus and left amygdala ADC values in patients with left hemisphere-induced epilepsy

	Left hippocampus mean (SD)	Left amygdala mean (SD)
Study group (n=16)	0.898 (0.457)	0.860 (0.429)
Control group (n=20)	0.884 (0.628)	0.823 (0.441)
P-value	0.450	0.018

Table 5: Comparison of left hippocampus and left amygdala volumes in patients with left hemisphere-induced and left temporal epilepsy with the control group

	A (n=16) mean (SD)	B (n=20) mean (SD)	*P*-value	C (n=10) mean (SD)	D (n=20) mean (SD)	*P*-value
Left hippocampus	2.173 (0.393)	2.471 (0.302)	0.015	2.196 (0.366)	2.471 (0.302)	0.037
Left amygdala	1.034 (0.303)	1.106 (0.169)	0.374	1.056 (0.249)	1.106 (0.169)	0.522

A: Left hemisphere-induced study group, B: Left hemisphere-induced control group, C: Left temporal epilepsy study group, D: Left temporal epilepsy control group

Table 6: Comparison of ADC values of left hippocampus and left amygdala in patients with left hemisphere-induced and left temporal epilepsy

	A (n=16) mean (SD)	B (n=20) mean (SD)	*P*-value	C (n=10) mean (SD)	D (n=20) mean (SD)	*P*-value
Left hippocampus	0.898 (0.457)	0.884 (0.628)	0.450	0.903 (0.488)	0.884 (0.628)	0.394
Left amygdala	0.860 (0.429)	0.823 (0.441)	0.018	0.865 (0.492)	0.823 (0.441)	0.027

A: Left hemisphere-induced study group, B: Left hemisphere-induced control group, C: Left temporal epilepsy study group, D: Left temporal epilepsy control group

Discussion

The limbic lobe is formed by the combination of various structures in different anatomical lobes of the brain, namely, the frontal, temporal, and parietal lobes, and is not a real anatomical brain lobe. The concept of the limbic system refers to a larger area than the limbic lobe anatomically and is much more complex than the limbic lobe itself. The limbic lobe and all associated cortical and subcortical structures with intense synaptic connections which perform certain functions form the limbic system [12].

The limbic system contains important neuroanatomic formations such as thalamus, hypothalamus, hippocampus, pineal gland, pituitary gland and amygdala within the subcortical structures of the brain and is responsible for memory and mood changes [13].

Rosso et al. [14] reported a decrease in amygdala volumes of patients with major depression and no statistically significant difference between the hippocampus volumes compared to the control group. Szeszko et al. [15] found a decrease in the amygdala volumes of 11 patients with obsessive-compulsive disorder compared to the control group.

In Chang et al.'s study [16] in 20 pediatric patients diagnosed with bipolar disorder, no significant difference was detected in the hippocampus, thalamus, and caudate nucleus volumes of the patients, but bilateral amygdala volumes were reportedly decreased. Keller et al. [17] found decreased hippocampus volumes in right and left hemisphere induced TLE patients compared to the control group, but no significant difference was found in amygdala volumes.

Partial onset seizures are often caused by the temporal lobe. These seizures are called complicated partial seizures when consciousness changes are added. A considerable proportion of these patients are resistant to drug therapy [18]. The seizures of TLE patients who do not have drug-resistant non-hippocampal epileptogenic focus and whose hippocampal atrophies were documented by MRI can be controlled by surgical treatment. Surgical success rate is low in patients with TLE in whom hippocampal atrophy is not detected by MRI. With regards to preoperative strategizing, it is very important for the radiology to fully lateralize the focus of epilepsy in drug resistant TLE cases. The diagnosis and precise lateralization in patients with bilateral symmetrical involvement of both hippocampi before surgery requires significant experience [19].

Hakyemez et al. [20] found a significant decrease in right and left hippocampi volumes in 27 patients with complex temporal lobe epilepsy, but no significant difference in amygdala volumes compared to the control group.

Similarly, in our study, although the mean volumes of bilateral hippocampi were decreased in the study group, a statistically significant difference was found only on the left. Amygdala volumes were not significantly different.

Amygdala volume ranged from 1.1 to 1.6 cm^3 in postmortem studies. However, in different volumetric MRI analyses, values are measured in a wide range of 1 to 4 cm^3 [11,21-23]. The reason for this may be the preference of low-resolution or thick-sectioned MRI techniques. Therefore, in many volumetric studies, it is thought that the amygdala volume is measured more than its real value [24]. Volume values obtained by MRI with a section thickness of one mm and three-dimensional analysis should be preferred. Such results are similar to those of post-mortem studies [25].

In an experimental study on mice, spontaneous recurrent seizures were observed in 50% of the mice after amygdala stimulation, but none of them lost volume in the amygdala or parahippocampal region. Significant neuron loss was observed in the hippocampal dentate gyrus hilum, but there was no significant difference in neuron loss between mice with and without spontaneous recurrent seizures [26]. Kalviainen et al. [27] compared 29 new patients, 54 patients with chronic temporal lobe epilepsy, and 25 control subjects. Although there was no significant difference in amygdala volumes, approximately 20% of patients with chronic diagnosis had at least 20% reduction in amygdala volumes compared to the control group.

In our study, preference of patients without visible hippocampal atrophy in study groups may explain the absence of significant differences in amygdala volumes. A slight decrease in the amygdala volumes in the patient may herald the loss of amygdala volume in the future.

Mu et al. [28] found that amygdala and hippocampus volumes differed significantly among some age groups in healthy

adult subjects, but that gender and right-left sides did not differ significantly.

Although no statistical study was performed, the mean right hippocampus volume was higher and left hippocampus volume, lower in male patients. The mean amygdala volume of females was slightly higher than males bilaterally. Females were found to have outvalued males in all measurements in the control group.

Geuze et al. [29] emphasized in their study how MRI technical parameters may affect the consistency of volumetric results and reported that particularly image acquisition parameters such as image resolution may have caused heterogeneity. They reported that differences between patient and control groups occurred in studies with high resolution. Numerous anatomical protocols for demonstrating the hippocampus are an important source of variability between studies.

When evaluating the performance of different MR techniques in TLE lateralization, hippocampal volume measurement seems prominent. However, the long duration of measurements for a single patient and the conflicts and difficulties in determining the hippocampus limits to be included in the measurement are the two most important limitations in the application of this method. On the other hand, studies have shown no significant difference between volume measurement and visual assessment in detecting hippocampal atrophy for an experienced neuroradiology [30]. In light of this information, it may be recommended to use hippocampal volume measurement primarily in bilateral atrophy cases where contralateral hippocampus cannot be used as reference, in cases where hippocampal volume changes are diminished and in centers with insufficient experience in diagnosing epilepsy [31,32].

Hippocampal sclerosis is a disease characterized by hippocampal neuronal loss causing mesial temporal lobe epilepsy (MTLE). Many studies on patients with hippocampal sclerosis [33-36] have shown that magnetic resonance imaging (MRI) is a reliable method for identifying epileptogenic focus. Hippocampal sclerosis is best demonstrated using T2-weighted or fluid attenuated inversion-recovery (FLAIR) sequences and thin coronal sections perpendicular to the hippocampus, and the most reliable MR imaging findings of hippocampal sclerosis are atrophy and/or signal enhancement of the hippocampus on T2-weighted and FLAIR images [37]. According to the results of autopsy studies, 50% of MTLE cases have bilateral hippocampal sclerosis [38-41]. Although high sensitivity and specificity have been reported with MRI for the diagnosis of hippocampal sclerosis [42-44], bilateral hippocampal sclerosis is difficult to detect because interpretation of MR images depends on comparing signal changes and volumes of hippocampal formations in the same subject [45].

In their study on 13 patients diagnosed with complex temporal lobe epilepsy, Hakyemez et al. [10] showed that patients with hippocampal sclerosis had significantly higher ADC values on the pathological side compared to the contralateral side and control group, but no significant increase in amygdala ADC values was reported.

In our study, no significant difference was found between bilateral hippocampus and right amygdala ADC values, but left amygdala ADC values were higher in patients with temporal lobe epilepsy. This may be attributed to the fact that the left amygdala ADC values were high in the whole study group. The mean hippocampus ADC values were slightly and non-significantly higher in the study group, which may be due to the fact that patients with visible sclerosis were not included in our study group.

Limitations

As the number of patients was insufficient, temporal, and non-temporal epilepsy patients could not be compared in terms of amygdala and hippocampus volumes and ADC values. Although the average hippocampus volumes were not statistically analyzed, there was a decrease in the hippocampus and amygdala volumes of right-sided temporal epilepsy patients compared to non-temporal epilepsy patients.

The high male / female ratio in the gender distribution could be considered a limitation. Therefore, similar age and gender ratios were preferred in the control group. The fact that visible hippocampal sclerosis patients were not included in the study group may account for the fact that our findings do not resemble those of other studies. However, like other studies, non-significant decreases in hippocampus and amygdala volumes were found. There was no significant difference in ADC values due to the absence of apparent sclerosis.

Conclusion

The hippocampus and amygdala volumes of our pediatric patients diagnosed with idiopathic partial epilepsy were decreased ipsilateral to the seizure focus compared to the control group. There was an increase in ADC values in bilateral amygdala. Although our study showed that neuron loss and subsequent decrease in hippocampus and amygdala volumes may occur in idiopathic partial epilepsy patients, our findings were not as significant as chronic partial epilepsy cases.

References

1. Beaumanoir A, Nahory A. Benign partial epilepsies: 11 cases of frontal partial epilepsy with favorable prognosis. Rev Electroencephalogr Neurophysiol Clin. 1983;13:207-11.
2. Mega MS, Cummings JL. Frontal-subcortical circuits and neuropsychiatric disorders. J Neuropsychiatry Clin Neurosci. 1994;6:358-70.
3. Wieser HG. ILAE Commission Report. Mesial temporal lobe epilepsy with hippocampal sclerosis. Epilepsia. 2004;45:695-14.
4. Cendes F, Andermann F, Gloor P. Relationship between atrophy of the amygdala and ictal fear in temporal lobe epilepsy. Brain. 1994;4:739-46.
5. McLachlan RS, Blume WT. Isolated fear in complex partial status epilepticus. Ann Neurol. 1980;8:639-41.
6. Fedio P, Martin A. Ideative-emotive behavioral characteristics of patients following left or right temporal lobectomy. Epilepsia. 1983;24:117-30.
7. Watson C, Andermann F, Gloor P, Gotman M. Anatomic basis of amygdaloid and hippocampal volume measurement by magnetic resonance imaging. Neurology. 1992;42:1743-50.
8. Atmaca M, Yildirim H, Ozdemir H, Ozler S, Kara B, Ozler Z, et al. Hippocampus and amygdala volumes in patients with refractory obsessive-compulsive disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2008;32:1283-6.
9. Stejskal EO, Tanner JE. Spin diffusion measurements: spin echo in presence of a time dependent field gradient. J Chem Phys. 1965;42:288–92.
10. Hakyemez B, Erdoğan C, Yıldız H, Ercan I, Parlak M. Apparent diffusion coefficient measurements in the hippocampus and amygdala of patients with temporal lobe seizures and in healthy volunteers. Epilepsy Behav. 2005;6:250–6.
11. Herzog AG, Kemper TL. Amygdaloid changes in aging and dementia. Archives of Neurology. 1980;37:625-9.
12. Atlas SW, Zimmerman RA, Bilaniuk LT, Rorke L, Hackney DB, Goldberg HI, et al. Corpus callosum and limbic system: Neuroanatomic MR evaluation of developmental anomalies. Radiology. 1986;160:355–62.
13. Brick J, Erickson CK (eds). Drugs, the brain, and behavior. The Pharmacology of Abuse and Dependence. New York: The Haworth Medical Pres. 1998;119-31.
14. Rosso IM. Amygdala and hippocampus volumes in pediatric major depression. Biol Psychiatry. 2005;57:21-6.
15. Szeszko PR. Amygdala volume reductions in pediatric patients with obsessive compulsive disorder treated with paroxetine: preliminary findings. Neuropsychopharmacology. 2004;29:826-32.
16. Chang K, Karchemskiy A, Barnea-Goraly N. Reduced amygdalar gray matter volume in familial pediatric bipolar disorder. J Am Acad Child Adolesc Psychiatry. 2005;44:565-73.
17. Keller SS, Wieshmann UC, Mackay CE, Denby CE, Webb J, Roberts N. Voxel based orphometry of grey matter abnormalities in patients with medically intractable temporal lobe epilepsy: effects of side of seizure onset and epilepsy duration. J Neurol Neurosurg Psychiatry. 2002;73:648–56.

18. Achten E, Boon P, De Kerckhove TV. Value of single-voxel proton MR spectroscopy in temporal lobe epilepsy. Am J Neuroradiol. 1997;18:1131-9.
19. Cendes F, Leproux F, Melanson D, Ethier R, Evans A, Peters T. MRI of amygdala and hippocampus in temporal lobe epilepsy. J Comput Asist Tomog. 1993;17:206-10.
20. Hakyemez B, Yücel K, Yıldırım N, Erdoğan C, Bora I, Parlak M. Morphologic and volumetric analysis of amygdala, hippocampus, fornix and mamillary body with MRI in patients with temporal lobe epilepsy. Neuroradiol J. 2006;19:289-96.
21. Scott SK, Young AW, Calder AJ, Hellawell DJ, Aggleton JP, Johnson M. Impaired auditory recognition of fear and anger following bilateral amygdala lesions. Nature. 1997;385:254-7.
22. Glaser G. Historical perspectives and future directions. Wylie E (eds). The treatment of epilepsy: Principles and practise. Philedelphia: Febiger Press. 1993;3-9.
23. Sander JW, Hart YM. Epilepsy. In: Jack MA (eds). Florida: Merit Publishing International. 1998;12-29.
24. Berkovich SF, Andermann F, Oliver AA. Hippocampal sclerosis in temporal lobe epilepsy demonstrated by magnetic resonance imaging. Ann Neurol. 1991;29:175-82.
25. Bonilha L, Kobayashi E, Cendes F, Li LM. The importance of accurate anatomic assessment for the volumetric analysis of the amygdala. Braz J Med Biol Res. 2005;38:409-18.
26. Brandt C, Glien M, Potsckha H, Volk H, Loscher W. Epileptogenesis and neuropathology after different types of status epilepticus induced by prolonged electrical stimulation of the basolateral amygdala in rats. Epilepsy Res. 2010;55:83-103.
27. Kalviainen R, Salmenpera T, Partanen K, Vainio P, Riekkinen P, Pitkanen A. MRI volumetry and T2 relaxometry of the amygdala in newly diagnosed and chronic temporal lobe epilepsy. Epilepsy Res. 1997;28:39–50.
28. Qiwen M, Jingxia X, Zongyao W, Yaqin W, Zhang S. A Quantitative MR Study of the Hippocampal Formation, the Amygdala, and the Temporal Horn of the Lateral Ventricle in Healthy Subjects 40 to 90 Years of Age. AJNR Am J Neuroradiol. 1999;20:207–11.
29. Geuze E, Vermetten E, Bremner JD. MR-based in vivo hippocampal volumetrics: 1. Review of methodologies currently employed. Mol Psychiatry. 2005;10:147–59.
30. Jackson GD, Berkovic SF, Duncan JS, Connelly A. Optimizing the diagnosis of hippocampal sclerosis with MR imaging. AJNR. 1993;14:753-62.
31. Cendes F, Leproux F, Melanson D, Ethier R, Evans A, Peters T. MRI of amygdala and hippocampus in temporal lobe epilepsy. J Comput Asist Tomog. 1993;17:206-10.
32. Reutens D, Cook M, Kingsley D. Volumetric MRI is essential for reliable detection of hippocampal asymetry. Epilepsia. 1993;34:138-40.
33. Jackson GD, Berkovic SF, Tress BM, Kalnins RM, Fabinyi GC, Bladin PF. Hippocampal sclerosis can be reliably detected by magnetic resonance imaging. Neurology. 1990;40:1869–75.
34. Jack CR, Sharbrough FW, Twomey CK. Temporal lobe seizures: lateralization with MR volume measurements of the hippocampal formation. Radiology. 1990;175:423–9.
35. Berkovic SF, Andermann F, Olivier A. Hippocampal sclerosis in temporal lobe epilepsy demonstrated by magnetic resonance imaging. Ann Neurol. 1991;129:175–82.
36. Bronen RA, Fulbright RK, Kim JH, Spencer SS, Spencer DD, Al-Rodhan NR. Regional distribution of MR findings in hippocampal sclerosis. AJNR Am J Neuroradiol. 1995;16:1193–200.
37. Jack CR, Rydberg CH, Krecke KN. Mesial temporal sclerosis: diagnosis with fluid-attenuated inversion-recovery versus spin-echo MR imaging. Radiology. 1996;199:367–73.
38. Margerison JH, Corsellis JA. Epilepsy and the temporal lobes: a clinical, electroencephalographic and neuropathological study of the brain in epilepsy, with particular reference to the temporal lobes. Brain. 1966;89:499–530.
39. Dam AM. Epilepsy and neuron loss in the hippocampus. Epilepsia. 1980;21:617–29.
40. Babb T, Brown W. Pathological findings in epilepsy. Engel J (ed). Surgical Treatment of the Epilepsies. New York: Raven. 1987;511–40.
41. Jackson GD, Connelly A, Duncan JS, Grunewald RA, Gadian DG. Detection of hippocampal pathology in intractable partial epilepsy: increased sensitivity with quantitative magnetic resonance T2 relaxometry. Neurology. 1993;43:1793–9.
42. Tien RD, Felsberg GJ, Campi de Castro C. Complex partial seizures and mesial temporal sclerosis: evaluation with fast spin-echo MR imaging. Radiology. 1993;189:835–42.
43. Cendes F, Andermann F, Gloor P. MRI volumetric measurement of amygdala and hippocampus in temporal lobe epilepsy. Neurology. 1993;43:719–25.
44. Kim JH, Tien RD, Felsberg GJ, Osumi AK, Lee N, Friedman AH. Fast spin-echo MR in hippocampal sclerosis: correlation with pathology and surgery. AJNR Am J Neuroradiol. 1995;16:627–36.
45. Cheon JE, Chang KH, Kim HD. MR of hippocampal sclerosis: comparison of qualitative and quantitative assessments. AJNR Am J Neuroradiol. 1998;19:465–8.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):746-748.
DOI: 10.28982/josam.636918

Research article
Araştırma makalesi

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

Rectal flap experience in high transsphincteric cryptoglandular anal fistula

Yüksek transsfinkterik kriptoglandüler anal fistülde rektal flep deneyimi

Ali Kılıç [1], Sırma Mine Tilev [2], Fatih Başak [1], Abdullah Şişik [1]

[1] University of Health Sciences, Umraniye Training and Research Hospital, Department of General Surgery, Istanbul, Turkey
[2] University of Health Sciences, Zeynep Kamil Women and Children's Diseases Training and Research Hospital, Department of Pediatric Surgery, Istanbul, Turkey

ORCID ID of the author(s)
AK: 0000-0002-4948-0055
SMT: 0000-0002-9606-3326
FB: 0000-0003-1854-7437
AŞ: 0000-0002-7500-8651

Corresponding author / Sorumlu yazar:
Sırma Mine Tilev
Address / Adres: Sağlık Bilimleri Üniversitesi, Zeynep Kamil Kadın ve Çocuk Hastalıkları Eğitim ve Araştırma Hastanesi, Çocuk Cerrahisi Kliniği, İstanbul, Türkiye
e-Mail: stilev@gmail.com

Ethics Committee Approval: Ethics committee approval was not received due to 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.

Published: 10/23/2019
Yayın Tarihi: 23.10.2019

Abstract

Aim: Despite many treatment modalities, anal fistula disease remains an important problem. High recurrence rates have been reported in the surgical treatment of complicated anal fistulas. We hereby present complicated anal fistula patients treated with rectal advancement flaps.

Methods: Patients who underwent rectal advancement flap surgery by a single surgeon between 2009 and 2019 were analyzed in this retrospective cohort study. Demographic data, number of previous operations, recurrence rate and complications were recorded.

Results: Twenty patients (15 males and 5 females) underwent surgery with the rectal advancement flap technique. Nine patients had more than one previous operation. Seton, partial fistulectomy and curettage were the most performed operative techniques in their previous surgeries. The mean follow-up period was 31 months (3-74). Among 13 patients with follow up periods longer than 12 months, 3 patients had recurrences (23%), all of which had been previously operated twice or more.

Conclusion: Although rectal advancement flap is not the first choice in the treatment of complicated and high transsphincteric fistulas, it still maintains its importance. Experienced surgeons prefer this method due to its sphincter-sparing nature. In our study we detected a recurrence rate of 23% and incontinence rate of 5%, which was thought to be related to previous surgeries.

Keywords: Complicated anal fistula, Rectal advancement flap

Öz

Giriş: Birçok tedavi yöntemine rağmen, anal fistül hastalığı önemli bir problemdir. Özellikle komplike anal fistüllerin cerrahi tedavisinde yüksek nüks oranları bildirilmiştir. Bu çalışmada rektal ilerletme flepleri ile tedavi edilen karmaşık anal fistül hastalarını analiz etmek amaçlandı.

Yöntemler: 2009-2019 yılları arasında tek cerrah tarafından rektal ilerleme flep yapılan hastalar bu retrospektif kohort çalışmada incelendi. Demografik veriler, önceki operasyon sayısı, nüks oranı ve komplikasyonlar kaydedildi.

Bulgular: Yirmi hastaya (15 erkek ve 5 kadın) rektal ilerleme flep tekniği uygulandı. Dokuz hasta önceden birden fazla ameliyat geçirmişti. Hastalara daha önce seton, parsiyel fistülektomi ve küretaj yapılmıştı. Ortalama takip süresi 31 aydı (3-74). 12 aydan daha uzun takip süreleri olan 13 hastanın 3'ünde nüks (%23) saptandı, bunların hepsi daha önce iki kez veya daha fazla ameliyat geçiren hastalardı.

Sonuç: Rektal ilerletme flebi, komplike ve yüksek transsfinkterik fistüllerin tedavisinde ilk seçenek olarak kullanılmamasına rağmen, önemini korumaktadır. Deneyimli cerrahlar sfinkter koruyucu yapısı nedeniyle bu yöntemi tercih ediyorlar. Çalışmamızda, önceki ameliyatlara bağlı olarak düşünülebilecek %23'lük bir rekürrens oranı ve %5 inkontinans oranı analiz edildi.

Anahtar kelimeler: Komplike anal fistül, Rektal ilerletme flebi

How to cite / Atıf için: Kılıç A, Tilev SM, Başak F, Şişik A. Rectal flap experience in high transsphincteric cryptoglandular anal fistula. J Surg Med. 2019;3(10):746-748.

Introduction

Perianal fistula disease is an ancient disease of which the gold standard treatment is yet to be found [1]. Diversity of treatment and differences in practice are indications that the search continues. Although sphincter sparing therapies have gained importance with advancing technology, surgery remains the main treatment. Difficulties persist in the treatment of high transsphincteric and complicated fistulas [2]. In cases where the fistula tract is complicatedly related to the sphincter, treating the disease without damaging the sphincter structure and continence constitutes a difficult part of perianal fistula treatment. In order to cope with this situation, the surgeon must know the different treatment methods and choose the most appropriate one for the patient. Several methods have been described for the treatment of high transsphincteric fistulas without damaging the sphincter mechanism. Rectal advancement flaps are one of the sphincter-preserving methods based on the closure of the internal fistula orifice [3]. Other methods such as fibrin glue [4,5], seton [6-8], collagen plugs [9,10], OTSC® (Over-The-Scope Clip) system [11,12] have also been described.

In this study, we aimed to share the results of perianal fistula patients treated with the rectal advancement flap method.

Materials and methods

Patients who were operated by a single surgeon with 10 years of anal fistula surgery experience for perianal fistula between January 2009 and January 2019 were evaluated retrospectively from the hospital registry and surgical procedures were recorded. Among them, patients who underwent rectal advancement flap procedure were included in the study. Demographic data, physical examination findings, fistula types according to preoperative imaging (based on Parks classification), previous number of operations and methods used, postoperative complications and recurrences were evaluated from hospital registry or by telephone.

Surgical technique of rectal mucosal advancement flap

Preoperative intestinal cleansing was performed to all patients with 210 ml of sodium dihydrogenphosphate + disodium hydrogenphosphate enemas, and they were operated after the administration of a single dose of 1st generation cephalosporin. An anoscope was placed in the anus in the lithotomy position and internal orifice was visualized under general or spinal anesthesia. A probe was advanced through the outer orifice towards the inner orifice. If probe could not be advanced, the internal orifice was found by administering oxygenated water from external orifice. Subsequently, wedge excision was performed to the mucosa and submucosa of the internal orifice. The edges of the excised part were released, and the inner orifice was closed with 2 or 3 sutures. Then, the probe-guided fistula tract was cored out starting from the external orifice.

Statistical analysis

SPSS (Statistical Package for Social Sciences) 22.0 program was used for statistical analysis. Descriptive data were expressed by mean, standard deviation, frequency, and median.

Results

184 male and 40 female (n_{total}=224) patients were operated on for anal fistula, 29 of whom had undergone multiple surgeries. A total of 260 surgical records were found. Fistulotomy or fistulectomy were performed in 145 patients due to low transsphincteric or simple fistulas and one or more setons were placed in 40 patients.

Twenty patients (15 males and 5 females), all of which had high transsphincteric fistulas, underwent rectal advancement flap technique including the mucosa and submucosa, and core out excision was performed for the part of the fistula outside the rectum wall. The mean age of the patients was 41.2 (17-71) years. 9 patients had more than one operation. Two patients had been operated four times, two patients had been operated three times and five patients had been operated twice. Seton, partial fistulectomy and curettage were the most performed techniques to patients in their previous operations. The mean follow-up period was 31 months (3-74). Recurrence was detected in 4 patients. Among 13 patients with follow up periods longer than 12 months, 3 patients had recurrences (23%), all of which had been previously operated twice or more. One patient had incontinence classified as Wexner incontinence score 2.

Discussion

Perianal fistula is an ancient disease dating back to the 4th century BC, and a gold standard treatment is yet to be found. There are few diseases with more treatment options than anal fistula. According to Parks classification, fistulas can be suprasphincteric, extrasphincteric, transsphincteric or intersphincteric [2]. Perianal fistulas can be classified as simple or complex. Intersphincteric and low transsphincteric fistulas, which constitute about 90-95% of all fistulas, are simple fistulas that are easier to treat. Favorable results are obtained with non-sphincter-sparing procedures such as fistulotomy and fistulectomy [13]. If a high transsphincteric fistula is misdiagnosed as a low transsphincteric fistula during preoperative evaluation, the wrong surgical method may be chosen, resulting in inadequate treatment and recurrence. Complicated fistulas and high fistulas require alternative surgical procedures with careful evaluation [14]. Many sphincter and anal continence-sparing methods have been developed for the treatment of complicated fistulas, and research is still underway [4-12]. The main sphincter-sparing methods include seton, fibrin glue application, LIFT, rectal mucosal flap, clip application and stem cell injections. Each method is presented with high success rates when first described, after which these rates decrease with the increasing number of studies. Individual differences in the implementation of the procedures and differences in patient preference likely play a role in this decrease.

