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Transcutaneous carbon dioxide monitoring during flexible bronchoscopy under sedation: A prospective observational study

Sedasyon eşliğinde fleksibl bronkoskopi sırasında transkütanöz karbondioksit monitorizasyonu: Prospektif gözlemsel çalışma

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Ethics Committee Approval: The approval for this study was obtained from the Kırıkkale University Ethical Committee of