Flap technique for the treatment of anal fistula was first described by Noble for the treatment of rectovaginal fistula in 1902, after which Elting and Leird modified this operation to use it for treating anal fistulas [15,16]. Although it is not used as the first choice in the treatment of complicated and high transsphincteric fistulas, it still maintains its importance. Experienced surgeons prefer this method due to its sphincter-sparing nature. The basic principle of the operation is based on the closure of the cavity formed by the excision of the primary

orifice of the fistula with mucosal (mucosa and submucosa), partial-thickness (with a portion of the mucosa and internal sphincter fibers) or a full-thickness flap prepared from the rectum wall. Core out excision or curettage is preferred for the fistula tract outside the rectum wall [17]. Rectal sleeve flap advancement is another operation method developed to treat complicated fistulas which occurred due to radiotherapy or Crohn's disease [18]. In the meta-analysis performed by Balciscueta et al. [16], recurrence rate was reported as 21% (0-40), and full-thickness flaps had better results. It was determined that all patients developed some degree of incontinence correlating with the flap thickness. Core out and curettage methods did not have any effect on the results.

Approximately half of the patients in our study had previously undergone multiple operations due to fistula and had had recurrences. Since flap surgery will not be the right option when perianal sepsis is present, procedures like Seton may be considered as preparation for this operation to eliminate sepsis. Rectal advancement flap should not be preferred in patients in which the internal orifice cannot be detected. We believe that rectal advancement flap surgery may be the first choice of treatment in high transsphincteric complicated fistulas without perianal sepsis and with one, easily visualized inner orifice. The lower incontinence rate in our study compared to those in the literature may be due to the implementation of mucosal flap technique. Previous and unsuccessful surgical interventions should be considered among the causes of incontinence. Recurrence rates in our study were similar with those in the literature [16,19].

Conclusion

In recurring cases of high transsphincteric fistulas, rectal advancement flap technique may be preferred as a feasible method with low complication rates by experienced surgeons.

References

1. De Parades V, Zeitoun JD, Atienza P. Cryptoglandular anal fistula. Journal of Visceral Surgery. 2010;147.4:e203-e215.
2. Parks A G, Gordon PH, Hardcastle JD. A classification of fistula in ano. Br J Sur. 1976;63:1-12.
3. Khafagy W, Omar W, El Nakeeb A, Fouda E, Yousef M, Farid M. Treatment of anal fistulas by partial rectal wall advancement flap or mucosal advancement flap: a prospective randomized study. International Journal of Surgery. 2010;8(4):321-5.
4. 4.Cirocchi R, Farinella E, La Mura F, Cattorini L. Fibrin glue in the treatment of anal fistula: a systematic review. Ann Surg Innov Res. 2009;3:12-15.
5. Sentovich SM. Fibrin glue for anal fistulas: long-term results. Dis Colon Rectum. 2003 Apr;46(4):498-502.
6. Ritchie RD, Sackier JM, Hodde JP. Incontinence rates after cutting seton treatment for anal fistula. Colorectal Dis. 2009 Jul;11(6):564-71. doi: 10.1111/j.1463-1318.2008.01713.x.
7. Christensen A, Nilas L, Christiansen J. Treatment of transsphincteric anal fistulas by the seton technique. Dis Colon Rectum. 1986 Jul;29(7):454-5.
8. Garcia-Aguilar J, Belmonte C, Wong WD, Goldberg SM, Madoff RD. Anal fistula surgery. Factors associated with recurrence and incontinence. Dis Colon Rectum.1996 Jul;39(7):723-9.
9. Safar B, Jobanputra S, Sands D, Weiss EG, Nogueras JJ, Wexner SD. Anal fistula plug: initial experience and outcomes. Dis Colon Rectum. 2009 Feb;52(2):248-52.
10. Ky AJ, Sylla P, Steinhagen R, Steinhagen E, Khaitov S, Ly EK. Collagen fistula plug for the treatment of anal fistulas. Dis Colon Rectum. 2008 Jun;51(6):838-43.
11. Mennigen R, Laukötter M, Senninger N, Rijcken E. The OTSC(®) proctology clip system for the closure of refractory anal fistulas. Tech Coloproctol. 2015 Apr;19(4):241-6. doi: 10.1007/s10151-015-1284-7.
12. Prosst RL, Herold A, Joos AK, Bussen D, Wehrmann M, Gottwald T, Schurr MO. The anal fistula claw: the OTSC clip for anal fistula closure. Colorectal Dis. 2012 Sep;14(9):1112-7. doi: 10.1111/j.1463-1318.2011.02902.x.
13. Sangwan YP, Rosen L, Riether RD, Stasik JJ, Sheets JA, Khubchandani IT. Is simple fistula-in-ano simple? Dis Colon Rectum. 1994;37(9):885-9.
14. Davies M, Harris D, Lohana P, Chandra Sekaran TV, Morgan AR, Beynon J, et al. The surgical management of fistula-in-ano in a specialist colorectal unit. Int J Colorectal Dis. 2008;23(9):833-8.
15. Noble G. New operation for complete laceration of the perineum designed for the purpose of eliminating danger of infection from the rectum. Trans Am Gynecol Soc. 1902;27:357–63.
16. Balciscueta Z, Uribe N, Balciscueta I, Andreu-Ballester JC, García-Granero E. Rectal advancement flap for the treatment of complex cryptoglandular anal fistulas: a systematic review and meta-analysis. Int J Colorectal Dis. 2017 May;32(5):599-609. doi: 10.1007/s00384-017-2779-7.
17. Akiba RT, Rodrigues FG, da Silva G. Management of Complex Perineal Fistula Disease. Clin Colon Rectal Surg. 2016 Jun;29(2):92-100. doi: 10.1055/s-0036-1580631.
18. Marchesa P, Hull TL, Fazio VW. Advancement sleeve flaps for treatment of severe perianal Crohn's disease. Br J Surg. 1998;85(12):1695–8.
19. Jorge JM, Wexner SD. Etiology and management of fecal incontinence. Dis Colon Rectum. 1993 Jan;36(1):77-97.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):749-753.
DOI: 10.28982/josam.632294

Research article
Araştırma makalesi

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

Role of contrast-enhanced breast magnetic resonance angiography in characterizing suspicious breast lesions and evaluating the relationship between prognostic factors

Şüpheli meme lezyonlarını karakterize etmede ve prognostik faktörler arasındaki ilişkiyi değerlendirmede kontrastlı meme manyetik rezonans anjiyografisinin rolü

Ali Küpeli [1], Mehmet Koçak [1], Gürkan Danışan [2], Furkan Ufuk [3], Furkan Kaya [4], İsmail Taşkent [2]

[1] Department of Radiology, Faculty of Medicine, Erzincan Binali Yıldırım University, Erzincan, Turkey
[2] Mus State Hospital, Department of Radiology, Mus, Turkey
[3] Department of Radiology, Faculty of Medicine, Pamukkale University, Denizli, Turkey
[4] Department of Radiology, Faculty of Medicine, Afyonkarahisar University of Health Sciences, Afyon, Turkey

ORCID ID of the author(s)
AK: 0000-0002-5322-2972
MK: 0000-0003-3590-0327
GD: 0000-0003-2052-0006
FU: 0000-0002-8614-5387
FK: 0000-0001-8619-7593
İT: 0000-0001-6278-7863

Corresponding author / Sorumlu yazar:
Ali Küpeli
Address / Adres: Erzincan Binali Yıldırım Üniversitesi Tıp Fakültesi, Radyoloji Anabilim Dalı, Erzincan, Türkiye
e-Mail: dr.ali_3383@hotmail.com

Ethics Committee Approval: Ethics committee approval was received from Erzincan Binali Yıldırım University Ethics Committee (number 2019.38.19).
Etik Kurul Onayı: Etik kurul onayı Erzincan Binali Yıldırım Üniversitesi Etik Kurulu'ndan alınmıştır (no: 2019.38.19).

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.

Published: 10/25/2019
Yayın Tarihi: 25.10.2019

Abstract

Aim: Breast cancer is the most commonly diagnosed cancer in women, and mammography and ultrasonography are the most frequently used diagnostic radiological methods. Although they are highly sensitive, their specificity is low. Angiography can be added as a standard breast magnetic resonance imaging (MRI) protocol to increase specificity. In this study, we aimed to investigate the effectiveness of breast vascularity by evaluating the presence of an adjacent vessel sign (AVS) and increased ipsilateral breast vascularity (IIBV) in characterizing breast masses.

Methods: 135 patients with a mean age of 47 years with radiologically or clinically suspicious breast masses underwent breast MRI before biopsy. The contrast-enhanced three-dimensional MR angiograms of the breasts were investigated for the presence of AVS and IIBV to characterize suspicious breast masses, and their correlation with histopathological prognostic factors were evaluated.

Results: Patients' age, tumor size, and the presence of AVS and IIBV were significantly higher in malignant masses than in benign masses (P<0.001). The sensitivity, specificity, and accuracy of AVS and IIBV in predicting malignant masses from benign ones were 75%, 79.3%, 77% and 56.9%, 90.4% and 72.5%, respectively. In malignant masses, AVS and IIBV were both significantly associated with ER (P=0.005, P<0.001) and PR expression (P=0.003, P<0.001). We found no relationship between AVS, IIBV and C-ERBB2 expression (P=0.245 and P=0.085, respectively).

Conclusion: The presence of AVS and IIBV as determined from contrast-enhanced 3D MR angiograms may be reliable parameters for further characterizing suspicious breast masses, both of which seem to be related with ER and PR expression.

Keywords: Angiography, Breast, Magnetic resonance imaging

Öz

Amaç: Meme kanseri, kadınlarda en sık tanı alan kanser olup, mamografi ve ultrasonografi en sık kullanılan radyolojik yöntemlerdir. Bu yöntemlerin duyarlılığı yüksek olmasına rağmen, özgüllükleri düşüktür. Anjiyografi, özgüllüğü artırmak için standart bir meme manyetik rezonans görüntüleme (MRG) protokolü olarak eklenebilir. Bu çalışmada amacımız, komşu damar işareti (KDİ) ve artmış ipsilateral meme vaskülaritesi (AİMV) içeren meme damarlanmasının, meme kitlelerini karakterize etmedeki etkinliğini araştırmak ve histopatolojik prognostik faktörlerle korelasyonunu ortaya koymaktır.

Yöntemler: Mart 2017 - Ocak 2019 tarihleri arasında radyolojik veya klinik olarak şüpheli meme kitleleri olan 135 hastaya (yaş aralığı: 19-79 yıl, ort. Yaş: 47 yıl) biyopsi öncesi meme MRG yapıldı. Kontrastlı 3D meme MR anjiyografileri, KDİ ve AİMV varlığı açısından şüpheli meme kitlelerini karakterize etmek için incelendi. Bu bulgular histopatolojik prognostik faktörler ile korele edildi.

Bulgular: Hastaların yaşı, tümör boyutu, KDİ ve AİMV bulunsı malign kitlelerde benign kitlelere göre anlamlı derecede yüksekti (P<0,001). KDİ %75 duyarlılık, %79,3 özgüllük ve %77 doğrulukla, AİMV varlığı ise %56,9 duyarlılık, %90,4 özgüllük ve %72,5 doğrulukla benign kitleleri malign olanlardan ayırt etmiştir. Malign kitlelerde KDİ ve AİMV, ER (sırasıyla P=0,005, P<0,001) ve PR ekspresyonuyla (sırasıyla P<0,001, P=0,003) ilişkiliydi. Ancak çalışmamızda, KDİ, AİMV ile C-ERBB2 ekspresyonu arasında ilişki saptanmadı (P=0,245 ve P=0,085, sırasıyla).

Sonuç: Kontrastlı 3D MR anjiyogramlarından elde edilen KDİ ve AİMV varlığı, şüpheli meme kitlelerinin karakterize edilmesi için güvenilir bir yöntemdir ve ER ve PR ekspresyonu ile ilişkili görünmektedir.

Anahtar kelimeler: Anjiyografi, Meme, Manyetik rezonans görüntüleme

How to cite / Atıf için: Küpeli A, Koçak M, Danışan G, Ufuk F, Kaya F, Taşkent İ. Role of the contrast-enhanced breast MR angiography in characterizing suspicious breast lesions and evaluating the relationship between prognostic factors. J Surg Med. 2019;3(10):749-753.

Introduction

Breast cancer is the most commonly diagnosed cancer in women, and mammography and ultrasonography are the most commonly used radiological methods [1,2]. Although these methods have high sensitivity, their specificity is low [3,4]. For this reason, magnetic resonance imaging (MRI) is an increasingly applied diagnostic method for the evaluation of breast masses.

Angiogenesis plays a significant role in the uncontrolled growth, invasion and metastasis of malignant tumors, similar to the other major prognostic factors of breast cancer, such as size, histologic grade, tumor type, and lymph node and distinct metastasis [5-7]. The contrast enhancement features, including the kinetic curve and enhancement ratio from the breast MR images, are related to microvessel density and hypervascularity [8-10]. Because of the relationship between hypervascularity and these enhancement features, angiogenesis can be assessed through breast MRI.

MR angiography can be added as a standard breast MRI protocol to increase specificity. No additional time is required to perform dynamic contrast enhanced (DCE) imaging. The maximum intensity projection (MIP) images are acquired from post processing the obtained images, and MIP images can provide useful information for tumor characterization by visualizing the feeding vascular structures and enhancing the lesions on the vascular map [11]. The adjacent vessel sign (AVS) is identified by the existence of one or more vessels in contact with the breast lesion and can be employed as a marker of tumor angiogenesis [12-14]. Increased ipsilateral breast vascularity (IIBV) is described as an increased number of vascular structures compared with the vascularity of the contralateral normal breast [15-17].

There are several studies concerning the use of MR angiography for evaluating breast masses, but few studies include histopathologic predictors. In this study, we aimed to determine the diagnostic efficacy of contrast-enhanced MR angiography for evaluating the presence of an AVS and IIBV to characterize suspicious breast masses and to investigate the relationship between the presence of an AVS and IIBV and histopathologic factors in malignant breast masses.

Materials and methods

Study group

Patients who underwent breast MRI between March 2017 and January 2019 due to suspicious mammographic, ultrasonographic or clinical findings were retrospectively determined with a keyword search in our patient database. Among the 389 patients identified, those with unilateral and histopathologically diagnosed breast masses were included in our study. Patients who underwent unilateral mastectomy, had bilateral breast cancer or a history of radiation therapy were excluded from the study. Ultimately, 135 patients were included. This study was approved by the institutional ethics committee (Approval number 2019.38.19).

Magnetic resonance imaging protocol

All patient examinations were performed with a 1.5 T device (Aera, Siemens, Erlangen, Germany) with an eight-channel breast receiver coil. The patients were placed in the prone position with their arms beside their bodies during the examination. A standard breast DCE-MRI protocol was applied with fat suppression and three-dimensional (3D) T1-weighted spoiled gradient-echo sequences for all patients. The parameters were as follows: repetition time (TR)/echo time (TE): 2/4.5, flip angle: 18°, matrix size: 290 × 320, field of view: 380 × 420 mm, and slice thickness. 1.5 mm. First, one unenhanced pre-contrast image was obtained. Then, a single dose of 0.1 mmol/kg body weight gadobutrol (Gadovist, Bayer Schering Pharma) was administered intravenously at a rate of 2 mL/s, followed by a 20-mL saline flush, and six postcontrast axial 3D data sets were obtained within 56 seconds each. The MR angiogram images were obtained by subtracting the contrast-enhanced images from the unenhanced images, on which MIP reconstruction was performed.

Analysis of the magnetic resonance imaging

The MR images of the patients were evaluated together by two radiologists (A.K. with 8 years of experience and M.K. with 7 years of experience) at a workstation (Syngo, Siemens Healthcare) to reach a consensus. The radiologists were blinded to histopathologic outcomes. After identifying the suspicious index lesion on the sonograph or the mammograph, the longest diameter of the identified lesion was measured on the DCE-MR images. The largest tumor was evaluated for multifocality or multicentricity. The vascularity of the lesion and breast were evaluated with free windowing rotation.

Based on the description of Sardanelli et al. [11], we identified the following four vascularity grades for both breasts: Absent (no 3-cm-long and 2-mm-wide vessels), low (one 3-cm-long and 2-mm-wide vessel), moderate (two to four 3-cm-long and 2-mm-wide vessels), and marked (more than four 3-cm-long and 2-mm-wide vessels). IIBV was defined as the breast lesion showing at least two more vessels than the contralateral normal breast. The AVS was defined as the presence of a vessel entering or contacting the enhanced lesion on MIP images.

Regarding the histopathologic features, estrogen receptor (ER) and progesterone receptor (PR) expression were categorized as negative when the immunoreactive cells were equal to or less than 10% positive. C-ERBB2 expression was scored between 0 and 3. Accordingly, a score less than 3 was classified as negative, and a score of 3 was classified as positive.

Statistical analysis

All data analyses were performed with MedCalc statistical software version 16.8 (MedCalc Software bvba, Ostend, Belgium) and SPSS 13.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics, including the means and ranges, were calculated for age, tumor size, and mean number of vessels of both breasts for benign and malignant breast tumors. Normal distributions were verified using the Kolmogorov-Smirnov test. The Mann-Whitney U test was used to analyze the mean number of vessels, and student's t-tests was used to analyze age and tumor size. Chi-square test was used to examine the differences in AVS and IIBV positivity for benign and malignant breast tumors. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of AVS and IIBV were calculated. To determine the effect of tumor size on the diagnostic performance of AVS and IIBV, the lesions

were classified into two groups: Those equal to or smaller than 2 cm and those larger than 2 cm. Chi-square test was used for the evaluation of the relationships between AVS, IIBV positivity and ER, PR and C-ERBB2 expression. *P*-value of less than 0.05 indicated statistical significance.

Results

Among 135 suspicious breast masses, 72 (53.3%) were malignant and 63 (46.7%) were benign. Malign histopathological diagnoses included 58 invasive ductal carcinomas (IDCs), 7 invasive lobular carcinomas (ILCs), 4 papillary carcinomas, 2 mucinous carcinomas and 1 ductal carcinoma in situ. Benign masses included 32 fibroadenomas, 11 fibrocystic changes, 9 sclerosing adenoses, 4 papillomas, 3 mastitises, 2 phyllodes tumors, and 2 lesions with other benign histopathologies. Among all masses, 10 (7.4%) were classified as Breast Imaging Reporting and Data System (BI-RADS) 3, 63 (46.6%) as BI-RADS 4 and 52 (45.9%) as BI-RADS 5. Biopsies were performed for BI-RADS 3 masses either because of clinically suspicious findings or patient preferences.

Patient age, tumor size, the mean number of vessels in the ipsilateral and contralateral breast, presence of AVS and IIBV, and ER, PR and C-ERBB2 expression in the benign and malignant tumors are presented in Table 1. The mean patient age was 42 years (range 19–65) and 51 years (range 25–79) for the benign and malignant groups, respectively (P<0.001). The malignant masses had more vessels that were longer than 3 cm and wider than 2 mm than the benign masses in the ipsilateral breast (P<0.001). However, there were no significant differences in the mean number of vessels between benign and malignant masses in the contralateral breast (P=0.199). The prevalence of AVS and IIBV positivity were significantly higher in malignant masses (P<0.001) (Figure 1, 2). The diagnostic performances of the AVS and IIBV are presented in Table 2. AVS and IIBV distinguished benign masses from malignant ones with 75.0% sensitivity, 79.3% specificity, and 77.0% accuracy and 56.9% sensitivity, 90.4% specificity, and 72.5% accuracy, respectively. When the masses were stratified into two groups according to size, it was found that sensitivity of AVS and IIBV was lower and specificity was higher in the small lesion group.

Among 72 malignant masses, 48 (66.6%), 52 (72.2%) and 31 (43.0%) masses were positive for ER, PR and C-ERBB2 expression, respectively (Table 3). AVS and IIBV were significantly associated with ER (P=0.005, P<0.001) and PR expression (P=0.003, P<0.001), and not associated with C-ERBB2 expression (P=0.245 and P=0.085, respectively).

Table 1: The comparison of age, mass size, number of vessels in ipsilateral and contralateral breasts and presence of adjacent vessel sign and increased ipsilateral breast vascularity between benign and malignant breast masses

	Benign	Malignant	*P*-value
Number	63	72	
Age (years)	42.3 (9.8)	51.9 (11.2)	<0.001
MS (mm)	21.7 (10.8)	24.1 (9.8)	<0.001
NVIB	1.12 (1.33)	2.88 (1.35)	<0.001
NVCB	1.01 (0.87)	1.05 (0.82)	0.459
Presence of AVS			<0.001
Present	13	54	
Absent	50	18	
Presence of IIBV			<0.001
Present	6	41	
Absent	57	31	

Results are presented as number, mean (standard deviation), MS: Mass Size, NVIB: Number of vessels in ipsilateral breast, NVCB: Number of vessels in contralateral breast, AVS: adjacent vessel sign, IIBV: increased ipsilateral breast vascularity, Values are mean values ± SD, *P*-value: significance level for all pairs

Table 2: Diagnostic performances of the adjacent vessel sign, increased ipsilateral breast vascularity

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
AVS (n=135)	75.0	79.3	80.5	73.5	77.0
IIBV (n=135)	56.9	90.4	87.2	64.7	72.5
Mass size ≤2cm (n=64)					
AVS	42.8	94.4	85.7	68.0	71.8
IIBV	42.8	100.0	100.0	69.2	75.0
Mass size >2cm (n=71)					
AVS	95.4	59.2	79.2	88.8	81.6
IIBV	65.9	77.7	82.8	58.3	70.4

AVS: adjacent vessel sign, IIBV: increased ipsilateral breast vascularity, PPV: positive predictive value, NPV: negative predictive value

Table 3: Relationship between adjacent vessel sign, increased ipsilateral breast vascularity and histopathological predictors

	ER		PR		C-ERBB2	
	Negative (n=24)	Positive (n=48)	Negative (n=20)	Positive (n=52)	Negative (n=41)	Positive (n=31)
AVS						
Present	13	41	10	44	29	25
Absent	11	7	10	8	12	6
P-value	0.005		0.003		0.248	
IIBV						
Present	4	37	4	37	20	21
Absent	20	11	16	15	21	10
P-value	<0.001		<0.001		0.085	

ER: estrogen receptor, PR: progesterone receptor, AVS: adjacent vessel sign, IIBV: increased ipsilateral breast vascularity, *P*-value: significance level for all pairs

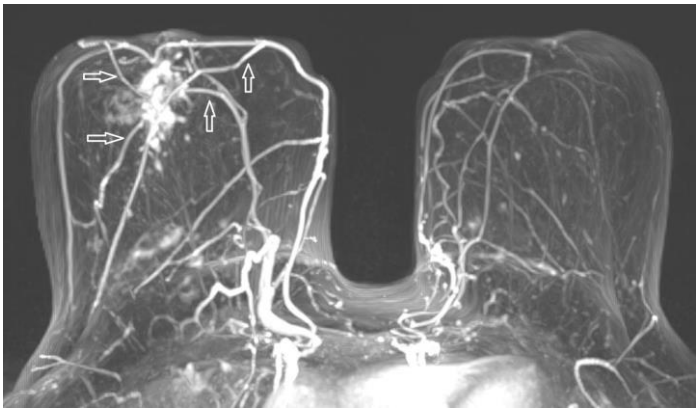

Figure 1: 43-year-old woman with invasive ductal carcinoma of right breast. Maximum-intensity-projection image shows presence of adjacent vessel sign (arrows) and increased ipsilateral breast vascularity.

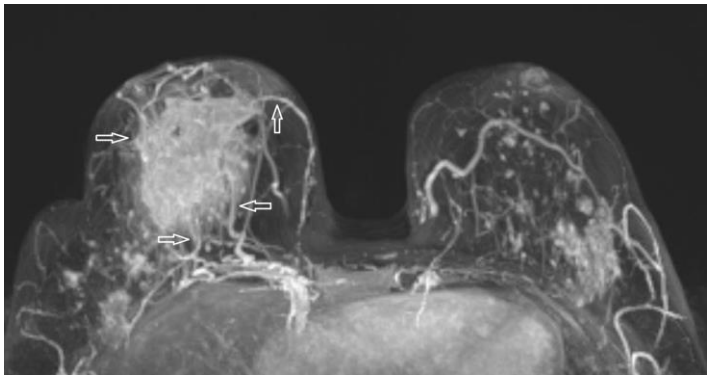

Figure 2: 27-year old woman with mastitis of right breast. Maximum-intensity-projection image represents false-positive findings for adjacent vessel sign (arrows) and increased ipsilateral breast vascularity.

Discussion

To grow and metastasize, tumor tissue requires nutrients and oxygen supplied by blood vessels with angiogenesis. Although physiological angiogenesis plays a significant role in embryo development, wound healing, and collateral vessel formation and abnormal angiogenesis in growing cancer tissue is related to active endothelial cells that release many angiogenic proteins [18]. The increased vascularity in breast cancer can be evaluated with Doppler ultrasound, positron emission tomography (PET) and MR angiograms [12,19,20].

MR angiography of the breast has been added to standard breast MRI to increase specificity when DCE images

are obtained. The obtained MIP images can provide a vascular map of the breast and the location of the enhanced masses. Additionally, arteries and veins of the breast and internal mammary vessels can be assessed for symmetry and the overall number of vessels.

Gadobutrol, gadobenate dimeglumine and gadopentetate dimeglumine are the main contrast agents for angiographic imaging. Herborn et al. [21] reported that gadobutrol and gadobenate dimeglumine showed better signal-to-noise and contrast-to-noise than gadopentetate dimeglumine. We used gadobutrol for vascular mapping of the breast from the DCE images in our study.

Several studies have investigated the relationship between asymmetrically increased vascularization and ipsilateral breast cancer and to reveal a strong association [11-16,22-25]. In these studies, the sensitivity and specificity of the AVS and IIBV for detecting breast cancer were quite different [11-16,22-25]. The sensitivity and specificity of AVS and IIBV were reported in the range of 68–92% and 57–100%, respectively. Consistent with these results, in our study, we obtained sensitivities of 75% and 56.9%, specificities of 79.9% and 90.4% and accuracies of 77% and 72.5% for AVS and IIBV, respectively. We also found that the AVS had a significantly higher degree of accuracy than IIBV in characterizing breast lesions. However, vascular evaluation alone was not sufficient for performing the isolation technique to characterize suspicious breast masses. The diagnostic performance of standard breast MRI can be enhanced with the addition of the AVS and IIBV to facilitate morphologic and dynamic analyses.

Mussurakis et al. [26] showed that the periphery of masses had greater diagnostic value than the central portion, and carcinomas revealed higher peripheral enhancement than benign masses. AVS may be related to neoangiogenesis and the higher microvessel density of the periphery of the lesion. We also investigated the relationship between the AVS and prognostic factors, including hormone expression, and found that AVS was significantly associated with ER and PR expression, but not with C-ERBB2 expression. Dietzel et al. [14] and Han et al. [27] reported that AVS was significantly associated with all histopathologic predictors of ER, PR and C-ERBB2 expression. However, AVS is a highly subjective parameter in terms of interpretation, and no criterion exists for the evaluation of the number and size of vessels in contact with the suspicious lesions. The vascularity of both breasts can be evaluated with MR angiograms, and IIBV is reportedly related to ipsilateral invasive breast cancer, multifocality and axillary lymph node metastasis [16].

In our study, the malignant masses had a significantly larger mean mass than the benign masses. When the masses were grouped according to size, the small masses showed decreased sensitivity and increased specificity compared to the large masses. These changes suggest that there may be a positive correlation between tumor size, AVS and IIBV. Additionally, Kul et al. [12] revealed sensitivity increased and specificity decreased with increasing lesion size, which may be due to angiogenic stimulation, increased metabolic demand and decreased flow resistance. Malignant breast masses are believed to induce angiogenesis for invasion, uncontrolled growth, and metastasis [5,6].

None of the fibroadenomas, except for five, were AVS-positive in our study. Similar to malignant masses, fibroadenomas can show higher degrees of vascularity with increased size. Although fibroadenomas are usually detected by ultrasound, a vascularity evaluation might be useful for differentiating a fibroadenoma from a well-marginated breast cancer.

There were three patients with mastitis in whom malignancy was suspected in our study. We found that all lesions with mastitis were positive for an AVS and IIBV. Breast inflammation is related to the angiogenic process, and mastitis can stimulate vascular structures to increase in both number and size [28]. For this reason, vascular evaluations with MR angiography may lead to false positive findings for inflammatory lesions.

None of the 11 fibrocystic changes had AVS or IIBV in our study. The ultrasound images of the cystic changes may vary with morphological changes. AVS and IIBV may be helpful in discriminating lesions with fibrocystic changes from malignant masses.

We detected eight papillary lesions, including four papillary carcinomas and four papillomas. We revealed that all papillary carcinomas, except for one, and three papillomas had an AVS. In total, two papillary carcinomas and papillomas had IIBV. Both benign and malignant papillary lesions can show high vascularity, so the AVS and IIBV have limited efficacy in characterizing papillary lesions.

Limitations

This study has several limitations. First, we evaluated the MRI images based on a consensus and did not take into consideration the inter- and intraobserver variability. Second, the sample sizes were also relatively small for subtypes of benign and malignant masses. Further prospective studies with large sample sizes are required to clarify the effectiveness of these methods and the relationship between various prognostic factors. Third, we only evaluated contrast-enhanced lesions, so our results cannot be applied to all lesions. Fourth, we did not evaluate other prognostic factors such as lymph node involvement, distant metastasis, or follow-up results.

Conclusion

Breast vascularity can be evaluated with MR angiograms obtained from DCE images without the need for additional acquisition time. MR angiography might increase the specificity of breast MRI and become a reliable method of further characterizing suspicious breast masses. In addition, AVS and IIBV both seem to be related with ER and PR expression.

References

1. Jatoi I, Miller AB. Why is breast-cancer mortality declining? Lancet Oncol. 2003;4(4):251-4.
2. Berry DA, Ravdin PM. Breast cancer trends: a marriage between clinical trial evidence and epidemiology. J Natl Cancer Inst. 2007;99(15):1139-41.
3. Brancato B, Crocetti E, Bianchi S, Catarzi S, Risso GG, Bulgaresi P, et al. Accuracy of needle biopsy of breast lesions visible on ultrasound: audit of fine needle versus core needle biopsy in 3233 consecutive samplings with ascertained outcomes. Breast. 2012;21(4):449-54.
4. Zhou JY, Tang J, Wang ZL, Lv FQ, Luo YK, Qin HZ, et al. Accuracy of 16/18G core needle biopsy for ultrasound-visible breast lesions. World J Surg Oncol. 2014;12:7.
5. Weidner N, Folkman J, Pozza F, Bevilacqua P, Allred EN, Moore DH, et al. Tumor angiogenesis: a new significant and independent prognostic indicator in early-stage breast carcinoma. J Natl Cancer Inst. 1992;84(24):1875-87.
6. Goede V, Fleckenstein G, Dietrich M, Osmers RG, Kuhn W, Augustin HG. Prognostic value of angiogenesis in mammary tumors. Anticancer Res. 1998;18(3C):2199-202.

7. Mungan İ, Doğru O, Aygen E, Dağlı AF. The relations of vascular endothelial growth factor–C and lymph node metastasis in breast cancer patients. J Surg Med. 2019;3(2):124-7.
8. Frouge C, Guinebretière JM, Contesso G, Di Paola R, Bléry M. Correlation between contrast enhancement in dynamic magnetic resonance imaging of the breast and tumor angiogenesis. Invest Radiol. 1994;29(12):1043-9.
9. Mussurakis S, Buckley DL, Horsman A. Prediction of axillary lymph node status in invasive breast cancer with dynamic contrast-enhanced MR imaging. Radiology. 1997;203(2):317-21.
10. Szabó BK, Aspelin P, Kristoffersen Wiberg M, Tot T, Boné B. Invasive breast cancer: correlation of dynamic MR features with prognostic factors. Eur Radiol. 2003;13(11):2425-35.
11. Sardanelli F, Fausto A, Menicagli L, Esseridou A. Breast vascular mapping obtained with contrast-enhanced MR imaging: implications for cancer diagnosis, treatment, and risk stratification. Eur Radiol. 2007;17:F48-51.
12. Kul S, Cansu A, Alhan E, Dinc H, Reis A, Çan G. Contrast-enhanced MR angiography of the breast: Evaluation of ipsilateral increased vascularity and adjacent vessel sign in the characterization of breast lesions. AJR Am J Roentgenol. 2010;195(5):1250-4.
13. Fischer DR, Malich A, Wurdinger S, Boettcher J, Dietzel M, Kaiser WA. The adjacent vessel on dynamic contrast-enhanced breast MRI. AJR Am J Roentgenol. 2006;187(2):147-51.
14. Dietzel M, Baltzer PA, Vag T, Herzog A, Gajda M, Camara O, et al. The adjacent vessel sign on breast MRI: new data and a subgroup analysis for 1,084 histologically verified cases. Korean J Radiol. 2010;11(2):178-86.
15. Mahfouz AE, Sherif H, Saad A, Taupitz M, Filimonow S, Kivelitz D, et al. Gadolinium-enhanced MR angiography of the breast: is breast cancer associated with ipsilateral higher vascularity? Eur Radiol. 2001;11(6):965-9.
16. Wright H, Listinsky J, Quinn C, Rim A, Crowe J, Kim J. Increased ipsilateral whole breast vascularity as measured by contrast-enhanced magnetic resonance imaging in patients with breast cancer. Am J Surg. 2005;190(4):576-9.
17. Kang DK, Kim EJ, Kim HS, Sun JS, Jung YS. Correlation of whole-breast vascularity with ipsilateral breast cancers using contrast-enhanced MDCT. AJR Am J Roentgenol. 2008;190(2):496-504.
18. Pavlakovic H, Havers W, Schweigerer L. Multiple angiogenesis stimulators in a single malignancy: implications for anti-angiogenic tumour therapy. Angiogenesis. 2001;4(4):259-62.
19. Kupeli A, Kul S, Eyuboglu I, Oguz S, Mungan S. Role of 3D power Doppler ultrasound in the further characterization of suspicious breast masses. Eur J Radiol. 2016;85(1):1-6.
20. Wilson CB, Lammertsma AA, McKenzie CG, Sikora K, Jones T. Measurements of blood flow and exchanging water space in breast tumors using positron emission tomography: a rapid and noninvasive dynamic method. Cancer Res. 1992;52(6):1592-7.
21. Herborn CU, Lauenstein TC, Ruehm SG, Bosk S, Debatin JF, Goyen M. Intraindividual comparison of gadopentetate dimeglumine, gadobenate dimeglumine, and gadobutrol for pelvic 3D magnetic resonance angiography. Invest Radiol. 2003;38(1):27-33.
22. Carriero A, Di Credico A, Mansour M, Bonomo L. Maximum intensity projection analysis in magnetic resonance of the breast. J Exp Clin Cancer Res. 2002;21(3):77-81.
23. Schmitz AC, Peters NH, Veldhuis WB, Gallardo AM, van Diest PJ, Stapper G, et al. Contrast-enhanced 3.0-T breast MRI for characterization of breast lesions: increased specificity by using vascular maps. Eur Radiol. 2008;18(2):355-64.
24. Ando Y, Fukatsu H, Ishiguchi T, Ishigaki T, Endo T, Miyazaki M. Diagnostic utility of tumor vascularity on magnetic resonance imaging of the breast. Magn Reson Imaging. 2000;18(7):807-13.
25. Verardi N, DiLeo G, Carbonaro LA, Fedeli MP, Sardanelli F. Contrast-enhanced MR imaging of thebreast: association between asymmetric increased breast vascularity and ipsilateral cancer in a consecutive series of 197 patients. Radiol Med. 2013;118(2):239-50.
26. Mussurakis S, Gibbs P, Horsman A. Peripheral enhancement and spatial contrast uptake heterogeneity of primary breast tumours: quantitative assessment with dynamic MRI. J Comput Assist Tomogr. 1998;22(1):35-46.
27. Han M, Kim TH, Kang DK, Kim KS, Yim H. Prognostic role of MRI enhancement features in patients with breast cancer: value of adjacent vessel sign and increased ipsilateral whole-breast vascularity. AJR Am J Roentgenol. 2012;199(4):921-8.
28. Jackson JR, Seed MP, Kircher CH, Willoughby DA, Winkler JD. The codependence of angiogenesis and chronic inflammation. FASEB J. 1997;11(6):457-65.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):754-758.
DOI: 10.28982/josam.632224

Research article
Araştırma makalesi

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

Investigation of respiratory syncytial virus in children with respiratory tract infection by real-time polymerase chain reaction

Solunum yolu enfeksiyonu olan çocuklarda respiratuvar sinsityal virusun gerçek zamanlı polimeraz zincir reaksiyonu ile araştırılması

Ayfer Bakır [1], Nuran Karabulut [1], Sema Alaçam [1], Sevim Meşe [1], Murat Yaman [1], Ayper Somer [2], Ali Ağaçfidan [1]

[1] Istanbul University, Istanbul Faculty of Medicine, Department of Medical Microbiology, Division of Virology and Fundamental Immunology, Istanbul, Turkey
[2] Istanbul University, Istanbul Faculty of Medicine, Department of Pediatric Infectious Disease, Istanbul, Turkey

ORCID ID of the author(s)
AB: 0000-0002-9006-5267
NK: 0000-0003-3550-2599
SA: 0000-0001-7957-2906
SM: 0000-0001-9992-4489
MY: 0000-0002-3685-0483
AS: 0000-0002-7827-1113
AA: 0000-0002-5470-296X

Corresponding author / Sorumlu yazar:
Ayfer Bakır
Address / Adres: İstanbul Üniversitesi, İstanbul Tıp Fakültesi, Tıbbi Mikrobiyoloji Anabilim Dalı, Viroloji ve Temel İmmünoloji Anabilim Dalı, 34000 İstanbul, Türkiye
e-Mail: dr.ayfer.bakir@gmail.com

Ethics Committee Approval: This study was performed with the approval of the Non-Interventional Clinical Research Ethical Committee of Istanbul University (reference number: 2018/08/662).
Etik Kurul Onayı: Bu çalışma, İstanbul Üniversitesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu'nun onayı ile yapıldı (referans numarası: 2018/08/662).

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.

This study is presented as an oral presentation at 2nd International Congress on Multidisciplinary Studies held in Adana on 04th-05th May 2018.

Published: 10/27/2019
Yayın Tarihi: 27.10.2019

Abstract

Aim: Respiratory syncytial virus (RSV) is the most common agent of respiratory tract infections (RTIs) in the early stages of life. This study aimed to investigate RSV A/B in children with RTIs by multiplex Polymerase Chain Reaction (PCR) and evaluate the distribution of RSV among age groups, concurrent co-infections, and features of its seasonal distribution.

Methods: Zero to eighteen-year-old patients whose nasopharyngeal swab samples were analyzed with the pre-diagnosis of RTI between April 2015 - March 2018 were included in this cross-sectional study. RSV A/B and other viruses of the respiratory panel were investigated with the multiplex real-time PCR method.

Results: Median age of 2707 patients was 1 (age range: 0-18) and 57.4% (1554) of them were male. RSV positivity was found in 14.4% (390). Prevalence of RSV in females and males were 13.6% and 15.5% respectively (P=0.16). The highest RSV rate was 18.1% in those younger than one year. Mixed infection factors were found in 5.4%, the most common ones being RSV and human rhinovirus (1.8%). RSV was mostly seen in December, followed by January and February (P<0.001).

Conclusion: RSV was found in 14.4% of the pediatric patients with RTI. We found that RSV was more common under the age of 1. In this study, we determined that RSV was commonly seen in winter. Early diagnosis of RSV with real-time PCR plays a crucial role in the prevention of unnecessary use of antibiotics and nosocomial infections. It may also help to implement an effective approach to the prevention, control, and treatment of RTIs during winter when the incidence increases.

Keywords: Respiratory syncytial virus, Real-time PCR, Respiratory tract infection

Öz

Amaç: Respiratuvar sinsityal virus (RSV), yaşamın ilk yıllarında solunum yolu enfeksiyonlarının (SYE) en sık etkenidir. Bu çalışmada SYE olan çocuklarda RSV A/B'nin multipleks polimeraz zincir reaksiyonu (PCR) ile araştırılması, yaş grupları arasında RSV dağılımı, eşlik eden koenfeksiyonlar ve mevsimsel dağılım özelliklerini değerlendirmeyi amaçladık.

Yöntemler: Bu çalışma çapraz kesitsel olarak planlanmıştır. Çalışmaya Nisan 2015 – Mart 2018 tarihleri arasında, 0-18 yaş arasında SYE ön tanısı ile gönderilen nazofaringeal sürüntü örnekleri dahil edildi. Örneklerden nükleik asit ekstraksiyon işlemi, EZ1 Virus Mini Kit V 2.0 (Qiagen, Almanya) ile EZ1 Advanced XL (Qiagen, Almanya) cihazında yapıldı. RSV A/B ve solunum paneline ait diğer viruslar, FTD Respiratory pathogens 21 (Fast-Track Diagnostics, Luxembourg) kiti kullanılarak multipleks real-time PCR yöntemi ile araştırıldı.

Bulgular: Yaş aralığı 0-18 olan 2707 hastanın medyan yaşı 1 idi ve %57,4'ü (1554) erkekti. RSV pozitifliği %14,4'ünde (390) tespit edildi. Kız ve erkeklerde RSV sıklığı sırasıyla %13,6 ve %15,5 idi (P=0,16). En yüksek RSV oranı <1 yaş grubunda %18,1 idi (P<0,001). Mikst etken ile enfeksiyonu %5,4'ünde saptandı. En fazla RSV ve HRV (%1,8) birlikteliği görüldü. RSV en sık Aralık (%27,9), ardından Ocak ve Şubat ayında saptandı (P<0,001).

Sonuç: SYE olan pediatrik hastaların %14,4'ünde RSV saptadık. RSV'nin 1 yaş altında daha yaygın olduğu tespit ettik. Bu çalışmada, RSV'nin kış mevsiminde sık görülen bir patojen olduğunu belirledik. Real-time PCR ile RSV tanısının erken konulması, gereksiz antibiyotik kullanımının ve nozokomiyal enfeksiyonların önlenmesi açısından önem taşımaktadır. Ayrıca, insidansın arttığı kış mevsimi boyunca SYE'lerin önlenmesi, kontrolü ve tedavisi için etkili bir yaklaşımın uygulanmasına yardımcı olabilecektir.

Anahtar kelimeler: Respiratuvar sinsityal virus, Real-time PCR, Solunum yolu enfeksiyonu

How to cite / Atıf için: Bakır A, Karabulut N, Alaçam S, Meşe S, Yaman M, Somer A, Ağaçfidan A. Investigation of respiratory syncytial virus in children with respiratory tract infection by real-time polymerase chain reaction. J Surg Med. 2019;3(10):754-758.

Introduction

Respiratory syncytial virus (RSV) is an enveloped, negative-stranded RNA virus of the *Pneumoviridae* family [1]. RSV is known as an important respiratory tract pathogen since it was isolated from infected children in 1957 [2,3], which affects all age groups. Virus transmission occurs through contact with infected persons or contaminated materials through the eye, nose or mouth mucosa. Inhaled fomites may be the cause of infection, which is generally limited to the upper respiratory tract [4]. However, it may also evolve into a serious lower respiratory tract infection (RTI). RSV constitutes the most common cause of pneumonia and bronchiolitis in children [5]. Sixty-seventy percent of the children under the age of 1 and almost all children under the age of 2 are affected by this virus [6]. RSV is associated with recurrent wheezing and pediatric asthma [7].

According to the data of 2015, it is estimated that RSV is responsible for 33.1 million lower RTI attacks, 3.2 million admissions to hospital and 118.200 deaths under the age of 5 around the world [8]. Although it is reported that the rate of RSV infection is higher in pediatric patients, some life-threatening infections may be seen in healthy children and the elderly, especially over the age of 65 [9]. Comorbid conditions such as congenital heart disease, chronic lung disease, Down syndrome, premature birth, cystic fibrosis and immune deficiency may increase morbidity and mortality [8,10-12]. RSV infection may cause more serious symptoms in cases of bacterial infection and superinfection [13]. Factors such as low education, decreased family income, and residing in crowded environments increase the probability of the transmission of RSV infection. It is concluded that there is a strong relationship between RSV infection and seasonal changes [14]. The prevalence of the infection differs according to geographical location, climate changes, genetic disposition, socioeconomic factors and regional virus strains [15].

In this study, a retrospective epidemiological analysis was performed to determine the prevalence of RSV in the age group of 0-18, outpatients and inpatients, its seasonal distribution and its peak season as well as the frequency of concurrent co-infections.

Materials and methods

Zero to eighteen-year-old patients whose nasopharyngeal swab samples were analyzed with the pre-diagnosis of RTI between April 2015 and March 2018 in the Medical Microbiology department were included in this cross-sectional study. RSV and other viruses of the respiratory panel such as Adenovirus, Bocavirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Enterovirus, Human metapneumovirus A/B, Influenza A, Influenza A (H1N1), Influenza B, Parainfluenza 1-4, Parechovirus, and RSV A/B were investigated with multiplex real-time PCR using FTD Respiratory pathogens 21 (Fast-Track Diagnostics, Luxembourg) kit in nasopharyngeal swab samples sent to the Virology Laboratory. Samples, which were transported under appropriate conditions for the microbiology laboratory, were stored at +4˚C until analysis. Viral genome extraction was performed by Qiagen EZ1 Virus Mini Kit v2.0 (Qiagen, Germany). The product obtained after the extraction underwent an amplification process in Rotor Gene Q Real-Time PCR device (Qiagen, Hilden, Germany).

This study was performed with the approval of the Non-Interventional Clinical Research Ethical Committee of Istanbul University (reference number: 2018/08/662).

Statistical analysis

SPSS 25 (SPSS Inc, Chicago, IL, USA) package program was used for statistical evaluation of the data. Continuous data were given as mean (standard deviation), and categorical data were given as number and percentage. Visual properties (histogram and probability graphs) and Kolmogorov-Smirnov test were used for normal distribution of variables. Student's T test or Mann-Whitney U test were used to compare the variables. Qualitative variables were compared using Pearson Chi-Square or Fisher exact tests. A *P*-value of <0.05 was considered statistically significant.

Results

A total of 2707 respiratory tract samples were obtained from 1863 (68.8%) outpatients and 844 (31.2%) inpatients. Median age of the pediatric patients in this study was 1 (age range: 0-18). One thousand, five hundred and fifty-two (57.3%) were males and 1155 (42.7%) were females. 390 out of 2707 pediatric patient samples (14.4%) were RSV positive. The prevalence of RSV in females and males were 13.6% (211) and 15.5% (179) respectively (P=0.16). Median age of the patients with RSV infection was 1. The highest rate of RSV was seen in patients under the age of 1, which was statistically significant (P<0.001).

Single infection with RSV was found in 9.1% (244/2707) of the patients and multiple factors with identified in 5.4% (146/2707). The rate of single and concurrent RSV infections were 8.8% (31/352) and 2.8% (10/352), respectively, in the age group of 6-10 years. The difference between the two was statistically significant (P=0.04) (Figure 1). Human rhinovirus (HRV) was the most commonly found pathogen concurrent with RSV (P<0.001) (Table 1). HRV was isolated in 59 of RSV-positive respiratory samples, human metapneumovirus was isolated in 16 and HBoV, in 15 samples. Parechovirus was not found in any RSV-positive patients (Table 2).

Among outpatients and inpatients, the rates of single infection with RSV were 8.7% (162/1863) and 9.8% (83/844) respectively, while the rates of concurrent infection were 5.8% (108/1863) and 4.4% (37/844) respectively (P=0.22) (Table 2). The most common multiple infection factor in RSV-positive respiratory samples was HRV (15.1%) (P=0.12) (Table 2, Figure 2).

Forty-one out of 120 inpatients had a comorbid disease, 10 of which were diagnosed with lower RTI (bronchiolitis and pneumonia). The most common comorbid diseases in patients with RSV infection were congenital metabolic diseases, renal diseases, hematologic malignancy and neurological disorders (Table 3).

When the distribution of RSV positivity according to the months was evaluated, it was found that RSV was mostly seen in December (27.9%), followed by January (21.3%) and

February (17.2%) (P<0.001). The lowest positivity rates were detected in July (0.8%) and August (1.4%) (Figure 3). Multiple infections with RSV were mostly seen in January (9.9%) and December (9.8%) (P<0.001).

Table 1: Demographic and laboratory features of the patients

		% (n)	*P*-value
RSV positive patients	Total	14.4 (390/2707)	
	Male	13.6 (211/1552)	0.16
Age (median)		1(range=0-18)	
Single infection		9.1 (244/2707)	0.29
Multiple infection		5.4 (146/2707)	
Double pathogens	RSV+HRV	1.8 (50)	<0.001
	RSV+EV	0.04 (1)	
	RSV+HBoV	0.3 (8)	
	RSV+HCoV-229E	0.2 (6)	
	RSV+HCoV-HKU1	0.2 (6)	
	RSV+HCoV-NL63	0.04 (1)	
	RSV+HCoV-OC43	0.1 (2)	
	RSV+hMPV	0.5 (14)	
	RSV+ADV	0.2 (5)	
	RSV+INF A	0.5 (13)	
	RSV+INF A H1N1	0.4 (11)	
	RSV+INF B	0.1 (3)	
	RSV+PIV-1	0.1 (2)	
	RSV+PIV-2	0.04 (1)	
	RSV+PIV-3	0.1 (2)	
	RSV+PIV-4	0.1 (2)	
Triple and four pathogens	RSV+ADV+EV	0.1 (2)	
	RSV+ADV+hMPV	0.04 (1)	
	RSV+ADV+INF-A H1N1	0.04 (1)	
	RSV+HBoV+hMPV	0.04 (1)	
	RSV+HBoV+INF-A H1N1	0.1 (2)	
	RSV+ADV+HCoV-229E	0.04 (1)	
	RSV+HCoV-NL63+HCoV-229E	0.04 (1)	
	RSV+HCoV–HKU1+PIV-4	0.04 (1)	
	RSV+HRV+HCoV–HKU1	0.1 (2)	
	RSV+HRV+ADV	0.04 (1)	
	RSV+HRV+EV	0.04 (1)	
	RSV+HRV+HboV	0.1 (4)	
	RSV+HRV+HCoV-229E	0.04 (1)	
	RSV+INF-A+HCoV–HKU1+PIV-4	0.04 (1)	

HRV: human rhinovirus; INF-A: influenza A virus; H1N1: pandemic influenza A H1N1 virus; hMPV: human metapneumovirus; HBoV: human bocavirus; HCoV: human coronavirus; PIV: parainfluenza virus ADV: adenovirus

Table 2: Distribution of multiple infections detected with Respiratory syncytial virus (RSV) positive samples in outpatients and inpatients

Infection	Outpatient n (%) 1863	Inpatient n (%) 844	*P*-value
Single infection	162 (8.7)	83 (9.8)	0.22
Multiple infection	108 (5.8)	37 (4.4)	
Human rhinovirus	40 (2.1)	19 (2.3)	0.80
Human metapneumovirus	11 (0.6)	5 (0.6)	1.00
Human Bocavirus	11 (0.6)	4 (0.5)	1.00
Influenza virus type A H1N1	11 (0.6)	3 (0.4)	0.56
Influenza virus type A	10 (0.5)	4 (0.5)	1.00
Adenovirus	9 (0.5)	2 (0.2)	0.52
Coronavirus-HKU1	8 (0.4)	2 (0.2)	0.73
Coronavirus-229E	7 (0.4)	1 (0.1)	0.44
Coronavirus-OC43	3 (0.2)	1 (0.1)	1.00
Parainfluenza virus type 4	2 (0.1)	2 (0.2)	0.59
Influenza virus type B	3 (0.2)	0 (0)	0.56
Coronavirus- NL63	1 (0.1)	1 (0.1)	0.52
Enterovirus	2 (0.1)	0 (0)	1.00
Parainfluenza virus type 1	2 (0.1)	0 (0)	1.00
Parainfluenza virus type 3	2 (0.1)	0 (0)	1.00
Parainfluenza virus type 2	1 (0.1)	0 (0)	1.00
Parechovirus	0 (0)	0 (0)	-

Table 3: Distribution of comorbid diseases in RSV-positive inpatients (n=43)

Comorbid diseases		n (%)
Congenital metabolic disease		9 (20.9)
	Propionic acidemia	4
	Maple syrup urine disease	1
	Fructose 1.6 diphosphatase	1
	Gaucher	1
	Metabolic disease, undefined	2
Renal disease		4 (9.3)
	Chronic renal failure	1
	Membranoproliferative glomerulonephritis	1
	Renal transplantation	2
Hematologic malignancy		4 (9.3)
	Acute lymphoblastic leukemia	4
Neurologic disease		4 (9.3)
	Cerebral palsy	1
	Epilepsy	1
	West syndrome	1
	Guillain-barre sydrome	1
Congenital heart disease		2 (4.7)
	Fallot tetralogy	1
	Ventricular septal defect	1
Liver disease		2 (4.7)
	Liver transplantation	2
Chronic lung disease		2 (4.7)
	Asthma	2
Other		16 (37.2)
	Inguinal hernia, umbilical hernia, cleft palate, pyloric stenosis, biliary atresia, low-birth-weight baby, premature baby	
Total		43

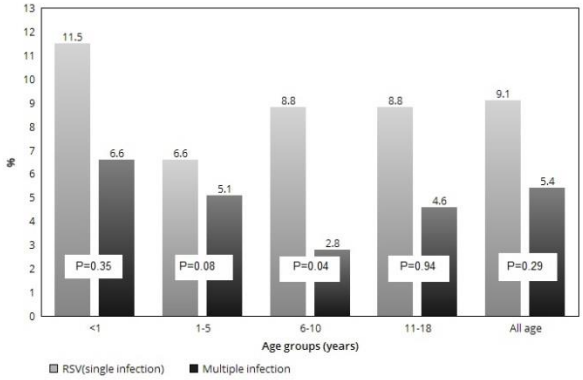

Figure 1: Distribution of single-infection (RSV) and multiple-infections according to the age groups

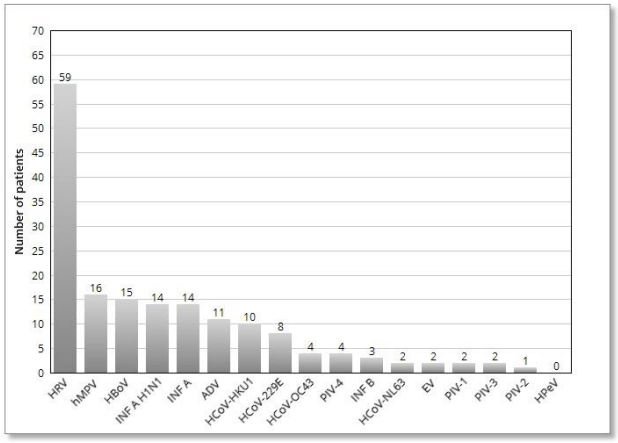

Figure 2: Distribution of co-infections in RSV-positive samples (number) (HRV: human rhinovirus, hMPV: human metapneumovirus, HBoV: human bocavirus, INF: influenza, ADV: adenovirus, HCoV: human coronavirus, PIV: parainfluenza virus, EV: enterovirus, HPeV: human parechovirus)

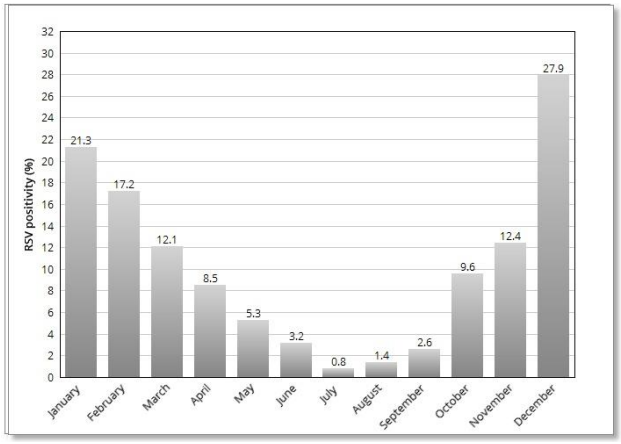

Figure 3: Distribution of human RSV according to the months

Discussion

RSV is the most common factor of RTIs in the early ages of life. Epidemiological studies are crucial as they help determine the timing of RSV outbreaks. In the studies conducted in our country, viral etiology is observed at a rate between 41.8% and 85% in acute RTIs. Also in these studies, RSV was found at a rate between 0% and 63% in different age groups (Table 4) [16-23]. In our study, we found RSV in 14% (390/2707) of the children diagnosed with RTI in the age group of 0-18. The highest rate of RSV was 18.1% (92/1060) in those younger than one year. Studies report that more than 80% of the children have RSV infection until the age of 2 [24]. Age and gender are important risk factors for serious RSV disease and children and the elderly are the groups at the highest risk for serious complications of the infection [25,26]. Incidence of RTI secondary to RSV decreases by age until late adulthood [27,28].

Asymptomatic infection is more commonly seen in adults and may contribute to the spread of the infection [29]. In our study, we did not find any difference between genders in terms of positivity rates of RSV infection.

Table 4: Characteristics of RSV infections in patients in Turkey

Location	Viral etiology %	Age	Respiratory tract infection	Prevalence (RSV)	Years	References
Aegean region						
Izmir	41.8	0-10 years	Lower	61	2009-2010	Akçalı S. et al. [22]
Izmir	75	<24 months	Lower	76.24	2013-2016	Gökçe Ş. et al. [23]
Central Anatolia						
Ankara†	25/39	20-67	Upper/ Lower	32	2013	Atilla E. et al. [19]
Ankara‡	51.8	90.4± 63.1 months	Upper/ Lower	17/86	2012-2014	Aldemir Kocabaş B. et al. [20]
Konya	58.2	0-18	Acute	ᵠ17.8, 27.9	2013-2015	Tüzüner U. et al. [21]
Marmara region						
Istanbul	85*	All age 0-5 6-23 24-59 ≥60	Upper	13.5 50 13 27 0	2005-2006	Ünüvar E. et al. [16]
Istanbul	78.6	2-16 years	Upper/ Lower	13–9.2	2013-2014	Aktürk H. et al. [17]
Sakarya		1-24 months	Lower	63	2018	Karakoyun M. et al. [18]
In this study (Istanbul)		0-18 years	Upper/Lower	14.4	2015-2018	

*Acute upper respiratory tract infections, †Adult recipients of allogeneic hematopoietic stem cell transplantation (Allo-HSCT) upper and lower respiratory tract infections, ‡The pediatric hematology and oncology department, ᵠ RSV-A, RSV-B respectively

The incidence of RSV differs according to the geographical regions and seasonal differences around the world. In mild climates, it is significantly more common in winter and spring. RSV outbreaks are very rare between June and September [30]. It causes outbreaks in the northern hemisphere between November and April and in southern hemisphere between March and October [31,32]. In the studies conducted in tropical regions, it is asserted that high humidity and year-round high temperatures allow air-borne transmission via droplet nuclei throughout the year [33]. In this study, we found that the highest and lowest rates of RSV positivity occurred between December-February and July-August, respectively. In a study in which the seasonal distribution of RTIs in Izmir in Aegean Region was investigated, the respiratory viruses were mostly isolated in winter (44.4%) and least during the summer (8.3%). Similarly, multiple infection factors were mostly seen in winter (46.9%) and least during the summer (8.8%) [34]. RSV was mostly found in Autumn (40%) and least during summer in children pre-diagnosed with RTI under the age of 5 in Konya, the Central Anatolia Region [10,35]. It was found that average RSV season began in early December and continued until early April in 15 European countries [36].

RSV infection is more severe in patients with a comorbid disease. Groups at the highest risk are children and the elderly with suppressed immune systems or cellular immunodeficiency. Low socioeconomic condition, malnutrition and some environmental factors such as crowded residential conditions and indoor air pollution may also lead to the development of more severe disease [37,38]. Prematurity, congenital heart diseases, congenital lung anomalies, cystic fibrosis, pulmonary malformations, and neurogenic disorders render children more prone to severe RSV disease [37]. In this study, the comorbid diseases in inpatients with RSV infection were mostly congenital metabolic diseases, renal diseases, hematologic malignancies, and neurological disorders.

Limitations

The retrospective nature of this study was the primary limitation, which made it impossible to distinguish the upper and lower RTIs due to the fact that no such records existed in the hospital registry.

Conclusion

RSV positivity was found in 14.4% of the samples of pediatric patients in the age group of 0-18 years. Consistent with the literature, we found that RSV was more common under the age of 1. We also found that RSV was a pathogen mostly seen in winter. Early diagnosis of RSV with real-time PCR is crucial in terms of the prevention of unnecessary use of antibiotics and nosocomial infections, as it allows timely intervention to control the spread of the disease. Further epidemiological studies are needed.

References

1. Rima B, Collins P, Easton A, Fouchier R, Kurath G, Lamb RA, et al. ICTV Report Consortium. J Gen Virol. 2017;98:2912-3.
2. Falsey AR, Hennessey PA, Formica MA, Cox C, Walsh EE. Respiratory syncytial virus infection in elderly and high-risk adults. N Engl J Med. 2005;352:1749-59.
3. Ruuskanen O, Lahti E, Jennings LC, Murdoch DR. Viral pneumonia. Lancet. 2011;377:1264-75.
4. Weir E, Fisman DN. Respiratory syncytial virus:pervasive yet evasive. CMAJ. 2004;170:191.
5. Stewart DL, Romero JR, Buysman EK, Fernandes AW, Mahadevia PJ. Total healthcare costs in the US for preterm infants with respiratory syncytial virus lower respiratory infection in the first year of life requiring medical attention. Curr Med Res Opin. 2009;25:2795-804.
6. Stein RT, Bont LJ, Zar H, Polack FP, Park C, Claxton A, et al. Respiratory syncytial virus hospitalization and mortality:Systematic review and meta-analysis. Pediatr Pulmonol. 2017;52:556-69.
7. Brüggmann D, Köster C, Klingelhöfer D, Bauer J, Ohlendorf D, Bundschuh M, et al. Respiratory syncytial virus:a systematic scientometric analysis of the global publication output and the gender distribution of publishing authors. BMJ Open. 2017;7:e013615.
8. Scheltema NM, Gentile A, Lucion F, Nokes DJ, Munywoki PK, Madhi SA, et al. Global respiratory syncytial virus-associated mortality in young children (RSV GOLD):a retrospective case series. Lancet Glob Health. 2017;5:e984-e991.
9. Mazur NI, Higgins D, Nunes MC, Melero JA, Langedijk AC, Horsley N, et al. The respiratory syncytial virus vaccine landscape:lessons from the graveyard and promising candidates. Lancet Infect Dis. 2018;18:e295-e311.
10. Stensballe LG, Trautner S, Kofoed PE, Nante E, Hedegaard K, Jensen IP, et al. Comparison of nasopharyngeal aspirate and nasal swab specimens for detection of respiratory syncytial virus in different settings in a developing country. Trop Med Int Health. 2002;7:317-21.
11. Borchers AT, Chang C, Gershwin ME, Gershwin LJ. Respiratory syncytial virus--a comprehensive review. Clin Rev Allergy Immunol. 2013;45:331-79.
12. Walsh EE, Peterson DR, Falsey AR. Risk factors for severe respiratory syncytial virus infection in elderly persons. J Infect Dis. 2004;189:233-8.
13. Rodríguez-Martínez CE, Rodríguez DA, Nino G. Respiratory syncytial virus, adenoviruses, and mixed acute lower respiratory infections in children in a developing country. J Med Virol. 2015;87:774-81.
14. Teck KS, Mac Guad R, Van Rostenberghe AH, Hua GS. Prevalence, risk factors and clinical characteristics of respiratory syncytial virus-associated lower respiratory tract infections in Kelantan, Malaysia. J Med Virol. 2019;91:1608-15.
15. Nair H, Simões EA, Rudan I, Gessner BD, Azziz-Baumgartner E, Zhang JSF, et al. Global and regional burden of hospital admissions for severe acute lower respiratory infections in young children in 2010: A systematic analysis. Lancet. 2013;381:1380-90.
16. Ünüvar E, Yildiz I, Kiliç A, Aslan SS, Çakal B, Toprak S, et al. Viral etiology and symptoms of acute upper respiratory tract infections in children. Turkish Journal of Medical Sciences. 2009;39:29-35.
17. Aktürk H, Sütçü M, Badur S, Törün SH, Çıtak A, Erol OB, et al. Evaluation of epidemiological and clinical features of influenza and other respiratory viruses. Turk Pediatri Ars. 2015;50:217-25.
18. Karakoyun M, Ataoğlu EA, Büyükkayhan D, Elevli M. Solunum yolu enfeksiyonu bulguları ile başvuran 2 yaş altı çocuklarda respiratory syncytial virus enfeksiyonlarının sıklığı ve klinik özellikleri. Online Türk Sağlık Bilimleri Dergisi. 2018;3:56-69.
19. Atilla E, Sahin D, Atilla PA, Dolapci I, Tekeli A, Bozdag SC, et al. Upper respiratory viral infections in patients with haematological malignancies after allogeneic haematopoietic stem cell transplantation:a retrospective study. Antivir Ther. 2018;23:523-7.
20. Aldemir-Kocabaş B, Karbuz A, Pekpak E, Karahan ZC, Dolapçı İ, İnce E, et al. Effects of respiratory viruses on febrile neutropenia attacks in children. Turk J Pediatr. 2017;59:511-9.
21. Tüzüner U, Akkaya O, Özdemir M, Kurtoğlu MG. Prevalence and Concomitancy of Respiratory Viruses in Children with Acute Respiratory Tract Infections. J Pediatr Infect. Dis. 2016;11:001-5.
22. Akçalı S, Yılmaz N, Güler Ö, Şanlidağ T, Anıl M. Alt solunum yolu enfeksiyonu olan çocuklarda solunum yolu viral etkenlerinin sıklığı. Türk Ped Arş. 2013;215-20.
23. Gökçe Ş, Kurugöl Z, Koturoğlu G, Çiçek C, Aslan A. Etiology, Seasonality, and Clinical Features of Viral Respiratory Tract Infections in Children Hospitalized With Acute Bronchiolitis:A Single-Center Study. Glob Pediatr Health. 2017;22;4:2333794X17714378.
24. Janet S, Broad J, Snape MD. Respiratory syncytial virus seasonality and its implications on prevention strategies. Hum Vaccin Immunother. 2018 ;14:234-44.
25. Sommer C, Resch B, Simões EA. Risk factors for severe respiratory syncytial virus lower respiratory tract infection. Open Microbiol J. 2011;5:144-54.
26. Langley GF, Anderson LJ. Epidemiology and prevention of respiratory syncytial virus infections among infants and young children. Pediatr Infect Dis J. 2011;30:510-7.
27. Glezen WP, Taber LH, Frank AL, Kasel JA. Risk of primary infection and reinfection with respiratory syncytial virus. Am J Dis Child. 1986;140:543-6.
28. Henderson FW, Collier AM, Clyde WA Jr, Denny FW. Respiratory-syncytial-virus infections, reinfections and immunity. A prospective, longitudinal study in young children. N Engl J Med. 1979;300:530-4.
29. Munywoki PK, Koech DC, Agoti CN, Kibirige N, Kipkoech J, Cane PA, et al. Influence of age, severity of infection, and co-infection on the duration of respiratory syncytial virus (RSV) shedding. Epidemiol Infect. 2015;143:804-12.
30. Stensballe LG, Devasundaram JK, Simoes EA. Respiratory syncytial virus epidemics:the ups and downs of a seasonal virus. Pediatr Infect Dis J. 2003;22:S21-32.
31. Mullins JA, Lamonte AC, Bresee JS, Anderson LJ. Substantial variability in community respiratory syncytial virus season timing. Pediatr Infect Dis J. 2003;22:857-62.
32. Dawson-Caswell M, Muncie HL Jr. Respiratory syncytial virus infection in children. Am Fam Physician. 2011;83:141-6.
33. Yusuf S, Piedimonte G, Auais A, Demmler G, Krishnan S, Van Caeseele P, et al. The relationship of meteorological conditions to the epidemic activity of respiratory syncytial virus. Epidemiol Infect. 2007;135:1077-90.

34.Çiçek C, Arslan A, Karakuş HS, Yalaz M, Saz EU, Pullukçu H, et al. Prevalence and seasonal distribution of respiratory viruses in patients with acute respiratory tract infections, 2002-2014. Mikrobiyol Bul. 2015;49:188-200.
35.Ture E, Yazar A. Distribution of Respiratory Viral Agents in Patients Being Followed-Up in Our Pediatric Emergency Department. Online Turkish Journal of Health Sciences. 2019;4:94-104.
36.Broberg EK, Waris M, Johansen K, Snacken R, Penttinen P. European Influenza Surveillance Network. Seasonality and geographical spread of respiratory syncytial virus epidemics in 15 European countries, 2010 to 2016. Euro Surveill. 2018;23:1-11.
37.Law BJ, Carbonell-Estrany X, Simoes EA. An update on respiratory syncytial virus epidemiology:a developed country perspective. Respir Med. 2002;96 Suppl B:S1-S7.
38.Simoes EA. Respiratory syncytial virus infection. Lancet. 1999;354:847-52.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):759-762.
DOI: 10.28982/josam.605123

Research article
Araştırma makalesi

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

The measurement of skin to epiglottis length for difficult airway prediction by ultrasonography in obese pregnant women: Prospective cohort study

Obez gebelerde zor havayolunu tahmin etmek için cilt-epiglot mesafesinin ultrasonografi ile ölçümü: Prospektif kohort çalışma

Çiğdem Ünal Kantekin [1], Mustafa Fatih Erkoç [2], Gamze Talih [1]

[1] Department of Anesthesiology and Reanimation, Bozok University, Yozgat, Turkey
[2] Department of Radiology, Bozok University, Yozgat, Turkey

ORCID ID of the author(s)
ÇÜK: 0000-0001-6758-7764
MFE: 0000-0002-6266-5177
GT: 0000-0003-4743-9734

Corresponding author / Sorumlu yazar:
Çiğdem Ünal Kantekin
Address / Adres: Bozok Üniversitesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Yozgat, Türkiye
e-Mail: drcgdm@hotmail.com

Ethics Committee Approval: Approval for the study was granted by Bozok University Clinical Research Ethics Committee (Decision number: 2017-KAEK-189_2018.02.27_08).
Etik Kurul Onayı: Çalışma için onay Bozok Üniversitesi Klinik Araştırmalar Etik Kurulu tarafından verildi (Karar numarası: 2017-KAEK-189_2018.02.27_08).

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.

Published: 10/27/2019
Yayın Tarihi: 27.10.2019

Abstract

Aim: The risk of difficult airway is high in obstetric anesthesia, and weight gain above physiological limits further increases this risk. Ultrasonography (USG) has often been used recently in airway evaluation of all patient groups. The aim of this study was to investigate the effect of weight gain beyond physiological limits on the measurement of the distance of the skin-to epiglottis (DSE) with USG.

Methods: 50 pregnant women aged between 20-40 years, half of which had gained weight within physiological limits during pregnancy (<15kg) (Group 1) and the other half whose weight gain was equal to or greater than 15 kilograms (Group 2) were included in this study. The measurements were labelled as "a" and "b" for the first and third trimesters. Mallampati evaluation was made during ultrasonographic measurements in all pregnant patients by an anesthesiologist blinded to the study.

Results: No statistically significant difference was determined between the Group 1 and Group 2 pregnant patients with respect to age, BMI, and distance of skin to epiglottis (DSE) values (P=0.293, P=0.281, P=0.515). A statistically significant increase in BMI and DSE was detected in Group 2b when compared to Group 1b (both: P<0.001).

Conclusion: Ultrasonographic DSE measurement in pregnant women with weight gain above the physiological limit during pregnancy may be used to predict difficult airways when utilized together with Mallampati scoring, especially during the third trimester.

Keywords: Obesity, Pregnancy, Difficult airway, Ultrasonography

Öz

Amaç: Obstetrik anestezide zor havayolu riski yüksektir. Fizyolojik sınırların üzerinde kilo artışı ile bu risk daha da artmaktadır. Son yıllarda bütün hasta gruplarında havayolu değerlendirilmesinde ultrasonografi sıklıkla kullanılmaktadır. Bu çalışmada gebelerde fizyolojik sınırların üzerindeki kilo artışının ultrasonografi ile cilt epiglot mesafesi ölçümüne etkisinin araştırılması amaçlanmıştır.

Yöntemler: 20-40 yaş arası gebeliği boyunca beklenen fizyolojik sınırda kilo artışı gösteren Grup 1 olarak isimlendirilen (n:25) ve aynı yaş grubunda gebeliği boyunca beklenenden daha fazla (fizyolojik sınır olan 15kg ve üstü) kilo artışı gösteren ve Grup 2 olarak isimlendirilen (n:25) toplam 50 gebe çalışmaya alınmıştır. Radyoloji kliniğine gebelikle ilgili rutin USG kontrolü için başvuran gebelere birinci ve üçüncü trimesterde eş zamanlı olarak boyun USG yapılarak cilt-epiglot mesafesi ölçülmüştür. 1. trimester ölçümler 'a', 3. trimester ölçümler 'b' harfi ile isimlendirilmiştir. Ultrasografik ölçümler sırasında tüm gebelerin mallampati değerlendirmesi çalışmayı bilmeyen bir anestezi uzmanı tarafından yapılmıştır.

Bulgular: Grup 1 ve 2'de bulunan gebelerin yaş, beden kitle indeksi ve ölçülen cilt-epiglot mesafesi yönünden istatistiksel olarak anlamlı bir fark olmadığı bulunmuştur (P=0,293, P=0,281, P=0,515). Grup 1b ve 2b değerlendirildiğinde beden kitle indeksi ve ölçülen cilt-epiglot mesafesi değerlerinde istatistiksel olarak anlamlı bir artış tespit edildi (P<0,001).

Sonuç: Üçüncü trimesterde preoperatif havayolu değerlendirilmesinde, özellikle fizyolojik sınırların üstünde kilo alımı olan gebelerde non-invaziv bir teknik olaran ultrasonografi ile cilt epiglot mesafesi ölçümü ve mallampatinin birlikte değerlendirilmesi zor havayolu tahmininde güvenilir bir belirteçtir.

Anahtar kelimeler: Obezite, Gebelik, Zor havayolu, Ultrasonografi

How to cite / Atıf için: Kantekin ÇÜ, Erkoç MF, Talih G. The measurement of skin to epiglottis length for difficult airway prediction by ultrasonography on obese pregnant women: Prospective cohort study. J Surg Med. 2019;3(10):759-762.

Introduction

The risk of difficult airway is high in obstetric anesthesia [1]. The most important cause of maternal morbidity and mortality related to anesthesia is difficulty in intubation. The oxygen reserves in pregnant patients are reduced, which makes it necessary to take precautions by estimating difficult airway preoperatively [1]. The recent Obstetric Anesthetists' Association/Difficult Airway Society Guidelines emphasize that an airway assessment should be performed before induction of general anesthesia [2]. This evaluation should be made not only to decrease difficult intubation, but also to evaluate the possibility of difficult mask ventilation and the difficulty of placement of the supraglottic airway device [2].

The dramatically increasing rate of obesity in the general population also extends to women of reproductive age. The anesthesiologist must be prepared to customize a perioperative plan to take care of these patients in the operating rooms [3]. Obesity increases the risk for cesarean delivery significantly and anesthesiologists are increasingly faced with morbidly obese patients. Several studies have reported that obesity was a major risk factor for maternal mortality. Obesity and its associated comorbidities, including obstructive sleep apnea, right ventricular failure, cardiomyopathy, diabetes mellitus, hypertension, and thromboembolic disease pose anesthetic challenges with failed intubation and aspiration representing the cause of death in most cases [4,5].

Airway ultrasonography (USG) is a simple, safe and noninvasive technique that can provide images of the concealed upper airway from the uvula to the glottis [6,7]. The engorgement of the oropharyngeal mucosa leads to an increase in Mallampati score, which this causes difficulties in intubation [8]. In addition to these factors, weight gain above the physiological limits may cause differences in airway evaluation with USG. Pinto et al. [9] reported that measuring the distance of the skin-to epiglottis (DSE) was a bedside test that could be used to estimate difficult laryngoscopy, and a cutoff value of 27.5mm provided an accuracy, sensitivity and specificity of 74.3%, 64.7% and 77.1%, respectively.

The aim of this study was to investigate the effect of weight gain above the physiological limits on the measurement of the skin to epiglottis distance with USG, a non-invasive technique which can be used daily to evaluate the obese pregnant individuals' airways.

Materials and methods

Approval for the study was granted by the Institutional Ethics Committee (Decision number: 2017-KAEK-189_2018.02.27_08).

50 pregnant women aged between 20-40 years, half of which had gained weight within physiological limits during pregnancy (<15kg) (Group 1) and the other half whose weight gain was equal to or greater than 15 kilograms (Group 2) were included in this study [10].

The patients were selected from those who were referred to the Radiology Clinic for routine antenatal ultrasonographic examination during the first and third trimesters and whose DSE were measured with neck ultrasonography. The measurements were labelled as "a" and "b" for the first and third trimesters. Mallampati evaluation was made during ultrasonographic measurements in all pregnant patients by an anesthesiologist blinded to the study.

Sonographic evaluation

DSE measurements were performed by the same radiologist blinded to the study, using a Ge-Health Care Logiq S7 device with a 10-13-MHz linear transducer. Patients were placed supine with their head and neck in a neutral position. Until the epiglottis was visible through the thyrohyoid membrane as a curvilinear hypoechoic structure, the airway was systematically imaged along its course using the linear transducer oriented transversely across the anterior surface of the neck. Swallowing facilitated identification of the epiglottis as a discrete mobile structure. The borders of the epiglottis were delineated by the brighter linear air-mucosa (A-M) interface (posterior) and pre-epiglottic space (anterior). DSE values were calculated with three measurements (central axis and the left - right extremities of the epiglottis) obtained from each patient and the mean value was used in the analysis [9].

Statistical analysis

Data obtained in the study were analyzed with SPSS v25.0 software. Conformity of the data to normal distribution was assessed with the Kolmogorov-Smirnov test, which showed that the data were non-normally distributed. Mann Whitney U-test was used for comparisons between the groups, and Wilcoxon Signed Ranks test was used for repeated measurements. Relationships between variables were evaluated with Spearman's rho correlation test. $P<0.05$ was considered statistically significant.

Power analysis was performed with G*Power 3.1.9.2 software. The power of this data was calculated as $1-\beta=0.82$ with $n_1=25$, $n_2=25$, $\alpha=0.05$ and an effect size of $d=0.85$.

Results

No statistically significant difference was determined between Group 1a and Group 2a with respect to age, body mass index (BMI), and DSE values ($P=0.293$, $P=0.281$, $P=0.515$, respectively) (Table 1). A significant increase was detected in BMI and DSE increases in each group (both: $P<0.001$) and between Groups 1b and 2b (both: $P<0.001$) (Table 2).

Table 1: Comparisons of age, BMI, and DSE values between Groups 1a and 2a

	Group 1a (n=25)	Group 2a (n=25)	Z	*P*-value
Age (years)	27 (18 - 35)	29 (18 - 37)	-1.052	0.293
BMI (kg/m2)	23.3 (20.8-34.2)	24.5 (20.1-31.3)	-1.078	0.281
DSE (mm)	24.2 (20.3-31.3)	24.9 (20-29)	-0.650	0.515

*: Mann-Whitney U Test (median [minimum-maximum])

Table 2: Comparisons of BMI, and DSE values between Group 1b and Group 2b

	Group 1b (n=25)	Group 2b (n=25)	Z	*P*-value
BMI (kg/m2)	23.3 (20.8-34.2)	25.6 (21-33.2)	-4.377	<0.001
DSE (mm)	24.2 (20.3-31.3)	26.2 (20.5-31)	-4.375	<0.001

*: Wilcoxon Signed Ranks Test (median [minimum-maximum])

A significantly positive correlation was determined between BMI and DSE in Group 1 in both trimesters ($r=0.856$, $P<0.05$) (Figure 1). The correlation coefficients of the first and third trimesters in Group 1 were 0.697 and 0.689, respectively. The overall correlation coefficient between BMI and DSE was 0.764.

No statistically significant difference was determined between Group 1a and Group 2a with respect to Mallampati

scores (P=0.249). The Mallampati scores of Group 2b were significantly higher than those of Group 1b and Group 2a (both: P<0.001) (Table 3). Mallampati scores and DSE values of the groups were not significantly correlated (P>0.05).

Table 3: Comparisons of Mallampati values between Group 1b and Group 2a

	Group 1b (n=25)	Group 2a (n=25)	Group 2b (n=25)	*P*-value
Mallampati	2 (1 - 3)	2 (1 - 3)	3 (2 - 4)[a]	<0.001

a: Group 2b values were significantly higher than Group 1b and Group 2a (z values -5.139, -4.796 respectively), *: Mann-Whitney U Test (median [minimum-maximum])

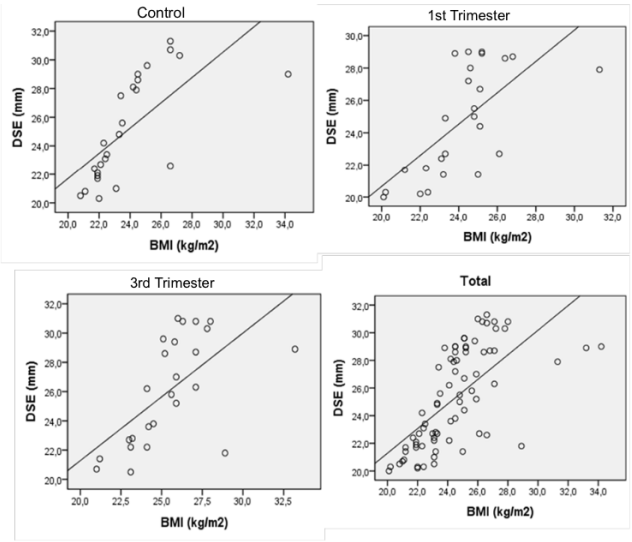

Figure 1: The correlations of DSE with BMI in Group 2

Discussion

Airway ultrasonography is a simple, safe, noninvasive technique that can provide images of the concealed upper airway from the uvula to the glottis. Hui et al. [11] used ultrasonography to image the sublingual space in a non-pregnant population. Sublingual USG has been shown to be well tolerated, and it has been reported that this technique may be relevant in pregnant women [12].

In another study of airway evaluation with USG in non-pregnant, morbidly obese patients, the distance between the midline skin and the larynx, the tracheal anterior wall at the level of the vocal cords and suprasternal notch, was found high in patients with difficult laryngoscopic findings [13]. Specific predictors for USG assessments of airway have not yet been established and there is a need for standardized USG scan measures for preoperative airway assessments. The cut off value of 27.5mm for difficult laryngoscopy was considered as the reference value for the current study in which soft tissue thickness was measured with USG between the skin and the epiglottis at the level of the thyroid membrane in elective patients [9]. In this study, no difficulties were encountered in any of the pregnant patients during DSE measurements.

Obesity is currently the most frequently seen global epidemic eating disorder with increasing incidence. Increased BMI is correlated with an increase in morbidity and mortality. In pregnancy, the growing fetus, placental and amniotic components, and increases in adipose tissue and fluid cause changes in the body. Generally, the increase in body weight during pregnancy is difficult to differentiate from obesity in obstetric patients. The incidence of unsuccessful intubation in the general population is approximately 1:2500 and this rate increases to 1:280 in obstetric cases. The addition of obesity to pregnancy not only increases the frequency of unsuccessful intubation but also complicates mask ventilation. The incidence of failed intubation in the morbidly obese pregnant women was reported as high as 33% [14]. The results of our study showed a positive correlation between increased BMI and DSE measurement. Therefore, a high DSE measurement on USG suggests that meticulous preoperative preparations should be made for difficult airway in obese pregnant patients.

Although the Mallampati score is widely used in preoperative airway evaluation, this scoring system has low sensitivity (50%) and specificity (89%) [11]. In a study examining the changes in Mallampati classification during pregnancy, birth, and the postpartum period, the incidence of Mallampati 3 and 4 reportedly increased from the 8th month of pregnancy until birth and these changes reversed within 48 hours after delivery [15]. In other studies in literature, Pilkington et al. [16] observed an increase in Mallampati scores during the course of pregnancy, and Abe et al. [4] confirmed these observations and reported that the engorgement of the oropharyngeal mucosa leads to an increase in Mallampati scores during labor and delivery. In accordance with those findings, Mallampati scores in our study were observed to increase in association with pregnancy and weight gain beyond the physiological limits, but no correlation was determined between Mallampati scores and DSE. This result may have been affected by the low number of patients. Nevertheless, both parameters are important in the evaluation of difficult airway, and when either is elevated, great care is required with respect to preparation for a difficult airway.

Limitation

An important limitation of this study is that as none of the pregnant patients underwent caesarean section under general anesthesia, hence, there was no actual evaluation of whether the airways were difficult. In our hospital, the rates of normal spontaneous vaginal delivery with epidural analgesia are extremely high. When indications for caesarean delivery arise, surgery is performed under epidural analgesia, which decreases the number of pregnant patients who received general anesthesia.

Conclusion

Weight gain in pregnancy over the expected physiological limit, especially during the 3rd trimester, increases DSE values measured ultrasonographically. Although no correlation was found between Mallampati scores and DSE, ultrasonographic DSE measurement, a non-invasive and easily performable technique, may be considered a more reliable warning of a difficult intubation than expected.

References

1. Girard T, Palanisamy A. The obstetric difficult airway: if we can't predict it, can we prevent it? Anaesthesia. 2017;72:143-7.
2. Mushambi MC, Kinsella SM, Popat M, Swales H, Ramaswamy KK, Winton AL et al. Obstetric Anaesthetists' Association and Difficult Airway Society Guidelines for the management of difficult and failed tracheal intubation in obstetrics. Anaesthesia. 2015;70:1286-306.
3. Riveros-Perez E, McClendon J, Xiong J, Cheriyan T, Rocuts A. Anesthetic and obstetric outcomes in pregnantwomen undergoing cesarean delivery according to body mass index: Retrospective analysis of a single-center experience. Ann Med Surg. 2018;36:129-34.
4. Abe H, Sumitani M, Uchida K, Ikeda T, Matsui H, Fushimi K, et al. Association between mode of anaesthesia and severe maternal morbidity during admission for scheduled Caesarean delivery: a nationwide population-based study in Japan, 2010-2013. Br J Anaesth. 2018;120:779-89.
5. Patel S, Weierstahl KL, Shah S, Fidkowski CW. Anesthetic Management for Cesarean Delivery in a Patient With Pulmonary Emboli, Pulmonary Hypertension, and Right Ventricular Failure. A Case Rep. 2016;7:146-9.
6. Singh M, Chin KJ, Chan VW, Wong DT, Prasad GA, Yu E. Use of sonography for airway assessment: an observational study. J Ultrasound Med 2010;29:79–85.
7. Adhikari S, Zeger W, Schmier C, Crum T, Craven A, Frrokaj I, et al. Pilot study to determine the utility of point-of-care ultrasound in the assessment of difficult laryngoscopy. Acad Emerg Med 2011;18:754–8.

8. Gaiser R. Maternal and fetal physiology. In: Chestnut DH, Wong LC, Tsen LC, Ngan Kee WD, Beilin Y, Mhyre J, editors. Obstetric anesthesia: principles and practice. 5th ed. Philadelphia: Saunders; 2014. p. 15–38.
9. Pinto J, Cordeiro L, Pereira C, Gama R, Fernandes HL, Assunção J. Predicting difficult laryngoscopy using ultrasound measurement of distance from skin to epiglottis. J Crit Care. 2016;33:26-31.
10. Bulut B, Mihmanlı, V. Obesity and Pregnancy. Okmeydanı Med J. 2014;30: 24-8.
11. Hui CM, Tsui BC. Sublingual ultrasound as an assessment method for predicting difficult intubation: a pilot study. Anaesthesia. 2014;69:314–9.
12. Weiniger CF, Sharoni L.The use of ultrasound in obstetric anesthesia.Curr Opin Anaesthesiol. 2017;30:306-12.
13. Ezri T, Gewürtz G, Sessler DI ,Medalion B, Szmuk P, Hagberg C, et al. Prediction of difficult laryngoscopy in obese patients by ultrasound quantification of anterior neck soft tissue. Anaesthesia. 2003;58:1111-4.
14. D'Angelo R, Habib AS. Obesity. In: Chestnut DH, ed. Obstetric anesthesia: principles and practice, 5th edn. Philadelphia: Elsevier Mosby, 2014:1141–56.
15. Boutonnet M,Faitot v, Katz A, Salomon L, Keita H. Mallampati class changes during pregnancy,labour, and after delivery: can these be predicted? Br J Anaesth. 2010;104:67-70.
16. Pilkington S, Carli F, Dakin MJ, Romney M, De Witt KA, Doré CJ, et al. Increase in Mallampati score during pregnancy. Br J Anaesth. 1995;74:638–42.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):763-765.
DOI: 10.28982/josam.547091

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

Multiple enterogluteal fistulas, Crohn's disease: A case report

Multipl enterogluteal fistüller, Crohn hastalığı: Bir olgu sunumu

Karam Aziz [1], Abdelouhab El Marouni [1], Houssam Belghali [1], Tarik Souiki [1], Karim Ibn Majdoub [1], Imane Toughrai [1], Khalid Mazaz [1], Ahmed Zerhouni [1]

[1] Visceral surgery service, Hassan II University hospital, Faculty of Medicine and Pharmacy of Fez, Sidi Mohammed Ben Abdallah University, Fez, Morocco

ORCID ID of the author(s)

KA: 0000-0002-3330-7311
AEM: 0000-0003-2035-7982
HB: 0000-0002-6734-2094
TS: 0000-0001-5657-7253
KIM: 0000-0002-0421-7296
IT: 0000-0003-0401-3012
KM: 0000-0001-7779-7802
AZ: 0000-0001-8441-016X

Corresponding author / Sorumlu yazar:
Karam Aziz
Address / Adres: Visceral surgery service, Hassan II University hospital, Faculty of Medicine and Pharmacy of Fez, Sidi Mohammed Ben Abdallah University, Fez, Morocco
e-Mail: karamaziz87@gmail.com

Informed Consent: The authors stated that the written consent was obtained from the patient presented with images in the study.
Hasta Onamı: Yazar çalışmada görüntüleri 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.

Published: 10/4/2019
Yayın Tarihi: 04.10.2019

Abstract
Crohn's disease is a type of chronic inflammatory bowel disease (IBD) of unknown etiology that may affect any part of the gastrointestinal tract from mouth to anus and shows extra-intestinal involvement. It characteristically shows skip lesions. This case report reported in 2018 describes a 40 years old Moroccan female not known to have documented evidence of significant Crohn's disease. She was diagnosed with multiple fistulas that are a rare entity of patients with Crohn's disease, which is itself a rare disease in African countries.
Keywords: Crohn's disease, Fistulas, Ileocecal resection

Öz
Crohn hastalığı, gastrointestinal sistemin ağızdan anusa kadar herhangi bir bölümünü etkileyebilen ve ekstra bağırsak tutulumu gösteren, etiyolojisi bilinmeyen bir tür kronik enflamatuar barsak hastalığıdır (IBD). Karakteristik olarak atlama lezyonlarını gösterir. 2018'de bildirilen bu vaka raporunda, 40 yaşındaki Faslı kadın, önemli Crohn hastalığı olduğuna dair kanıtları belgelemediği biliniyor. Kendisi Afrika ülkelerinde nadir görülen bir hastalık olan Crohn hastalığı olan hastaların nadir bir varlığı olan çoklu fistül tanısı aldı.
Anahtar kelimeler: Crohn hastalığı, Fistüller, İleoçekal rezeksiyon

Introduction

Crohn's disease is a type of chronic inflammatory bowel disease (IBD) of unknown etiology that may affect any part of the gastrointestinal tract from mouth to anus [1,2]. It typically presents as a recurrent course of patchy transmural inflammation with normal intestinal mucosa in between the diseased part followed by relapses [3,4]. It also manifests with extra intestinal complications most common being arthralgia/arthritis, and cutaneous, ophthalmologic and hepatobiliary manifestations. Smoking is considered as an important risk factor [5]. The treatment of this incurable disease aims at reducing the disease process, decreasing the number of relapses and improving the quality of life [6].

This case report describes a 40 years old Moroccan female known to have documented evidence of significant Crohn's disease since past 10 years. She is diagnosed with multiple fistulas that are a rare entity of patients with Crohn's disease, which is itself a rare disease in African countries.

How to cite / Atıf için: Aziz K, El Marouni A, Belghali H, Souiki T, Ibn Majdoub K, Toughrai I, Mazaz K, Zerhouni A. Multiple enterogluteal fistulas, Crohn's disease: A case report. J Surg Med. 2019;3(10):763-765.

Case presentation

A 40 years old Moroccan female with a past history of significant Crohn's disease since last 10 years presented to emergency room with severe gluteal and abdominal pain as well as a febrile condition (Figure 1). She denied the presence of chills, nausea and vomiting in her presenting complains and stated that she had normal bowel movements over the past one week.

The patient stated that she had occasional nausea and vomiting, crampy abdominal pain with bloating associated with meal intake and occasional diarrhea in the last 10 years leading to significant weight loss of 15 pounds over the previous 1–2 months. She denied any extra intestinal manifestations of her disease.

She was medically managed on infliximab for approximately 5 years but switched later to cetolizumab due to episodes of exaggerations between the doses. The next drug also failed after 1–2 months as she started having acute exaggerative episodes in the last few months. She had pre-operative colonoscopy, a year ago, after which she was recommended exploratory laparotomy with possible resection of diseased bowel but she denied it due to financial reasons.

Of all her past record of IV with oral contrast CT scans, the latest one that was performed approximately a year ago stated that the patient had moderately distended small bowel, compatible with small bowel obstruction, due to significant inflammatory edematous thickening of the terminal ileum. There was also evidence of multiple enteroenteric fistulas. In addition, there was an inflamed small bowel loop inseparable from the superior wall of bladder with presence of gas in the urinary bladder demonstrating evidence of enterovesicular fistula.

She also had colonoscopy a year ago that showed classical features of chronic inflammatory disease with tubulization in the sigmoid and the cecum except that there were no ulcerations present. The distal transverse colon and the entire descending colon appeared to be free of obvious disease. Overall pattern suggested of skip lesions with anal involvement classical for Crohn's disease.

The patient was operated with exploratory laparotomy discovering a fistula between sigmoid and cecum as well as a fistula between cecum and the right wall. We first did a fistulectomy of the fistula between the sigmoid and the cecum, then we proceeded to an ileocecal resection with ileocolic anastomosis then we tried a resection of 4 apparent fistulas tracks in the gluteal region (Figure 2, 3). Informed consent was taken from patient.

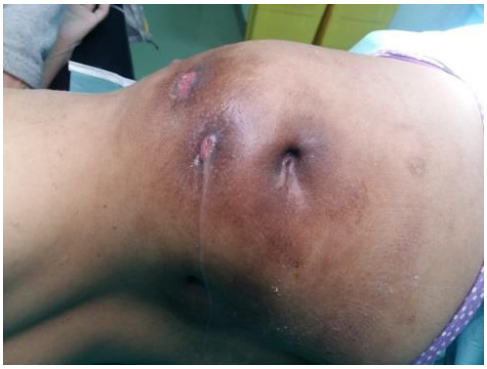

Figure 1: The patient gluteal fistulas at the emergency room

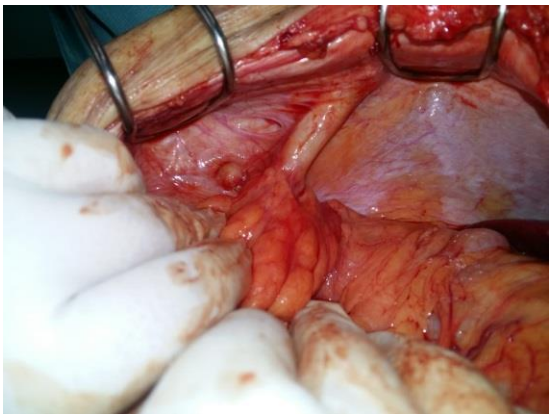

Figure 2: Peroperatory fistula between cecum and the wall

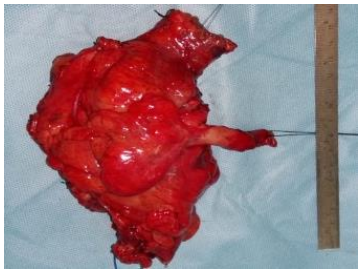

Figure 3: Ileocecal resection specimen

Discussion

The gluteal fistula and abscesses have been reported as complications of Crohn's disease, diverticulitis, colon carcinoma, and tuberculosis of lumbar vertebrae [7,8]. In our patient, recurrent abscesses history in gluteus suggested the possibility that there had been a fistula. In the case presented, initial diagnosis of a fistula could not be made till the visualization of fistulas. Computed tomography is helpful if exact spatial delineation of the tract is necessary or a suspect of associated abscess exists. Because CT results in high radiation, it should be used carefully in young children in selected indications. Ultrasound examination is generally not useful since it is limited by bowel gas and surgical incisions [9,10]. Magnetic resonance imaging (MRI) is reported as the golden standard in preoperative assessing and classifying of fistula, because MRI allows direct visualization of the tracts and abscesses through to high soft tissue resolution [11,12].

Surgery has been the main therapy for any sinus and fistula tracts. Open surgical exploration and repair provide definitive management, avoid recurrence, and prevent infection. Although surgical excision has been considered as a mode of treatment by most of the surgeons, the patient may be faced with some conditions such as nerve injuries, prolonged lymphatic drainage from the wound, recurrent lesions, wound infections, and unacceptable scar formations. Sclerotherapy using bleomycin is an established technique for the treatment of developmental vascular anomalies, also those which are at risk of developing intraoperative damage to vital organs and nerves, and lymphangiomas. Now sclerotherapy has been successfully used in the treatment of congenital sinus tracts [13,14].

Bleomycin is an antitumor agent and, besides its antineoplastic effect, bleomycin causes nonspecific inflammatory reaction leading to fibrosis in the surrounding tissues [15].

Conclusion

The present case is a description of a novel fistula tractus. To the best of our knowledge, this is the first case with

fistula deeply located and extending from the gluteus in the literature. Clinicians should consider underlying congenital malformation in the differential diagnosis of recurrent perineal and/or gluteal abscess. Catheter-based bleomycin injection could be applied as a safe, minimally invasive, and effective option for complex gluteal fistula, which makes it a suitable and durable alternative to open surgery. Treatment of this entity is individualized according to the site of fistula and associated anomalies.

References

1. Klein S, Kinney J, Jeejeebhoy K, Alpers D, Hellerstein M, Murray M, Twomey P, et al. Nutrition support in clinical practice: review of published data and recommendations for future research directions. Am J Clin Nut. 1997;66(3):683–706.
2. Lee Kang M, Ji ML. Crohn's disease in Korea: past, present, and future. Korean J Intern Med. 2014;29(5):558–70.
3. James Samuel D, Wise Paul E, Zuluaga-Toro Tania. Identification of pathologic features associated with "ulcerative colitis-like" Crohn's disease. World J Gastroenterol. 2014;20(36):13139–45.
4. Sica GS, Di Carlo S, Tema G, Montagnese F, Del Vecchio Blanco G, Fiaschetti V, Maggi G, Biancone L. Treatment of peri-anal fistula in Crohn's disease. World J Gastroenterol. 2014 Oct 7;20(37):13205-10.
5. Ott C, Takses A, Obermeier F. Smoking increases the risk of extraintestinal manifestations in Crohn's disease. World J Gastroenterol. 2014;20(34):12269–76.
6. Magalhães J, Castro FD, Carvalho PB, Moreira MJ, Cotter J. Quality of life in patients with inflammatory bowel disease: importance of clinical, demographic and psychosocial factors. Arq Gastroenterol. 2014;51(3):192–7.
7. Singh G, Kaur B, Gupta S. Gluteal fistula—an unusual manifestation of carcinoma colon. Indian Journal of Gastroenterology. 2001;11(4):171.
8. Hussien M, Mudd DG. Crohn's disease presenting as left gluteal abscess," International Journal of Clinical Practice. 2001;55(3):217–8.
9. Alexander ES, Weinberg S, Clark RA, Belkin RD. Fistulas and sinus tracts: radiographic evaluation, management, and outcome. Gastrointest Radiol. 1982;7(2):135-40.
10. Nicholson T, Born MW, Garber E. Spontaneous cholecystocutaneous fistula presenting in the gluteal region. J Clin Gastroenterol. 1999 Apr;28(3):276-7.
11. Buchanan GN, Halligan S, Bartram CI, Williams AB, Tarroni D, Cohen CR. Clinical examination, endosonography, and MR imaging in preoperative assessment of fistula in ano: comparison with outcome-based reference standard. Radiology. 2004 Dec;233(3):674-81.
12. Baskan O, Koplay M, Sivri M, Erol C. Our Experience with MR Imaging of Perianal Fistulas. Pol J Radiol. 2014 Dec 24;79:490-7. doi: 10.12659/PJR.892098
13. Nixon PP, Healey AE. Treatment of a branchial sinus tract by sclerotherapy. Dentomaxillofac Radiol. 2011 Feb;40(2):130-2.
14. Duman L, Karnak I, Akinci D, Tanyel FC. Extensive cervical-mediastinal cystic lymphatic malformation treated with sclerotherapy in a child with Klippel-Trenaunay syndrome. J Pediatr Surg. 2006 Jan;41(1):e21-4.
15. Erikçi V, Hoşgör M, Yıldız M, Örnek Y, Aksoy N, Okur Ö, Demircan Y, Genişol İ. Intralesional bleomycin sclerotherapy in childhood lymphangioma. Turk J Pediatr. 2013 Jul-Aug;55(4):396-400.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):766-768.
DOI: 10.28982/josam.570128

Case report
Olgu sunumu

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

A rare acute abdomen case: Acute appendicitis in a patient with situs inversus totalis

Nadir görülen bir akut batın olgusu: Situs inversus totalisli hastada akut apandisit

Mustafa Yeni [1], Rıfat Peksöz [2], Ali Dablan [3], Esra Dişçi [4]

[1] Department of General Surgery, Horasan State Hospital, Erzurum, Turkey
[2] Department of General Surgery, Malazgirt State Hospital, Muş, Turkey
[3] Department of Radiology, Horasan State Hospital, Erzurum, Turkey
[4] Department of General Surgery, Atatürk University Faculty of Medicine, Erzurum, Turkey

ORCID ID of the author(s)

MY: 0000-0003-2384-2094
RP: 0000-0003-4658-5254
AD: 0000-0003-4198-4416
ED: 0000-0003-3657-3620

Corresponding author / Sorumlu yazar:
Rıfat Peksöz
Address / Adres: Malazgirt Devlet Hastanesi, Genel Cerrahi Anabilim Dalı, Muş, Türkiye
e-Mail: kemal_peksoz@hotmail.com

Informed Consent: The authors stated that the written consent was obtained from the patient presented with images in the study.
Hasta Onamı: Yazar çalışmada görüntüleri 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.

Published: 10/11/2019
Yayın Tarihi: 11.10.2019

Abstract

Acute appendicitis is the most frequent disease requiring urgent surgery in the world. It may sometimes occur in atypical locations, such as the lower left quadrant of the abdomen. If previously unknown, some conditions such as situs inversus totalis make diagnosing acute appendicitis difficult. In those cases, surgeons primarily consider diverticulitis, gynecological diseases, or urinary pathologies, which present with lower left quadrant pain. Direct abdominal radiography, ultrasonography and computed tomography are the auxiliary imaging methods in the diagnosis of the disease. Dextrocardia and the observation of the gastric fundus gas in the right quadrant in direct abdominal radiograph are key features of situs inversus totalis. Considering the anatomical variation, laparoscopic exploration is recommended in these patients. We hereby present a forty-eight-year-old female patient with situs inversus totalis who was diagnosed with acute appendicitis.

Keywords: Acute appendicitis, Situs inversus totalis, Left lower quadrant pain, Computed tomography

Öz

Akut apandisit dünyada acil cerrahi gerektiren en sık hastalıktır. Akut apandisit bazen karnın sol tarafı gibi atipik yerlerde karşımıza çıkabilir. Situs inversus totalisde akut apandisit tanısını koymada zorluk oluşturabilecek durumlardan biridir. Situs inversuslu hastalarda eğer daha önce hastalığın tanısı bilinmiyorsa apendiks normal pozisyonda yerleşmediğinden apandisitin tanısı zordur. Cerrahlar öncelikle sol alt kadran ağrısı yapan divertikülit, jinekolojik hastalıklar veya üriner patolojileri düşünürler. Direk grafi, ultrasonografi, bilgisayarlı tomografi hastalık tanısında yardımcı radyolojik yöntemlerdir. Direkt grafilerde dekstrokardi ve mide fundus gazının sağda izlendiği durumlarda hastalıktan şüphelenilmelidir. Situs inversuslu hastalarda daha iyi eksplorasyon sağlayarak ayırıcı tanıyı yapmak ve anatomik varyasyon olabileceği de göz önünde tutularak laparoskopik cerrahi yapılması önerilmektedir. Bu olgu sunumunda tetkik edildikten sonra akut apandisit tanısı konulan sitüs inversus totalisli kırk sekiz yaşında kadın hastanın tanı ve tedavi süreci literatür eşliğinde tartışıldı.

Anahtar kelimeler: Akut apandisit, Situs inversus totalis, Sol alt kadran ağrısı, Bilgisayarlı tomografi

Introduction

Acute appendicitis is the most frequent disease requiring urgent surgery in the world [1]. Despite a usually typical anamnesis and physical examination findings, it may be wrongly or tardily diagnosed [2]. If previously unknown, some conditions such as situs inversus totalis (SIT) make diagnosing acute appendicitis difficult. SIT occurs when intraabdominal organs turn 270º clockwise during embryonic development [3]. The prevalence of acute appendicitis in SIT patients is similar to that in the general population, which is between 0.001% and 0.01% [4,5].

In patients with SIT, the diagnosis of other diseases, such as acute myocardial infarction, may also be delayed due to the reverse placement of the organs, which increases morbidity and mortality. Previous knowledge about the condition is critical to take measures against undesired clinical and surgical complications [6].

This case presentation discusses the diagnosis and treatment process of the forty-eight-year-old female patient with SIT who was diagnosed with acute appendicitis.

How to cite / Atıf için: Yeni M, Peksöz R, Dablan A, Dişçi E. A rare acute abdomen case: Acute appendicitis in the patient with situs inversus totalis. J Surg Med. 2019;3(10):766-768.

Case presentation

The forty-eight-year-old female patient arrived at the emergency department with complaints of abdominal pain in the lower left quadrant and appetite loss that began 12 hours ago. Physical examination revealed slight abdominal distention, pain and rebound in the lower left abdominal quadrant. There was no defense. She was incidentally diagnosed with SIT 2 years ago during her follow-ups for pregnancy. Her white blood cell count was $13.01x10^3/mm^3$. Computerized tomographic imaging of the abdomen revealed an edematous tubular structure, with a wall-thickness of 8 mm, extending from the cecum to the pelvis (Figure 1d), which was consistent with acute appendicitis. The liver was observed on the left while the spleen and the stomach were located on the right (Figure 1b, 1c). Electrocardiogram (ECG) and posteroanterior lung x-ray findings of the patient were compatible with dextrocardia: Right axis deviation, global negativity in D1 AVL and AVR, positive QRS complex, positive P, T waves with poor R progression and deep S loss in precordial derivations. All findings pointed to Situs Inversus Totalis. Laparoscopic exploration was planned, however, open appendectomy under spinal anesthesia was preferred due to the patient's Mallampati Class IV airway, which may have caused intubation difficulty. Abdomen was accessed via the paramedian incision made in the left lower quadrant. The appendix was hyperemic and edematous with a thickened wall as it extended into the pelvis (Figure 2). Appendectomy was performed. The patient was discharged uneventfully on the 3rd postoperative day. A written informed consent form was obtained prior to the operation.

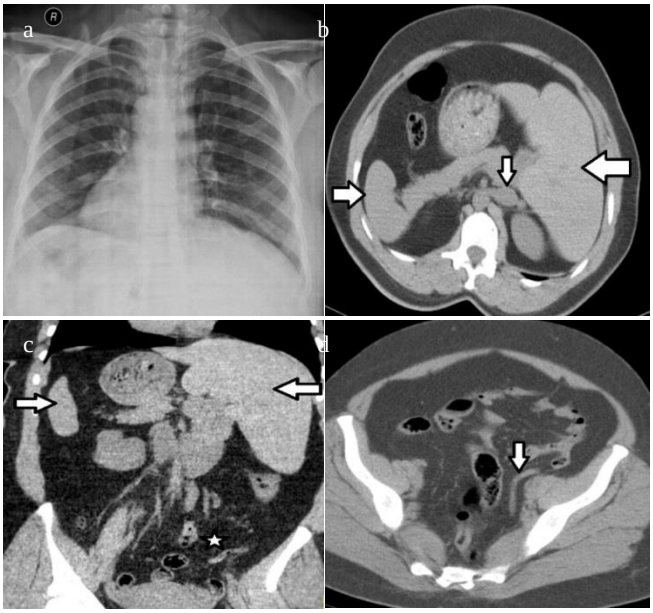

Figure 1: a: Dextrocardia in PA lung x-ray, b: Liver located on the left (right arrow), VCI located on the left (downward arrow), spleen (left arrow) located on the right, c: Liver located on the left (right arrow) and spleen located on the right (left arrow), inflamed appendix (star) in the lower left quadrant, d: Blind-ending of the inflamed appendix on the left lower quadrant

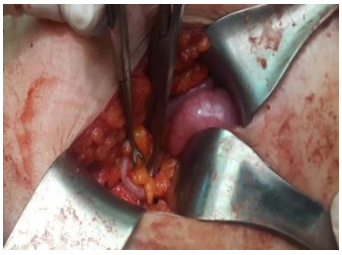

Figure 2: The appendix as visualized during the operation

Discussion

Sixty percent of patients with appendicitis present with pain originating from the umbilical region, which later migrates to the lower right quadrant, loss of appetite, nausea, vomiting, constipation, and sometimes diarrhea [7]. Although the appendix is usually located in the right lower quadrant, in rare cases such as SIT or intestinal malrotation, it may be found in the lower left abdominal quadrant [8]. Various other conditions may cause lower left abdominal pain, i.e., sigmoid diverticulitis, abdominal aortic dissection, cystitis, renal colic, prostatitis, testicular torsion, intestinal obstruction, incarcerated hernia, and psoas abscess.

In SIT, which is usually incidentally diagnosed, the organs are arranged in the mirror image of their normal locations [10]. Direct abdominal radiography, ultrasonography and computed tomography are the auxiliary diagnostic imaging methods [11]. In direct x-ray imaging, dextrocardia and observation of the gastric fundus gas on the right side of the patient lead to the diagnosis of SIT. In our patient, we cross-checked the direct abdominal x-ray findings with computerized tomographic images. Dextrocardia has specific electrocardiogram findings: Reverse P and T waves in D1, and poor R progression between V1-V6 [12]. The ECG findings of our patient were typical for dextrocardia.

In patients with Situs Inversus Totalis, loss of appetite, nausea, diarrhea, pain originating from the umbilical region, leukocytosis, defense and/or rebound in the lower left abdominal quadrant may be associated with acute appendicitis [13]. In our case, acute appendicitis was diagnosed with physical examination and radiological evaluation, after which it was verified with surgery. Considering anatomical variations, laparoscopic exploration is the preferred surgical treatment in SIT patients [14]. Open appendectomy was obligatory in our patient due to difficult intubation.

Conclusion

In evaluating pain in the lower left quadrant, physicians should be mindful of acute appendicitis in patients with rare conditions such as Situs Inversus Totalis and always bear in mind the possibility of an atypically placed appendix.

References

1. Sammalkorpi HE, Mentula P, Leppäniemi A. A new adult appendicitis score improves diagnostic accuracy of acute appendicitis-a prospective study. BMC Gastroenterology. 2014;14:114.
2. Merter A, Bilecik T, Mayır B, Doğan U, Koç Ü, Oruç T. Laparoscopic Appendectomy in a Patient with Situs Inversus Totalis: Case Report. FÜ Sağ Bil Tıp Derg. 2014;28(3):145.
3. Jaffe BM, Berger DH. The appendix. In: Brunicardi FC, Andersen KD, Billiar RT, Dunn LD, Hunter GC, Pollock RE, editors. Schwartz's Principles of Surgery. 8th ed. New York: McGraw-Hill; 2005. p. 1119-1137.
4. Akbulut S, Ulku A, Senol A, Tas M, Yagmur Y. Left-sided appendicitis: Review of 95 published cases and a case report. World J Gastroenterol. 2010;16:5598-602.
5. Oh JS, Kim KW, Cho HJ. Left-sided appendicitis in a patient with situs inversus totalis. J Korean Surg Soc. 2012;83:175-8.
6. Koç A, Sönmez Y, Balaban O. Anaesthetic Management for Appendectomy in a Patient with Situs Inversus Totalis. Turkish Journal of Anesthesia & Reanimation. 2016;44:105-7.
7. Karagülle E, Türk E, Yildirim E, Moray G. A rare cause of left lower quadrant abdominal pain: acute appendicitis with situs inversus totalis. Turkish Journal of Trauma & Emergency Surgery. 2010;16:268-70.
8. Kamiyama T, Fujiyoshi F, Hamada H, Nakajo M, Harada O, Haraguchi Y. Left-sided acute appendicitis with intestinal malrotation. Radiation Medicine. 2005;23:125-7.
9. Nelson MJ, Pesola GR. Left lower quadrant pain of unusual cause. The Journal of Emergency Medicine. 2001;20:241-5.
10. Sands SS, Taylor JF. Prescreen evaluation of situs inversus patients. International surgery 2001;86:254-8.
11. Yaghan RJ, Gharaibeh KI, Hammori S. Feasibility of laparoscopic cholecystectomy in situs inversus. Journal of Laparoendoscopic & Advanced Surgical Techniques. 2001;11:233-7.
12. Demangone DA. EKG findings associated with situs inversus. Journal of Emergency Medicine 2004;27:179-81.
13. Ünal O, Haberal K, Çolak A. Left sided acute appendicitis in a patient with situs inversus totalis, Türk Radyoloji Derg. 2018;37(1):13-5.

14. Yılmaz Ö, Bayrak V, Çallı İ, Demir A. Differential Diagnosis in Left Lower Quadrant Pain: Acute Appendicitis in Patients with Situs İnversus. Sakarya Med J. 2014;4(2):93-5.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):769-771.
DOI: 10.28982/josam.629561

Case report
Olgu sunumu

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

An unusual complication of septic sacroiliitis: Hepatic and splenic infarction after iliac vein thrombosis

Septik sakroileitin nadir bir komplikasyonu: İliak ven trombozu sonrası gelişen hepatik ve splenik enfarkt

Gürkan Danışan [1], Nurmuhammet Taş [2], Gökhan Polat [3], Hayri Oğul [3]

[1] Department of Radiology, Mus State Hospital, Mus, Turkey
[2] Department of Physical Medicine Rehabilitation and Rheumatology, Medical Faculty, Ataturk University, Erzurum, Turkey
[3] Department of Radiology, Medical Faculty, Ataturk University, Erzurum, Turkey

ORCID ID of the author(s)
GD: 0000-0003-2052-0006
NT: 0000-0002-8033-4208
GP: 0000-0002-4143-0344
HO: 0000-0001-5989-3729

Corresponding author / Sorumlu yazar:
Gürkan Danışan
Address / Adres: Muş Devlet Hastanesi, Muş, Türkiye
e-Mail: gurkandanisan@yahoo.com

Informed Consent: The authors stated that the written consent was obtained from the patient presented with images in the study.
Hasta Onamı: Yazar çalışmada görüntüleri 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.

Published: 10/14/2019
Yayın Tarihi: 14.10.2019

Abstract
Septic sacroiliitis typically presents with non-specific symptoms such as limping gait, radiating pain in the hip and lumbar region and fever. Differential diagnoses include pelvic abscess, lumbar disc herniation or septic arthritis of the hip, and misdiagnosis is common. Magnetic resonance imagining (MRI) greatly enhanced the ability to determine the extent of infection arising from the sacroiliac joint. We hereby present a rare case of hepatic and splenic infarction secondary to septic thrombophlebitis in a patient with sacroiliitis.
Keywords: Splenic infarct, Hepatic infarct, Septic sacroiliitis, Magnetic resonance imaging

Öz
Sakroileit genellikle topallama, kalça ve bel bölgesinde yayılan ağrı, ateş gibi non-spesifik semptomlarla prezente olabilir. Ayırıcı tanılar arasında pelvik abse, lumbar disk herniaayonu ve kalçanın septik artriti olup, yanlış tanı oranı yüksektir. Manyetik rezonans görüntüleme sakroiliak eklemden yayılan enfeksiyonun gösterilmesinde oldukça başarılıdır. Bu olgu sunumunda sakroileiti bulunan bir hastada septik trombofilebite bağlı gelişen hepatik ve splenik enfarkt sunulmuştur.
Anahtar kelimeler: Dalak enfarktı, Karaciğer enfarktı, Septik sakroileit, Manyetik rezonans görüntüleme

Introduction

The sacroiliac joint is a diarthrodial synovial joint with abundant innervation [1]. 10% to 25% of patients' persistent mechanical low back pain arise from the sacroiliac joint [2]. Infection of the sacroiliac joint is uncommon, representing 1–2% of septic arthritis cases. The predisposing factors for phylogenic sacroiliitis include parenteral drug abuse, systemic sclerosis, pregnancy, immunosuppression, trauma, hemoglobinopathies, diabetes mellitus, HIV infection, cancer, endocarditis, alcohol abuse, and skin, respiratory or genitourinary infections [1-3]. Differential diagnoses include pelvic abscess, lumbar disc herniation or septic arthritis of the hip, and misdiagnosis is common [2].

Septic sacroiliitis may get complicated in two ways: The infection can spread to adjacent tissue [1,3], or it can spread distantly with septic thrombophlebitis [4,5]. Due to nonspecific physical examination findings, diagnosis of septic sacroiliitis may be difficult. The availability of contemporary imaging techniques, such as magnetic resonance imaging, greatly enhances the ability to determine the precise location and extent of infection arising from the sacroiliac joint and other anatomic structures in the pelvis [6]. We hereby present a rare case of spleen infarction secondary to septic thrombophlebitis in a patient with sacroiliitis.

How to cite / Atıf için: Danışan G, Taş N, Polat G, Oğul H. An unusual complication of septic sacroiliitis: Hepatic and splenic infarction after iliac vein thrombosis. J Surg Med. 2019;3(10):769-771.

Case presentation

A 38-year-old man was referred to our clinic with low back pain. Physical examination showed a tender left abdominal quadrant and hepatomegaly. White blood cell (WBC) count was 30.900/mm3 with 6.62% bands, 84.53% polymorphonuclear leukocytes (PMNs), and 8.85% lymphocytes. The erythrocyte sedimentation rate (ESR) was 1mm/h and C-reactive protein (CRP) was 243mg/l. Creatinine was normal while liver function tests had increased (Alanine aminotransferase (ALT): 76 U/L, alkaline phosphatase (ALP): 343 U/L, aspartate transaminase (AST): 88 U/L, direct bilirubin: 7.93 mg/dl, indirect bilirubin: 1.77 mg/dl, total bilirubin: 9.70 mg/dl). The blood culture was positive for staphylococcus aureus. Pre- and post-contrast pelvic magnetic resonance imagining (MRI) was performed. Pelvic MRI scans revealed right septic sacroiliitis findings such as subarticular intense edematous signal changes, significant joint effusion, adjacent soft tissue inflammation and abscess formation (Figure 1A-B). The massive inflammation extended into the spinal canal via the neural foramens. Post-contrast MRI scans showed an epidural abscess at L5/S1 level. Contrast enhanced images also revealed luminal obliteration and intense contrast enhancement on the vessel wall compatible with thrombophlebitis in the right internal iliac vein (Figure 1C-D), a wedge-shaped infarction area of decreased enhancement in the spleen and the left lobe of the liver (Figure 2A-B). Anticoagulant therapy was started for thrombosis. The patient was administered intravenous antibiotic treatment for septic sacroiliitis and discharged uneventfully after 10 days of hospitalization.

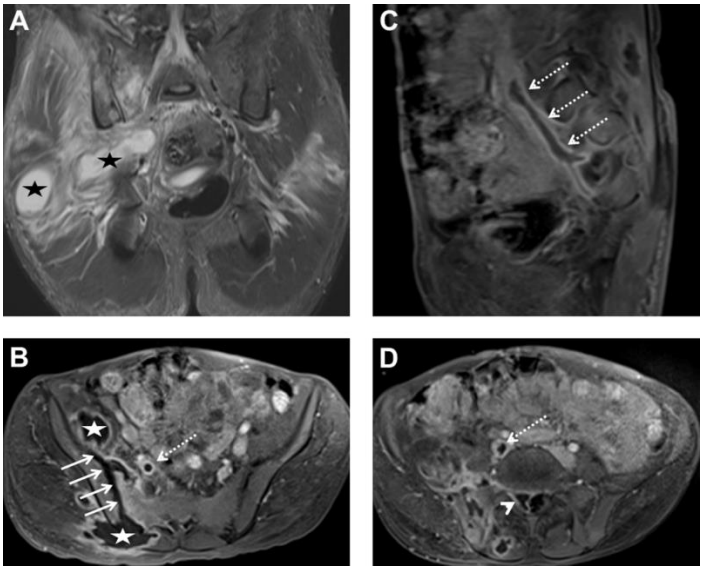

Figure 1: Coronal fat-sat T2 weighted (A) and post-contrast axial fat-sat T1 weighted (B) MR images of the pelvis reveal septic sacroiliitis (arrows) complicated by muscle abscesses (stars). Post-contrast fat-sat T1 weighted (B-D) images also show epidural involvement (arrowhead) of the abscess and right internal iliac vein thrombosis (dashed arrows).

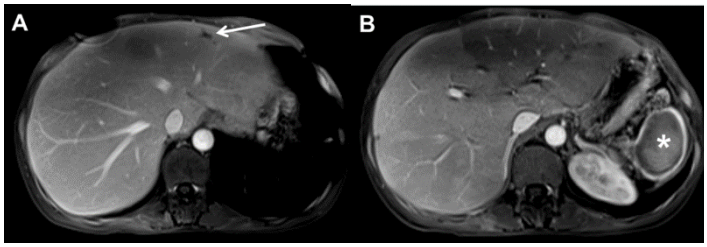

Figure 2: Contrast-enhanced fat-sat hepatic venous phase T1 weighted (A and B) MR images show a subsegmental hepatic infarct (arrow) with hypoperfused portion in left lobe. Post-contrast T1 weighted (B) MR image also demonstrates a large, global infarct (asterisk) of the spleen with only a tiny amount of enhancing splenic tissue (rim sign).

Discussion

Infection in the sacroiliac joint can spread to adjacent muscles. Pyomyositis of the iliopsoas muscle and gluteal abscesses have been very rarely reported [1,3]. MRI may provide more diagnostic accuracy in septic sacroiliitis than CT or radionuclide scanning. The authors emphasized that MRI has unique potential to delineate fluid in the sacroiliac joint, bone marrow edema, and soft tissue abscesses that may extend into the pelvic cavity [6]. MRI is also an important diagnostic tool for imaging vascular structures [7].

Septic sacroiliitis may present as acute, subacute, and chronic. ESR and CRP are almost always elevated in septic sacroiliitis. Leukocytosis, which is a nonspecific indicator of infection, may not always be encountered. Septic sacroiliitis is mostly observed unilaterally, but bilateral cases have also been reported. The primary infectious agent is usually *Staphylococcus aureus* [6]. ESR and CRP were higher than normal and leukocytosis was present in our patient. The infection was unilateral and blood culture was positive for *Staphylococcus aureus.*

Spinal epidural abscess and splenic infarction associated with septic sacroiliitis is uncommon. In our case, a spinal epidural abscess had developed after spreading via sacral neural foramen, and splenic infarction and iliac vein thrombosis had caused intense inflammation. The predisposing factors for spinal epidural abscess include diabetes mellitus, end-stage renal disease, endocarditis, urosepsis, intravenous drug use, rheumatoid arthritis, previous spinal procedure, previous spinal or dental trauma, alcoholic or viral cirrhosis and HIV infection. None of these etiologic factors were found in our case.

Septic thrombophlebitis or acute venous thrombosis may be associated with septicemia or bacteremia [6]. In our case, there were hepatic and splenic abscesses, for which the most frequent factor is metastatic hematogenous infection [4,8,9]. The spleen is a particularly easier target for embolism owing to the features of its anatomy and blood circulation [10].

Abscess treatment generally involves drainage by needle aspiration or surgery; however, cases of complete regression with antibiotics have also been reported [1]. There is no gold standard management for splenic abscesses. Splenectomy has been the most preferred method of treatment. Currently, conservative methods such as percutaneous drainage are performed in particularly in thick-walled, solitary abscesses [8,9].

Conclusion

We presented MRI findings of this exceedingly rare case of the hepatic and spleen infarction associated with septic sacroiliitis. Abdominopelvic MRI is the best diagnostic modality and should be performed particularly in septic sacroiliitis patients presenting with upper quadrant pain.

References

1. Llop Vilaltella M, Maldonado Romero V, Guillén Astete C, de la Puente Bujidos C, de Casanova Peña C. Sacroiliitis and gluteal abscess secondary to Staphylococcus aureus infection. Reumatol Clin. 2015 Nov-Dec;11(6):398-400.
2. Kim S, Lee KL, Baek HL, et al. A case of acute pyogenic sacroiliitis and bacteremia caused by community-acquired methicillin-resistant staphylococcus aureus. Infect Chemother. 2013;45:441–5.
3. Roca B, Torres V. Pyomyositis of the iliacus muscle complicated with septic sacroiliitis. QJM. 2008;101:983–4.

4. An S, Li B, Cui R, et al. Unusual complication of multiple splenic abscesses arising from a feeding jejunostomy tube subsequent to total gastrectomy: A case report and literature review. Oncol Lett. 2015;9:2398–400.
5. Lardo S, Ariane A, Chen K. Septic Pulmonary embolism following appendectomy surgery. Acta Med Indones. 2015;47:234–7.
6. Zimmermann B, Mikolich DJ, Lally EV. Septic sacroiliitis. Semin Arthritis Rheum. 1996;26:592–604.
7. Taydas O, Kantarci M, Bayraktutan U, Ogul H. Supradiaphragmatic origin of the renal artery; frequency on contrast-enhanced MR imaging. Clin Imaging. 2018;52:152-6.
8. Ulhaci N, Meteoglu I, Kacar F, Ozbas S. Abscess of the spleen. Pathol Oncol Res. 2004;10:234–6.
9. Lee WS, Choi ST, Kim KK. Splenic abscess: a single institution study and review of the literature. Yonsei Med J. 2011;52:288–92.
10. Luaces Mendez M, Vilacosta I, Sarria C, et al. Hepatosplenic and renal embolisms in infective endocarditis. Rev Esp Cardiol. 2004;57:1188–96.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):772-773.
DOI: 10.28982/josam.560112

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

Extraovarian granulosa cell tumor: A case report

Ekstraovaryen granulosa hücreli tümör: Olgu sunumu

Abdelouhab El Marouni [1], Karam Aziz [1], Imane Toughrai [1], Khalid Mazaz [1], Karim Ibn Majdoub Hassani [1]

[1] Visceral Surgery Service, Hassan II University Hospital, Faculty of Medicine and Pharmacy of Fez, sidi Mohamed Ben Abdullah University, Fez, Morocco

ORCID ID of the author(s)

AE: 0000-0003-2035-7982
KA: 0000-0002-3330-7311
IT: 0000-0003-0401-3012
KM: 0000-0001-7779-7802
KIMH: 0000-0002-0421-7296

Abstract

Granulosa cell tumor (GCT) of the ovary is a rare tumor representing 2 to 5% of all ovarian neoplasms. It can reproduce or metastasize several years after the initial treatment. In rare cases, CGT can develop on an extra-ovarian site, which is thought to originate from ectopic gonadal tissue along the embryonic genital ridge. We herein present a case of extraovarian granulosa tumor, the clinical and therapeutic aspects, and our approach.

Keywords: Extraovarian, Granulosa cell tumor, Histological diagnosis

Öz

Overin granuloza hücreli tümörü (GCT), tüm over neoplazmalarının %2-5'ini oluşturan nadir bir tümördür. Tedaviden birkaç yıl sonra yeniden ortaya çıkabilir veya metastaz yapabilir. Sık olmamakla birlikte, embriyonik genital katlantı üzerindeki ektopik gonadal dokudan köken alarak, ekstra-overyen bir bölgede de görülebilir. Burada bir ekstraovaryen granüloza tümörünü, klinik, terapötik yönleri ve kendi yaklaşımımızla birlikte sunuyoruz.

Anahtar kelimeler: Ekstraovaryan, Granulosa hücreli tümör, Histolojik tanı

Introduction

Tumors of adult granulosa cells are considered as sexual tumors of the cord and ovary [2]. There is considerable debate about the cellular origin of these tumors. In the literature, several cases of extraovarian tumors with granular cells have been reported [3].

Corresponding author / Sorumlu yazar:
Abdelouhab El Marouni
Address / Adres: Visceral Surgery Service, Hassan II University Hospital, Faculty of Medicine and Pharmacy of Fez, sidi Mohamed Ben Abdullah University, Fez, Morocco
e-Mail: elmarouniabdelouhab@hotmail.fr

Informed Consent: The authors stated that the written consent was obtained from the patient presented with images in the study.
Hasta Onamı: Yazar çalışmada görüntüleri 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.

Published: 10/18/2019
Yayın Tarihi: 18.10.2019

How to cite / Atıf için: El Marouni A, Aziz K, Toughrai I, Mazaz K, Hassani KIM. Extraovarian granulosa cell tumor: A case report. J Surg Med. 2019;3(10):772-773.

Case presentation

A 66-year-old female patient with no significant pathological history presented with severe abdominal pain. Physical examination revealed the presence of a large mass at the left flank. An abdominopelvic scan showed the presence of two large ganglionic clusters measured respectively at 13 and 11 cm, the first one extending from the subcarinal region to the renal hilum, and the second one extending along the left psoas muscle (Figure 1). Histopathological examination of the biopsy (confirmed by immunohistochemistry) revealed adult granulosa cell tumor characteristics (Figure 2). Patient was diagnosed with extra-ovarian GCT, and therapeutic strategy was based on chemotherapy.

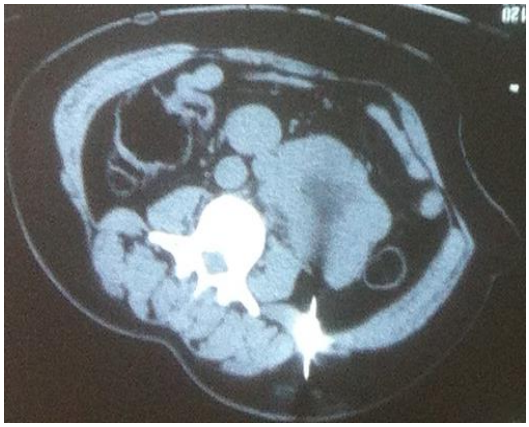

Figure 1: CT image shows the location of the granular tumor

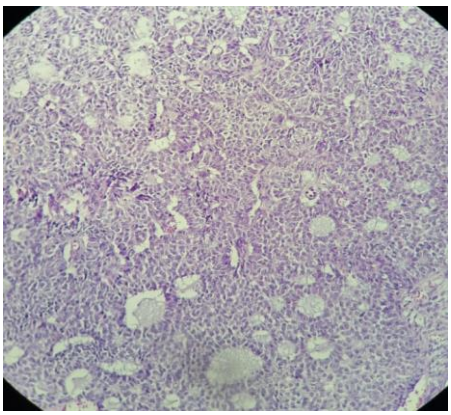

Figure 2: Microscopic image shows the histological appearance of the extraovarian granulosa tumor

Discussion

An uncommon ovarian cancer [1], adult and juvenile type GCTs exhibit different clinical and histological features. The more common adult type of GCT usually presents during the perimenopausal or the early menopausal period, the median age of diagnosis being 50-54 years [1]. GCT patients require long-term follow-ups with proper history-taking, physical examination, and tumor marker studies because 17% of relapses occur more than 10 years after diagnosis [3]. The most common site of recurrence is the pelvis. Rarely, extraovarian GCT can develop. Eight such cases have so far been reported in the English literature until 2001 [3], one of which was from India [5]. The tumors of four cases originated from the broad ligament, three from the retroperitoneum and one from the adrenal gland [3]. Recently, one case of GCT arising in a Müllerian cyst of the broad ligament has been reported [6].

The histogenetic origin of extraovarian sex-cord stromal tumors is considered as the ectopic gonadal stromal tissue, with the sex-cord originating from the mesonephros. A dual origin theory from both coelomic epithelium and mesonephros has also been proposed [7]. Mesonephros or its influence seems necessary for creating the sex-cord. This may explain why the sites of extraovarian sex-cord stromal tumors being limited to the broad ligament, the retroperitoneum, and the adrenal gland, all of which differentiate close to the mesonephros and the mesonephric duct [7]. The morphological differential diagnosis of GCT includes undifferentiated carcinoma, small cell carcinoma and endometrial stromal sarcoma [1]. However, characteristic histological findings and immunostaining are helpful in definitive diagnosis.

Several tumor markers are used for confirmation of histologic diagnosis of GCT, an important one being inhibin. The ovary is the only source of inhibin in non-pregnant woman whereas in pregnancy, it is also secreted from the placenta. It is reportedly a more reliable marker for GCT than estradiol. Although an elevated inhibin level may be observed in some epithelial ovarian cancers, confirmation is based on EMA positivity, which is negative in GCT [10].

Our patient presented with two separate intraabdominal ganglionic clusters, which is unusual for a primary tumor. GCT can recur or metastasize years after initial diagnosis and treatment, hence the strong possibility of metastatic deposit in intraabdominal sites. As slides of the excised ovaries were not available for thorough review, the possibility of late metastasis of a low-grade GCT could not be evaluated, and the diagnosis of extraovarian GCT was deemed most appropriate.

Conclusion

Tumors of adult granulosa cells are considered sexual tumors of the cord and ovary, which poses a diagnostic problem. A diagnosis of an extraovarian GCT can be made by excluding any history of ovarian GCT.

References

1. Schumer ST, Cannistra SA. Granulosa cell tumour of the ovary. J Clin Oncol. 2003;21:1180-9.
2. Serov SF, Scully RE, Sobin LH: International Histological Classification of Tumours, No. 9. Histological Typing of Ovarian Tumors. Geneva, World Health Organization, 1973
3. Kim SH, Park HJ, Linton JA, Shin DH, Yang WI, Chung WY, et al. Extraovarian granulosa cell tumour. Yonsei Med J. 2001;42:360-3.
4. Cronjı HS, Niemand I, Bam RH, Woodruff JD. Review of the ¬granulosa-theca cell tumors from the emil Novak ovarian tumor registry. Am J Obstet Gynecol. 1999;180:323-7.
5. Reddy DB, Rao DB, Sarojini JS. Extraovarian granulosa cell tumour. J Indian Med Assoc. 1963;41:254-7.
6. Sakai Y. Granulosa cell tumor arising in the wall of müllerian cyst of the broad ligament: Report of a case and immunohistochemical study. Arch Gynecol Obstet. 2007;275:145-8.
7. Motta PM, Makabe S. Germ cells in the ovarian surface during fetal development in humans. J Submicrosc Cytol 1986;18:271-90.
8. Lal A, Bourtsos EP, Nayar R, DeFrias DV. Cytologic features of granulosa cell tumours in fluids and fine needle aspiration specimens. Acta Cytol. 2004;48:315-20.
9. Stenwig JT, Hazekamp JT, Beecham JB. Granulosa cell tumours of the ovary: A clinico-pathological study of 118 cases with long term follow-up. Gynecol Oncol. 1979;7:136-52.
10. Lappǫhn RE, Burger HG, Bouma J, Bangah M, Krans M, de Bruijn HW. Inhibin as a marker for granulosa-cell tumors. N Engl J Med. 1989;321:790-3.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):774-776.
DOI: 10.28982/josam.630593

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

Situs inversus totalis with double superior vena cava: An unusual case report

Sitüs inversüs totalis ve çift superior vena kava: Nadir bir olgu

İsmail Taşkent [1], Gürkan Danışan [1], Ayşe Murat Aydın [2]

[1] Mus State Hospital, Department of Radiology, Mus, Turkey
[2] Firat University, School of Medicine, Department of Radiology, Elazig, Turkey

ORCID ID of the author(s)
İT: 0000-0001-6278-7863
GD: 0000-0003-2052-0006
AMA: 0000-0001-9619-4142

Corresponding author / Sorumlu yazar:
İsmail Taşkent
Address / Adres: Muş Devlet Hastanesi, Muş, Türkiye
e-Mail: dr.taskent@gmail.com

Informed Consent: The authors stated that the written consent was obtained from the patient presented with images in the study.
Hasta Onamı: Yazar çalışmada görüntüleri 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.

Published: 10/23/2019
Yayın Tarihi: 23.10.2019

Abstract
Situs inversus totalis (SIT) with double superior vena cava (SVC) is a rare congenital anomaly. Most cases are diagnosed incidentally after imaging for other reasons. Double SVC is usually asymptomatic, unless associated with other cardiac anomalies. A 22-year-old female patient with the complaints of cough, headache, weakness, and shortness of breath was admitted to the cardiology department. The patient, who was hospitalized with a diagnosis of pulmonary embolism and pulmonary hypertension, had a history of surgical repair of atrial septal defect and ventricular septal defect 7 years ago. Contrast-enhanced multislice computed tomography (CT) of the chest was obtained in our department. CT demonstrated SIT with double SVC, with the right SVC draining into the left atrium. The variations of anomalous venous connections accompanying cardiac anomalies should be fully defined before surgery with a combined imaging approach with echocardiography and CT.
Keywords: Situs Inversus, Superior Vena Cava, Imaging

Öz
Situs inversus totalis (SİT) ve çift superior vena kava (SVK) nadir görülen Konjenital anomalilerdir. Olguların çoğunluğu başka nedenlerle görüntülemede tesadüfen teşhis edilir. Diğer kardiyak anomalilerle birlikte olmadıkça çift SVK genellikle asemptomatiktir. 22 yaşındaki kadın hasta öksürük, baş ağrısı, halsizlik ve nefes darlığı şikayetleri ile kardiyoloji kliniğine başvurdu. 7 yıl önce atriyal septal defekt ve ventriküler septal defekt cerrahi onarım öyküsü olan hasta pulmoner emboli ve pulmoner hipertansiyon tanısı ile hastaneye yatırıldı. Göğüsün kontrastlı çok kesitli bilgisayarlı tomografisi (BT) kliniğimizde çekildi. BT, SİT ile çift SVK'ı gösterdi. Çift SVK'nın sağ SVK'sı sol atriuma drene idi. Kalp anomalilerinin eşlik ettiği anormal venöz bağlantı varyasyonları ekokardiyografi ve BT ile kombine görüntüleme yaklaşımıyla ameliyattan önce tam olarak tanımlanmalıdır.
Anahtar kelimeler: Situs İnversus, Superior Vena Kava, Görüntüleme

Introduction

Situs inversus is a rare congenital anomaly that occurs due to inhibition of visceral rotation during embryonic development, with an incidence of approximately 0.01% worldwide. In situs inversus, all thoracoabdominal and retroperitoneal organs (i.e., kidneys and adrenal glands) are positioned symmetrical to their normal localizations, which is often referred to as a mirror image [1]. When both abdominal and thoracic viscera are affected, it is called situs inversus totalis (SIT) [2]. It can be associated with Kartegener triad (bronchietasis, sinusitis, and situs inversus), cardiac anomalies, genitourinary anomalies, polysplenia syndrome and intestinal rotational disorders [1,3,4].

The most common congenital abnormality of the superior vena cava (SVC) is a double SVC [2,5]. Double SVC with persistence of a left SVC [PLSVC) is rarely encountered. The prevalence in the general population is 0.3% but may reach 1.3-11% in patients with congenital heart diseases [5-8].

In 90% of cases, PLSVC connects to the right atrium via the coronary sinus, but in 8-10% of cases, PLSVC connects to the left atrium causing a right-to-left shunt, and it is in this variant that there is a potential hazard of systemic embolization of thrombus or air. Cyanosis, sepsis, and cerebral abscess may occur [1,5,9,10]. PLSVC draining to the left atrium is associated with many types of congenital heart disease but is rare if the heart is normal [7].

How to cite / Atıf için: Taşkent İ, Danışan G, Aydın AM. Situs inversus totalis with double superior vena cava: An unusual case report. J Surg Med. 2019;3(10):774-776.

Case presentation

A 22-year-old female patient with complaints of cough, headache, weakness, and shortness of breath was admitted to the cardiology department of our hospital. The patient, who was hospitalized with a diagnosis of pulmonary embolism and pulmonary hypertension, had a history of surgical repair of atrial septal defect and ventricular septal defect 7 years ago.

Her heart rate was 80 beats/min and blood pressure was 110/90 mmHg. Body temperature was 37^{o}C and hemoglobin level was 12.4 g/dL. Peripheral capillary oxygen saturation was 91%. The patient had no cyanosis.

Transesophageal echocardiography (ECHO) was performed with a Sonos 5500 using (Hewlett Packard, Inc., Andover, MA, USA) a 5-MHz omniplane probe. ECHO revealed dextrocardia. Residual ventricular septal defect was detected. Systolic pulmonary artery pressure was 83 mm Hg, consistent with pulmonary arterial hypertension.

Contrast-enhanced multislice computed tomography (CT) of the chest was obtained in our department. 64-detector CT (Aquilion, Toshiba Medical Systems, Tokyo, Japan) was used for imaging. 60 ml non-ionic contrast medium (Omnipaque, Amersham Health, Cork, Ireland) was administered via the antecubital vein with an autoinjector. CT demonstrated SIT with double SVC. The Left SVC was draining directly into right atrium, while the right SVC was draining into left atrium (right-to-left shunt) (Figure 1). There was a horizontal communicating vein between upper parts of the SVCs (Figure 2). Pulmonary trunk diameter was measured as 32 mm. Pulmonary embolism wasn't detected.

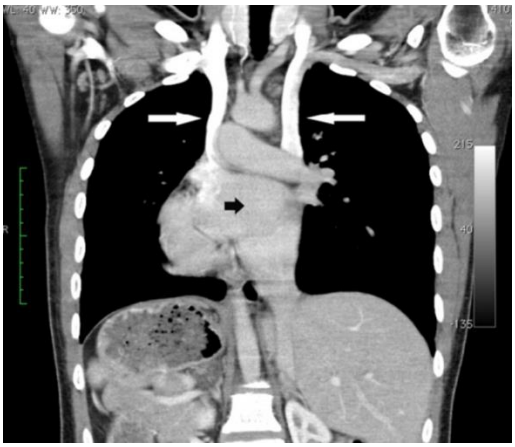

Figure 1: Contrast-enhanced chest computed tomography (CT); mediastinal window (coronal slice). Situs inversus totalis is shown. Apex of the heart is the right hemithorax. The stomach is on the right while the liver of the abdominal organs is seen on the left. Double superior vena cava is observed (white arrows). On the right superior vena cava is opened to the left atrium (black arrow).

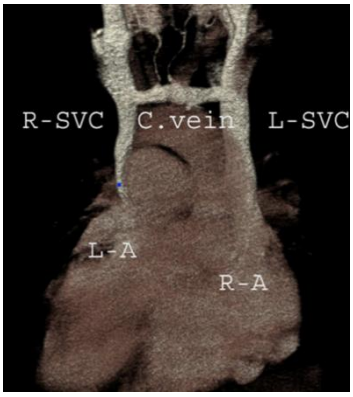

Figure 2: On three-dimensional volume rendering CT image, double superior vena cava is seen. On the right superior vena cava is opened to the left atrium. The horizontal communicating vein between upper parts of the superior vena cava is seen.

The patient was followed up 9 days in the cardiology clinic. Bosentan, sildenafil and iloprost triple combination therapy was administered to the patient for pulmonary hypertension secondary to congenital heart disease. Acetyl-salicylic acid and furosemide were also included in the treatment. The cardiovascular surgeon suggested surgery to treat the congenital abnormality of right SVC, which the patient refused. The patient was discharged with medical therapy and recommendations. The patient was later lost to follow-up.

Discussion

SIT is an unusual entity, first reported by Fabricius in 1600. SIT is usually incidentally detected on radiological images obtained due to another medical condition and does not threaten life [1,3,4].

The double superior vena cava with PLSVC is a disorder in the regression of the left anterior cardinal vein during the first weeks of embryological development [5-7]. In adults, the absence of right superior vena cava with PLSVC is rare and most patients with PLSVC have both right and left-sided SVC [10].

The presence of double SVC may be alone or concurrent with anomalies like double coronary sinus, absence of left brachiocephalic vein, atrial septal defect, common atrium, univentricular heart, transposition of large vessels, dextrocardia, conductive tissue abnormalities and horseshoe kidney [9]. Although it is a benign condition, PLSVC has important clinical implications. It may be associated with a variety of congenital malformations of the heart and great vessels, and it may technically complicate some endovascular and surgical procedures [11]. CT is a useful technique to investigate additional anomalies of SVC. Magnetic resonance imaging and venographic techniques can complement CT [5,6]. ECHO may be useful [2,5].

PLSVC rarely connects to the left atrium causing a right-to-left shunt responsible for cyanosis and heart failure. There was no evidence of cyanosis or systemic arterial desaturation in our patient.

PLSVC draining to the left atrium can result in a significant intracardiac shunt. Various surgical procedures have been reported to correct this anomaly. Some of these may include intra-atrial redirection of flow from the left SVC to the right atrium, and re-implantation of the left SVC into the right atrium, pulmonary artery, or SVC. If the LSVC is connected to the right SVC by a left innominate vein of adequate size, simple ligation is feasible. Polytetrafluoroethylene graft is a successfully used method for connecting SVCs [10,12].

The variations of anomalous venous connections accompanying cardiac anomalies such as ASD should be fully defined before surgery, preferably with a combined imaging approach with ECHO and CT.

Double SVC is usually asymptomatic unless it is associated with other cardiac anomalies. Therefore, it is diagnosed incidentally in surgery or autopsy [2]. The most commonly associated cardiac abnormality is ASD. Others include tetralogy of Fallot, coarctation of the aorta, pulmonary stenosis, interventricular septal defect [5].

Double SVC may cause enlarged mediastinum on chest radiography and the definitive diagnosis is made by CT. However, if chest CT scans are evaluated without proper attention, double SVC can be missed [2,5]. Unexpected double SVC may give rise to difficulties in venous catheterization, pacemaker insertion, radiofrequency ablation, coronary artery bypass graft, during cardiopulmonary bypass or surgery of the congenital heart diseases [2,6,9].

Although our case is a good example for showing these two anomalies together, the patient's refusal to accept the operation is a limiting factor in presenting the post-operative findings and clinical progress.

Conclusion

Situs inversus totalis with a double SVC is a rare congenital anomaly. Double SVC is benign condition unless it is associated with other cardiac anomalies. If double SVC with PLSVC draining to left atrium is detected, further cardiac evaluation with imaging methods becomes is necessary.

References

1. Sun XY, Qin K, Dong JH, Li HB, Lan LG, Huang Y, et al. Liver Transplantation Using a Graft from a Donor with Situs Inversus Totalis: A Case Report and Review of the Literature. Case Rep Transplant. 2013;2013:532865.
2. Argüder E, Köksal A, Gümüş B, Celenk MK. A case with double vena cava superior discovered during the investigating of persistent cough. Tuberk Toraks. 2012;60:199-200.
3. Arya SV, Das A, Singh S, Kalwaniya DS, Sharma A, Thukral BB. Technical difficulties and its remedies in laparoscopic cholecystectomy in situs inversus totalis: A rare case report. Int J Surg Case Rep. 2013;4:727-30.
4. Vijayakumar V, Kandappan G, Udayakumar P, Padmanabhan R. What is normal in an abnormality? Central venous cannulation in a patient with Situs inversus totalis with dextrocardia and polyCystic kidney disease. Indian J Crit Care Med. 2013;17:262-3.
5. Burney K, Young H, Barnard SA, McCoubrie P, Darby M. CT appearances of congential and acquired abnormalities of the superior vena cava. Clin Radiol. 2007;62:837-42.
6. Albay S, Cankal F, Kocabiyik N, Yalcin B, Ozan H. Double superior vena cava. Morphologie. 2006;90:39-42.
7. Demos TC, Posniak HV, Pierce KL, Olson MC, Muscato M. Venous anomalies of the thorax. Am J Roentgenol. 2004;182:1139-50.
8. Günay E, Halıcı B, Okur N, Aldemir M, Ünlü M. The coexistence of persistant left superior vena cava with a left intrathoracic subclavian artery aneurysm. Türk Göğüs Kalp Damar Cerrahisi Dergisi. 2013;21:843-4.
9. Cooper CJ, Gerges AS, Anekwe E, Hernandez GT. Double superior vena cava on fistulogram: A case report and discussion. Am J Case Rep. 2013;14:395-7.
10. Demirkan B, Gungor O, Turkvatan A, Guray Y, Guray U. Images of persistent left superior vena cava draining directly into left atrium and secundum-type atrial septal defect. J Cardiovasc Comput Tomogr. 2010;4:70-2.
11. Dogan E, Dogan MM, Gul S, Cullu N. Left persistent superior vena cava with large coronary sinus: A case report. J Surg Med. 2019;3(2):194-6.
12. Ugaki S, Kasahara S, Fujii Y, Sano S. Anatomical repair of a persistent left superior vena cava into the left atrium. Interact Cardiovasc Thorac Surg. 2010;11:199-201.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):777-781.
DOI: 10.28982/josam.635128

Case report
Olgu sunumu

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

Neuroacanthocytosis in a case presenting to emergency department with acute respiratory failure and loss of consciousness: A case report

Acil servise akut solunum yetmezliği ve bilinç kaybı ile başvuran bir olguda nöroakantositoz: Bir olgu sunumu

Muzaffer Gencer [1]

[1] **Department of Anesthesia, Istinye University Medical Faculty, Istanbul, Turkey**

ORCID ID of the author(s)
MG: 0000-0002-3324-5106

Abstract

The diagnosis of neuroacanthocytosis (NA) is made by the presence of acanthocytes via peripheral smear and by the accompanying clinical picture. Laboratory tests for diagnosis include blood smears to detect acanthocytosis, creatine kinase, genetic analysis and / or chorein level examination with western blot technique. This paper describes the case of a 34 year-old male patient who presented to the emergency department with acute respiratory failure and loss of consciousness. He was intubated and received mechanical ventilatory support after admission to the intensive care unit, and was diagnosed with Chorea akanthozytose (ChAc). We aim to emphasize the need to consider NA among the differential diagnoses for patients presenting with complex clinic such as acute respiratory failure and altered consciousness.

Keywords: Acute respiratory failure, Axonal neuropathy, Chorea akanthozytose, Intensive care unit, Neuroacanthocytosis

Öz

Nöroakantositoz (NA) tanısı, periferik yayma yoluyla akantositlerin varlığı ve beraberindeki klinik tablo ile yapılır. Teşhis için laboratuvar testler; akantosit tespit etmek için kan smear yapılması, kreatin kinaz, genetik analiz ve/veya western blot tekniği ile koreine düzey muayenesidir. Bu yazıda acil servise akut solunum yetmezliği ve bilinç kaybı şikayeti ile başvuran 34 yaşında bir erkek hasta sunulmuştur. Yoğun bakım ünitesine alındıktan sonra entübe edildi ve mekanik ventilatör desteği aldı ve Chorea akanthozytose (ChAc) tanısı aldı. Akut solunum yetmezliği ve bilinçte bozulma gibi karmaşık bir klinik ile başvuran hastalarda ayırıcı tanılar arasında NA düşünülmesinin gerekliliğini vurgulamayı hedefliyoruz.

Anahtar kelimeler: Akut solunum yetmezliği, Aksonal nöropati, Kore akantositozis, Yoğun bakım ünitesi, Nöroakantositozis

Corresponding author / Sorumlu yazar:
Muzaffer Gencer
Address / Adres: İstinye Üniversitesi Tıp Fakültesi, Anestezi Anabilim Dalı, İstanbul, Türkiye
e-Mail: dr.m.gencer07@gmail.com

Informed Consent: The authors stated that the written consent was obtained from the patient presented with images in the study.
Hasta Onamı: Yazar çalışmada görüntüleri 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.

Published: 10/26/2019
Yayın Tarihi: 26.10.2019

Introduction

The term "acanthocyte" describes the spiculated appearance of red blood cells [1]. Acanthocytosis is a condition in which more than 3% of all red blood cells in the peripheral smear are defined as acanthocytes [2]. Neuroacanthocytosis (NA) refers to a genetically heterogeneous group of diseases characterized by neurological signs and symptoms that are accompanied by spiculated red blood cells in the peripheral smear. Neurological signs of these diseases include choreiform movements at the end of the extremities, dysarthria, dysphagia, muscle atrophy, hypoactive deep tendon reflexes, and epilepsy. During the advanced stages of NA, patients may experience dementia, marked distal muscle atrophy and weakness, movement disorders (e.g., dystonia, orofacial dyskinesia, tics and ataxia), cognitive impairment and personality changes, axonal neuropathy, epilepsy, and possibly Parkinsonism [3,4]. NA syndromes can be divided into 2 groups as autosomal recessive Chorea akanthozytose (ChAc) and McLeod Syndrome (MLS) with X chromosomal transition. The first group includes ChAc syndromes that manifest with neurodegeneration and involve a genetic defect in their etiology. In ChAc, there is a mutation in the VPS13A gene found in 9q21 and a defect in the protein called chorein.

How to cite / Atıf için: Gencer M. Neuroacanthocytosis in a case presenting to emergency department with acute respiratory failure and loss of consciousness: A case report. J Surg Med. 2019;3(10):777-781.

These syndromes present with basal ganglia involvement, movement disorders, orofacial dyskinesia and common choreiform movements in the extremities, cognitive impairment, and psychiatric symptoms. In MLS, the XK gene in the Xp21 is affected. This group manifests with lipoprotein metabolism disorders. Dorsal column degeneration and polyneuropathy are the prominent features in the clinical picture [5]. Each of the two major types of NA described above has its own etiology. Although they generally have autosomal recessive inheritance, autosomal dominant and X-linked recessive inheritance have also been described. Sporadic cases have also been reported [6,7]. Although ChAc syndromes usually start in the third to fourth decades of life, patients with MLS are older persons. These syndromes are progressive and degenerative diseases in which the age of onset, clinical and laboratory findings, family history, neurological and systemic involvement, and treatment vary according to the subtypes [8]. The time during which acanthocytes are observed in peripheral smear may vary from patient to patient. Generally, acanthocytes may be observed at the initial stages of the disease; however, in some patients, they may only show up in the late stages [9]. The most important criterion for the diagnosis of NA is the detection of acanthocytes in peripheral blood smear; however, the presence of acanthocytes is not meaningful on its own, and should certainly be supported with clinical findings. Despite the significance of acanthocytes in the peripheral smear, because they may be observed only in the late stages of the disease, the absence of acanthocytes in peripheral blood should not exclude the diagnosis, and the peripheral smear should be re-evaluated after diluting with saline. Normal controls show less than 6 % acanthocytic red blood cells of their total erythrocytes. Indeed, the observation of acanthocytes in the early stage aids in the diagnosis [1]. Genetic analysis and / or chorein level examination with western blotting can be used as further investigations. Currently, the treatment of NA syndromes is entirely symptomatic. Some drugs that are used in their treatment include anticholinergics, antipsychotics, antiepileptics, and acetylcholine release inhibitors; in addition, lithium treatment and pallidotomy are also used. Additional beneficial treatment approaches include botulinum toxin injection, dietary supplementation, and assistive walking devices [8]. Recent studies report that deep brain stimulation and deep brain bilateral pallidal stimulation can provide favorable results, especially at the end of the first month [10,11].

This paper presents the case of a 34 year-old male patient who presented to the emergency department with loss of consciousness and acute respiratory failure. After his initial evaluation, he was intubated due to inadequacy of spontaneous respiration, and he received mechanical ventilatory support after admission to the intensive care unit. He was diagnosed with ChAc, and his general condition improved after approximately 15 days of intensive care and treatment.

Case presentation

A 34-year-old male patient was brought to the emergency department due to acute respiratory failure and loss of muscle strength (especially prominent at the lower extremities), which was followed by loss of consciousness. The patient was sent to us for consult. He had stupor at his initial examination, and according to the Glasgow coma scale, he had eye opening in response to painful stimuli, his verbal response was incomprehensible sounds, and his motor response was not localized to painful stimuli. His pupils were isochoric, and he had both direct and indirect light reflexes. His spontaneous respiration was insufficient, and arterial blood gas analysis indicated respiratory acidosis and severe hypercapnia. He was hemodynamically normotensive and had normal heart rhythm. Due to the risk of respiratory arrest, the patient was immediately intubated and received mechanical ventilatory support with bilevel mode following admission to the intensive care unit. According to the statement given by his spouse, he had been followed up with in a military hospital for 2 months approximately 10 years ago due to a rapidly developing acute respiratory failure. At that time, he was given an initial diagnosis of autonomic neuropathy, and sural nerve biopsy revealed findings suggestive of Guillain-Barre syndrome. During that same period, the patient was being seen in a psychiatry clinic due to the diagnosis of bipolar affective disorder, for which he was taking olanzapine and lithium. Regarding the current episode, the patient had complained of difficulty in standing and walking due to weakness at his lower extremities, which began one week ago and choreiform movements at the end of the extremities. His loss of strength was then accompanied by respiratory difficulty, and he was brought to the emergency department after he developed a state of altered consciousness. His deep tendon reflexes were normoactive at the upper extremities, but deep tendon reflexes could not be obtained at the lower extremities. He had hammer toe deformity in both big toes, and pes cavus deformity of his feet. He also had widespread muscle atrophy, which was particularly prominent in the gluteal muscles and the quadriceps femoris muscles in the lower extremities. His laboratory tests revealed mild leukocytosis and a mild elevation of creatinine kinase. Vitamin B12 level was within normal limits, and Lipoprotein electrophoresis evaluated as normal. Due to his altered consciousness and acute respiratory failure, we first considered whether he had a cerebrovascular accident, drug intoxication, or a new attack of Guillain-Barré syndrome. Cranial magnetic resonance imaging (MRI) revealed normal results, while lumbar MRI did not show any compression to the spinal canal or the nerve roots. His clinical and laboratory findings were not suggestive of drug intoxication. A lumbar puncture was performed; biochemical analysis of the cerebrospinal fluid revealed normal results and did not yield any findings that could be associated with Guillain-Barré syndrome. Electromyography examination results were consistent with sensorimotor axonal polyneuropathy predominant in the lower extremities. His family history did not include any features. Although we primarily interpreted his initial results as a sequel sign to axonal type Guillain-Barré syndrome, which he had experienced in severe form in the past, we realized that the presence of hammer toe and pes cavus deformities could also indicate a hereditary form of neuropathy. The patient was monitored in the intensive care unit with mechanical ventilatory support, and symptomatic treatment was continued. Since the patient had a history of ataxia, orofacial dyskinesia, and parkinsonism symptoms accompanied by dysarthria and polyneuropathy, and because he had had cognitive

and psychiatric diagnoses in the past, NA was suspected in the differential diagnosis; therefore, a peripheral blood smear was performed. The peripheral smear revealed acanthocytes at a ratio greater than 20%, and the patient was diagnosed with NA. Since Genetic testing for VPS13A mutations was unavailable, protein analysis was performed Western blotting technique from tissue samples. The diagnosis which ChAc was confirmed by detection of chorein deficiency with the help of the free chorein Western blot technique. The polyneuropathy present in the patient was thought to be associated with ChAc (Figure 1).

In addition to his symptomatic treatment, the patient was given 1 g/day methylprednisolone pulse therapy for 10 days while he was being monitored with mechanical ventilatory support. During this time, his level of hypercapnia regressed, his consciousness returned to normal, and he was extubated as his spontaneous respiration became sufficient. The patient then underwent respiratory physiotherapy, muscle strengthening, and walking and balance exercises. At the end of the treatment period, his muscle strength increased, his overall condition returned to normal, and he was able to walk without any support. He had a normal state of consciousness and showed complete orientation and cooperation. His speech was dysarthric and his apprehension was normal. His eyes were at midline, and his eye movements were free in all directions. The patient's Rankin scale score increased to 2. The patient was referred to the neurology-psychiatry department in his present clinical condition.

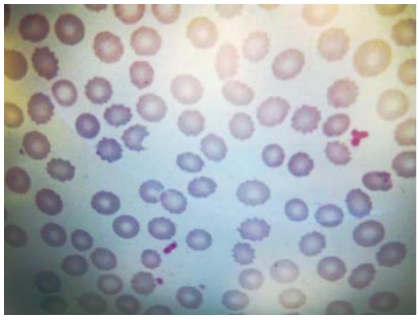

Figure 1: Acanthocytes observed in the peripheral blood smear of the patient

Discussion

NA Syndromes are composed of different diseases where nervous system abnormalities are seen together with red blood cell acanthocytosis [12]. NA is a neurodegenerative disease and the patients show some psychiatric signs, chorea, dementia as well as acanthocytes. In cranial MRI caudate nucleus atrophy may be present [13]. And patients mainly suffer because of the basal ganglia degeneration.

Presence of acanthocytosis on peripheral blood smear can vary, and they are not necessary to confirm the diagnosis. ChAc is an autosomal recessive, and MLS is an X-linked inherited NA syndrome. They share some similarities such as psychiatric symptoms, chorea, dystonia, myopathy, seizures, and peripheral neuropathy [5,14]. There are some additional sporadic conditions associated as well. For example, there has been a report of a NA case developing cerebellar atrophy [15].

Genes mutated in patients with MLS, ChAc, and Huntington's disease-like 2 have been identified. The mutations, the proteins and associated pathophysiological process have been identified [14,16], but the pathophysiology of the related red blood-cell anomalies is not yet clarified. There are studies focusing on the association between the integral membrane protein and the cytoskeleton [17]. Described herein is the case of a 34-year-old male patient. According to his history, symptoms of his disease were present at least 10 years prior to his current episode. This leads one to question whether the symptoms of NA begin when the patient is much younger, even though the diagnosis is typically made at later ages. Although there are reports of NA cases diagnosed in their first and seventh decades, the average age of onset for NA is 35 years [18]. A recent study from China including 66 cases reported that the age of onset of disease symptoms varied between 5 and 74 years [19].

NA disorders are extremely rare, and this rarity may be due to underdiagnosis. Thousands of ChAc and a few hundred MLS cases are thought to be present throughout the world. MLS are reported from Americas, Europe, and Japan and there seems to be no geographical selection [5]. ChAc seems to be common in Japan, and this may be related to some genetic predisposition [20], also some cases are present in geographically isolated communities of the French-Canadian population [21].

Psychiatric symptoms such as anxiety, depression, paranoid delusions, apathy, compulsive disorder (such as impulsivity), emotional lability, and cognitive disturbances are commonly observed in NA [18]. The case described herein was diagnosed with bipolar affective disorder, for which he was receiving treatment. NA is a rare, heterogeneous group of neurodegenerative diseases that can manifest diverse neurological signs. It has been reported that the possibility of developing dystonia and Parkinsonism are more likely than the possibility of developing chorea if the disease begins at an early age. Orofacial dyskinesia, dysarthria, and dysphagia can be observed in NA patients. These patients may also bite their own tongue and lip during eating due to orolingual dystonia (known as "eating dystonia") [13]. Our case had eating dystonia and tongue protrusion during the initial period after extubation; therefore, during that time, he was fed formula through a nasogastric tube. Oral intake was initiated later. Dementia is observed in approximately 50% of cases with NA. It is common for patients with the diagnosis of ChAc to have generalized type epileptic seizures [13]. Our patient had history of seizure. In a recent study including 66 cases [24]. accompanying findings are reported as hyperkinetic movements (88%), dyskinesia in orofacial region (80%), dystonia (67%), dysarthria (68%), caudate atrophy or enlarged lateral ventricles on neuroimaging (64%), and elevation in creatine kinase level (52%). Specific genetic tests or western blotting can use in confirmed the diagnosis as ChAc or MLS.

Studies show that myopathy and axonal type polyneuropathy are often found during electrophysiological examinations of patients with neuropathy. Histological examinations of these patients often reveal the involvement of generally large-diameter myelinated fibers and the presence of chronic axonal neuropathy [22]. In the electrophysiological examination of our current case, his sensory potential could not be obtained, and his motor potentials had significantly reduced amplitudes at the lower extremities. These findings are consistent with widespread, symmetrical, and sensorimotor axonal type polyneuropathy. NA syndromes are categorized as hereditary neuropathies that are associated with central nervous system

involvement, and nearly half of these patients have neuropathy [22]. Our current patient did not have deep tendon reflexes, and he had a loss of muscle strength at the lower extremities. NA patients may have elevated levels of creatinine kinase (CK) and may also suffer from amyotrophy. Elevated serum CK levels can also be observed without myopathy, especially in the ChAc and MLS subtypes, in which CK levels are usually between 300-3000 (U/L) [5]. The serum CK level of our current case was 920 (U/L). In NA, radiological imaging findings are not specific to the disease. For example, computed brain tomography, brain MRI, positron emission tomography (PET), and single-photon emission computed tomography can all be used as radiological examination methods. In patients with NA, brain MRI may reveal atrophy in the caudate and lentiform nuclei, as well as hyperintensity at the lateral putamina area in T2 sequence. Some cases may also show diffuse changes in white matter. In Figure 2 cranial MRI of several patients with NA are seen. In patients with NA, computed brain tomography can demonstrate caudate atrophy and ventricular enlargement, which is especially prominent in the anterior horns of the lateral ventricles. PET may show hypometabolic areas in the neostriatum and in the frontal cerebral cortical regions. Additionally, patients with NA often have reduced norepinephrine levels in the putamen and globus pallidus. Similar to findings in patients with Parkinson's disease, PET scans of patients with NA show a 42% reduction in DOPA re-uptake in the posterior putamen. Using single photon emission computed tomography (SPECT), the hypometabolic areas may be observed as areas of hypoperfusion [18,23]. Further, there have also been reports of cases with cerebellar atrophy [15]. Our current case only underwent brain MRI, the results of which were reported as normal. Autopsy examinations of NA cases demonstrate neuronal loss and gliosis in the caudate, putamen, globus pallidus, and substantia nigra, while the cerebral cortex is preserved. Apart from the basal ganglia, neuronal loss may also be profound in the thalamus and in the anterior horn of the spinal cord. As in Parkinson’s disease, in NA, neuronal loss in the substantia nigra is most profound in the ventrolateral region; however, nigral neuronal loss is more diffuse in neurodegenerative NA syndromes [24].

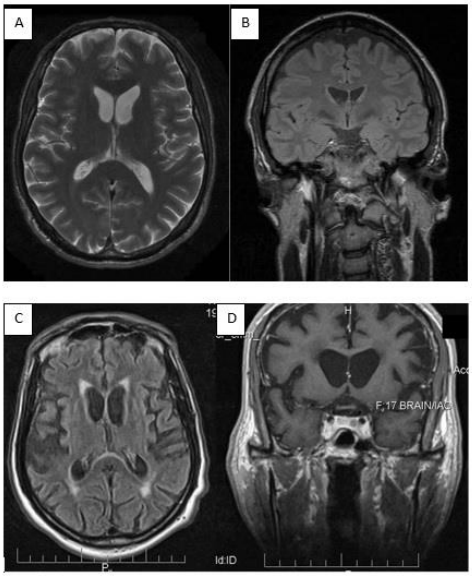

Figure 2: Cranial MRI images of Neuroacanthocytosis. Axial T2-weighted images demonstrate moderate atrophy of caudate nucleus and putamen (A).Coronal FLAIR-T1-weighted images demonstrate moderate atrophy of the caudate nucleus (B). Axial FLAIR- (C) and coronal T1-weighted images (D) demonstrate atrophy of the caudate nucleus and the fronto-temporal cortex. In addition, FLAIR images show periventricular white matter hyperintensities (courtesy of Nora Chan, MD, UCLA, Los Angeles, USA).

Diagnosis of NA is made using a combination of clinical properties, appropriate family history, and detection of acanthocytes in the peripheral blood smear and protein analysis the help of western blotting technique and/ or with genetic testes [24]. For neurodegenerative NA syndromes, demonstration of acanthocytes in the peripheral blood smear is the most important diagnostic criterion; nevertheless, clinical findings should not be underrated [25]. The percentage of acanthocytes in the blood smear of patients with NA varies between 5-50%; however, the ratio of acanthocytes does not reflect disease intensity. In our current case, we performed a peripheral blood smear upon the suspicion of NA due to the presence of suggestive clinical signs and symptoms, which revealed the presence of acanthocytes at a ratio of 20%, confirming the diagnosis of NA. Since acanthocytes may be present at various stages of the disease, it is not always possible to detect them, even though there may be clinical findings pointing towards the diagnosis of NA. In such conditions, it is recommended that the peripheral smear be repeated or re-evaluated after diluting with saline in a 1:1 ratio. Repeating the peripheral smear with a thinner layer of blood may increase the possibility of diagnosis [26]. The diagnosis was confirmed with western blotting from tissue samples as chorea ChAc.

The symptoms of NA syndromes may vary among patients, which causes misdiagnoses. In some, the disease starts with dominant psychiatric features like schizophrenia, obsessive-compulsive disorder, depression, cognitive impairment, tics, and Tourette's syndrome. In others neurological and muscular symptoms are dominant such as parkinsonism, chorea, epileptic seizures, dystonia, peripheral neuropathy, myopathy, or cardiomyopathy.

Although there have been several reports of NA cases in the literature in which neurological and psychiatric symptoms predominate the clinical condition, to our knowledge, ours is the first reported case of NA presenting to the emergency department with such severe clinical conditions as acute respiratory failure and altered conscious state. Therefore, we believe our case is significant for the literature. Moreover, it is also interesting that our case demonstrated almost all the clinical manifestations described within the context of ChAc. Our patient's presentation with acute respiratory failure suggested that his respiratory muscles were affected by his neuropathy. Our patient most likely received benefit from steroid treatment because steroids have known effectiveness in the treatment of neuropathy. It is clear that a successful emergent approach, early diagnosis, and appropriate treatment of the disease in a case presenting with such a severe condition are of vital significance. Failure to meet these requirements may lead to unwanted outcomes such as a requirement for long-term mechanical ventilation and hypoxic encephalopathy. Further, it is even possible that the clinical condition may become as dramatic as to cause the death of the patient.

Conclusion

Various presentations are known for these syndromes and, it should be noted that NA may manifest with a very severe unexpected presentation, as in our case. Therefore, we believe it is necessary to consider NA among the differential diagnoses in patients presenting with a complex clinical picture, including

acute respiratory failure, and altered consciousness. The diagnosis of NA syndromes can be made quite rapidly with the peripheral blood smear, which is an amazingly simple and cost-effective method; a rapid diagnosis leads to a prompt start to treatment. Western blotting for protein analysis and/ or genetic tests for mutations can be performed to confirm the diagnosis and to identify subgroups of NA syndromes.

References

1. Stevenson VL, Hardie RJ. Acanthocytosis and neurological disorders. J Neurol. 2001;248:87-94.
2. Kayahan B, Özdemir F, Bora E. Nöroakantositozis. Turkiye Klinikleri J Med Sci. 2005;25:576-80.
3. Rafalowska J, Drac H, Jamrozik Z. Neuroacanthocytosis. Review of literature and case report. Folia Neuropathol. 1996;34(4):178-83.
4. Lossos A, Dobson-Stone C, Monaco AP, Soffer D, Rahamim E, Newman JP, et al. Early clinical heterogeneity in choreoacanthocytosis. Arch Neurol. 2005;62(4):611-4.
5. Jung HH, Danek A, Walker RH. Neuroacanthocytosis Syndromes. Orphanet Journal of Rare Diseases. 2011;6:68.
6. Rubio JP, Danek A, Stone C, Chalmers R, Wood N, Verellen C, et al. Chorea acanthocytosis: genetic linkage to chromosome 9q21. Am J Hum Genet. 1997;61:899-908.
7. Walker RH, Morgello S, Davidoff-Feldman B, Melnick A, Walsh MJ, Shashidharan P, et al. Autosomal dominant chorea-acanthocytosis with polyglutamine-containing neuronal inclusions. Neurology. 2002 Apr 9;58(7):1031-7.
8. Walker RH, Danek A, Dobson-Stone C. Developments in neuroacanthocytosis: Expanding the spectrum of choreatic syndromes. Mov Disord. 2006;21:1794-805.
9. Sorrentino G, De Renzo A, Miniello S, Nori O, Bonavita V. Late appearance of acanthocytes during the course of choreaacanthocytosis.J Neurol Sci. 1999;163(2):175-8.
10. Di Biase L, Munhoz RP. Deep brain stimulation for the treatment of hyperkinetic movement disorders. Expert Rev Neurother. 2016 Jun 10:1-12.
11. Fernández-Pajarín G, Sesar A, Ares B, Jiménez-Martín I, Blanco-Arias P, Corredera E, et al. Deep brain bilateral pallidal stimulation in chorea-acanthocytosis caused by a homozygous VPS13A mutation. Eur J Neurol. 2016 Jan;23(1):e4-5. doi: 10.1111/ene.12833.
12. Walker RH, Jung HH, Dobson-Stone C, Rampoldi L, Sano A, Tison F, et al. Neurologic phenotypes associated with acanthocytosis. Neurology. 2007;68(2):92-8.
13. Fahn S, Jankovic J. Chorea, Ballism, Athetosis. Phenomenology and Etiology. In: Fahn S, Jankovic J, editors. Principles and Practice of Movement Disorders. London, UK: Churchill Livingstone/Elsevier; 2007. pp. 393–407.
14. Hermann A, Walker RJ. Diagnosis and treatment of chorea. Curr Neurol Neurosci Rep. 2015;15:514. doi: http://dx.doi.org/10.1007/s11910-014-0514-0.
15. Sharma C, Nath K, Acharya M, Kumawat BL, Khandelwal D, Jain D. Cerebellar atrophy in neuroacanthocytosis. BMJ Case Rep. 2014 Jun 6;2014. pii: bcr2014205232. doi: 10.1136/bcr-2014-205232.
16. Hayflick SJ, Westaway SK, Levinson B. Genetic, clinical, and radiographic delineation of Hallervorden-Spatz syndrome. New Engl J Med. 2003;348:33–40.
17. De Franceschi L, Bosman GJ, Mohandas N. Abnormal red cell features associated with hereditary neurodegenerative disorders: the neuroacanthocytosissyndromes. Curr Opin Hematol. 2014 May;21(3):201-9. doi: 10.1097/MOH.0000000000000035.
18. Luca R, Adrian D, Anthony PM. Clinical features and molecular basis of neuroacanthocytosis. J Mol Med. 2002;80:475-9.
19. Liu J, Bader B, Danek A. Neuroacanthocytosis in china: a review of published reports. Tremor Other Hyperkinet Mov (N Y). 2014 Oct 31;4:248. doi: 10.7916/D8Q23XDX.
20. Ueno S, Maruki Y, Nakamura M, Tomemori Y, Kamae K, Tanabe H, et al. The gene encoding a newly discovered protein, chorein, is mutated in chorea-acanthocytosis. Nat Genet. 2001;28(2):121-2.
21. Dobson-Stone C, Velayos-Baeza A, Jansen A, Andermann F, Dubeau F, Robert F. et al. Identification of a VPS13A founder mutation in French Canadian families with choreaacanthocytosis. Neurogenetics 2005, 6(3):151-158.
22. Marson AM, Bucciantini E, Gentile E, Geda C. Neuroacanthocytosis: clinical, radiological, and neurophysiological findings in an Italian family. Neurol Sci. 2003;24:188-9.
23. Storch A, Kornhass M, Schwarz J. Testing for acanthocytosis. A prospective reader-blinded study in movement disorder patients. J Neurol. 2005;252(1):84-90.
24. Jankovic J. Movement Disorders. In Bradley's Neurology in Clinical Practice. Robert B. Daroff, Gerald M. Fenichel, Joseph Jankovic, John C. Mazziotta Eds. 6.th. ed, Philadelphia, Saunders Elsevier Inc. 2012, pp. 1762-801.
25. Özer F, Özben S. Sekonder Parkinsonizm. İçinde Parkinson Hastalığı. Emre M Ed. 1st ed, Ankara, Güneş Tıp Kitabevi 2010, pp. 255-6.
26. Rampoldi L, Danek A, Monoca AP. Clinical features and molecular bases of neuroacanthocytosis. J Mol Med. 2002;80:475-91.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine

J Surg Med. 2019;3(10):782-784.
DOI: 10.28982/josam.635056

Case report
Olgu sunumu

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

Spinal cord intramedullary hemorrhage (hematomyelia) after use of sildenafil: A very rare complication

Çok nadir bir komplikasyon; Sildenafil kullanımı sonrasi gelişen spinal kord intramedüller kanaması (hematomiyeli)

İsmail Taşkent [1], Hanefi Yıldırım [2]

[1] Mus State Hospital, Department of Radiology, Mus, Turkey
[2] Firat University, School of Medicine, Department of Radiology, Elazig, Turkey

ORCID ID of the author(s)
İT: 0000-0001-6278-7863
HY: 0000-0002-6204-6392

Abstract
Sildenafil's complications include intracranial hemorrhage along with others, however, spinal cord intramedullary hemorrhage (Hematomyelia) after using sildenafil has not been previously reported. We herein present the case of a 50-year-old male patient who was referred to the Neurology department with pain and numbness radiating to the left arm after use of sildenafil. He was diagnosed with hematomyelia after various diagnostic tests. Other pathologies that might have caused hematomyelia were ruled out.
Keywords: Intramedullary hemorrhage, Hematomyelia, Cervical cord, Sildenafil

Öz
Sildenafil kullanımının çeşitli komplikasyonlarının yanında intrakranial kanamaya da neden olduğunu gösteren olgular bildirilmiş olmasına rağmen, sildenafil kullanımı sonrası spinal kord intramedüller kanaması (Hematomyelia) henüz bildirilmemiştir. Bu olguda, sildenafil kullandıktan sonra sol kola yayılan ağrı ve uyuşukluk şikayetleri ile nöroloji kliniğine başvuran 50 yaşında erkek hastadan bahsedildi. Görüntüleme yöntemlerinden sonra hematomiyeli tanısı aldı. Sildenafil kullanımı dışında hematomiyeliye neden olabilecek diğer patolojiler ekarte edildi.
Anahtar kelimeler: İntramedüller kanama, Hematomiyeli, Servikal kord, Sildenafil

Introduction

Sildenafil (UK-92,480), an orally active, selective inhibitor of phosphodiesterase type 5 (PDE-5), is a crucial regulator of cyclic guanosine monophosphate (cGMP). Its initial target at manufacturing was the corpus cavernosum in males. It causes muscle relaxation, vasodilatation, and penile erection by increasing cGMP and nitrous oxide (NO) in the smooth muscle of the corpus cavernosum [1]. Side effects include flushing, headache, nasal congestion, and changes in pulmonary blood flow, which shows that the vasodilatory effects are not confined to the corpus cavernosum [2,3]. Despite the lack of evidence confirming the exact cause of bleeding, there is enough data to suggest that sildenafil can cause the atraumatic hematomyelia [4-6]. Spinal cord intramedullary hemorrhage (Hematomyelia) after sildenafil use has not yet been reported. We herein present the case of a 50-year-old male patient who was referred to the Neurology department with pain and numbness radiating to the left arm after use of sildenafil. He was diagnosed with intramedullary hemorrhage of the cervical cord (hematomyelia) after various diagnostic tests.

Corresponding author / Sorumlu yazar:
İsmail Taşkent
Address / Adres: Muş Devlet Hastanesi, Muş, Türkiye
e-Mail: dr.taskent@gmail.com

Informed Consent: The authors stated that the written consent was obtained from the patient presented with images in the study.
Hasta Onamı: Yazar çalışmada görüntüleri 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.

Published: 10/27/2019
Yayın Tarihi: 27.10.2019

How to cite / Atıf için: Taşkent İ, Yıldırım H. Spinal cord intramedullary hemorrhage (hematomyelia) after use of sildenafil: A very rare complication. J Surg Med. 2019;3(10):782-784.

Case presentation

A fifty-year-old male patient was admitted to the Neurology Department with neck pain radiating to the left arm and shoulder and numbness which started 7-8 days ago after using 100 mg sildenafil thrice at short intervals. The physical examination and laboratory tests were normal. Cervical computerized tomography (CT) imaging revealed hyperdense intramedullary hemorrhage at between C2-C6 levels (Figure 1). Cervical magnetic resonance imaging (MRI) was recommended for differential diagnosis, which revealed subacute intramedullary hemorrhage with hyperintense, non-restricted lesions extending between C2-C6 levels in T1, T2 and diffusion-weighted images (Figure 2-3) respectively, which were non-enhancing after administration of intravenous contrast agent (IVCA). Lumbar puncture (LP) was performed for cytological examination, in which there were no significant findings. Contrast-enhanced cranial MRI performed for demyelinating disease showed no pathology, and all markers were negative for vasculitis. Steroid pulse therapy was planned for 7 days. The patient's complaints regressed after medical treatment and the control cervical MRI obtained after ten days showed a decrease in the hemorrhage. He was then discharged with recommendations (Figure 4). Follow-up MR imaging after 4 weeks showed that intramedullary hemorrhage had decreased, and cord swelling had resolved. Dual phase CT imaging did not reveal any vascular anomalies. Consequently, this case was evaluated as a complication of sildenafil use. The patient's complaints had completely resolved after 9 months and follow-up cervical MRI showed a significant decrease in hemorrhagic findings (Figure 5).

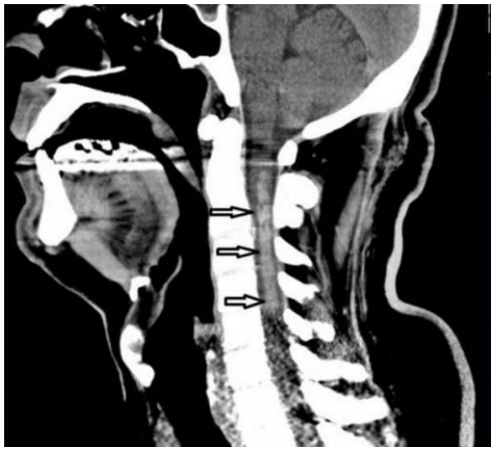

Figure 1: Non contrast enhanced cervical CT (sagittal image) showed hyperdense intramedullary hemorrhage between C2-6 levels (arrows)

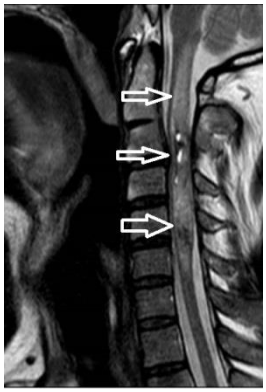

Figure 2: Sagittal T2-weighted magnetic resonance images of the cervical spine demonstrating intramedullary hemorrhage between C2-6 levels with abnormally increased T2 signalling and expansion of the cord (arrows)

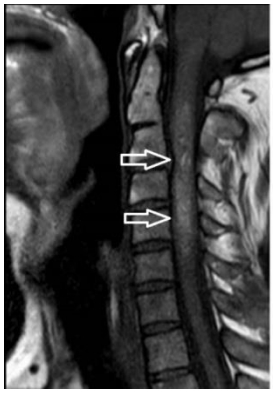

Figure 3: Sagittal T1-weighted magnetic resonance images of the cervical spine demonstrating intramedullary hemorrhage between C2-6 levels with abnormally increased T1 signaling and expansion of the cord (arrows)

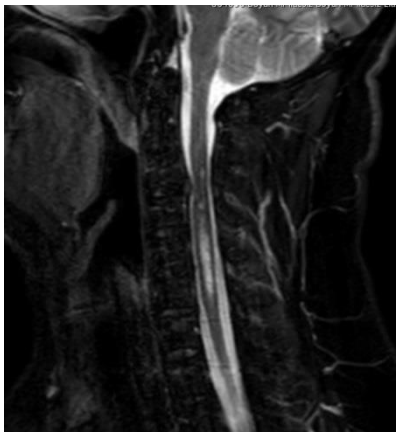

Figure 4: Sagittal magnetic resonance image of the cervical spine showing decreased intramedullary hemorrhage and expansion between C2-6 levels

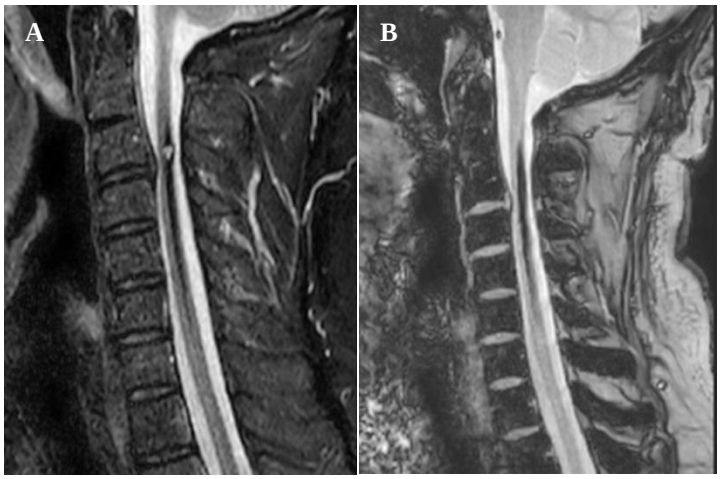

Figure 5: Follow-up magnetic resonance image, A, B: Sagittal STIR and T2-Gradient Echo resonance images of the cervical spine showing hypointense areas due to hemosiderin deposition in the old intramedullary hemorrhage area

Discussion

Intraspinal hemorrhage is much less common than intracranial hemorrhage and may present as epidural, subdural, subarachnoid, or intramedullary bleeding with devastating consequences. Intramedullary hemorrhage, also known as hematomyelia, is the rarest form of intraspinal hemorrhage [7]. Since the first report of spontaneous hematomyelia by Richardson, few other case reports of hematomyelia have been described, most in relation to anticoagulant treatment [8].

Spinal cord hematoma or hematomyelia is an infrequently encountered condition that is the result of several unusual disease processes. The causes of spontaneous, nontraumatic spinal cord hematoma most commonly include vascular malformations of the spinal cord, followed by clotting disorders, inflammatory myelitis, spinal cord tumors, abscess, syringomyelia, and unknown etiologies [9,10].

Sildenafil (UK-92,480), an orally active, selective inhibitor of phosphodiesterase type 5 (PDE-5), is a crucial regulator of cyclic guanosine monophosphate (cGMP) and causes muscle relaxation, vasodilatation, and penile erection by increasing cGMP and nitrous oxide (NO) in the smooth muscle of the corpus cavernosum [1]. This drug also redistributes the arterial flow and decreases perfusion, which may lead to acute myocardial infarction. For the above-mentioned reasons, it lowers systolic blood pressure by 8 to 10 mmHg in clinical trials [11].

The enzyme inhibited by the drug, cyclic guanosine monophosphate-specific phosphodiesterase type 5 (PDE5), is

present at several other sites than the corpus cavernosum. Known side-effects of vascular smooth muscle relaxation caused by sildenafil include headache in 16%, facial flushing in 10%, and hypotension and dizziness in 2% of patients [2]. In-vitro research suggests that sildenafil can also inhibit PDE5-induced platelet aggregation [12].

In this case, we excluded the common causes of atraumatic hematomyelia, including vascular malformations (arteriovenous fistula, cavernoma, capillary telangiectasia, venous angioma), neoplasms, Gowers' intrasyringal hemorrhage, spinal radiation, coagulation and bleeding disorders [13,14], concluding that the hematomyelia of the patient was a complication of multiple sildenafil use in a short period of time.

Sildenafil is a potentially dangerous drug that can provoke life-threatening intracranial and subarachnoid hemorrhage. To the best of our knowledge, this case report presents the first case of hematomyelia after using sildenafil.

References

1. Ballard SA, Gingell CJ, Tang K, Turner LA, Price ME, Naylor AM. Effects of sildenafil on the relaxation of human corpus cavernosum tissue in vitro and on the activities of cyclic nucleotide phosphodiesterase isozymes. J Urol. 1998;159:2164–71.
2. Morales A, Gingell C, Collins M, Wicker PA, Osterloh IH. Clinical safety of oral sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction. Int J Impot Res. 1998;10:69–73.
3. Morgan JC, Alhatou M, Oberlies J, Johnston KC. Transient ischemic attack and stroke associated with sildenafil (Viagra) use. Neurology. 2001;57:1730–1.
4. Alpsan MH, Bebek N, Ciftci FD, Coban O, Bahar S, Tuncay R. Intracerebral hemorrhage associated with sildenafil use: a case report. J Neurol. 2008;255:932–3.
5. Buxton N, Flannery T, Wild D, Bassi S. Sildenafil (Viagra)-induced spontaneous intracerebral haemorrhage. Br J Neurosurg. 2001;15:347–9.
6. Monastero R, Pipia C, Camarda LK, Camarda R. Intracerebral haemorrhage associated with sildenafil citrate. J Neurol. 2001;248:141–2.
7. Irazoque-Palazuelos F, Sosa-Espinosa PV, Andrade-Ortega L. Hematomyelia in systemic lupus erythematosus and secondary antiphospholipid syndrome: case report. Reumatol Clin. 2008;4:34-6.
8. Richardson JC. Spontaneous hematomyelia: a short review and a case report illustrating intramedullary angioma and syphilis of the spinal cord as possible causes. Brain. 1938;61:17-36.
9. Pobiel RS, Schellhas KP, Eklund JA, Golden MJ, Johnson BA, Chopra S, et al. Selective cervical nerve root blockade: prospective study of immediate and longer term complications.AJNR Am J Neuroradiol. 2009;30(3):507-11.
10. Miyakoshi N, Hongo M, Kasukawa Y, Ando S, Shimada Y. Thoracic disk herniation with hematoma-case report. Neurol Med Chir (Tokyo). 2008; 48(9):414-7.
11. Zusman RM, Morales A, Glasser DB, Osterloh IH. Overall cardiovascular profile of sildenafil citrate. Am J Cadiol. 1999;83:35–44.
12. Berkels R, Klotz T, Sticht G, Englemann U, Klaus W. Modulation of human platelet aggregation by the phosphodiesterase type 5 inhibitor sildenafil. J Cardiovasc Pharmacol. 2001;37:413–21.
13. Leep Hunderfund AN, Wijdicks EF. Intramedullary spinal cord hemorrhage (hematomyelia) Rev Neurol Dis. 2009;6:E54–61.
14. Heldner MR, Arnold M, Nedeltchev K, Gralla J, Beck J, Fischer U. Vascular diseases of the spinal cord: a review. Curr Treat Options Neurol. 2012;14:509–20. doi: 10.1007/s11940-012-0190-9.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.

Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine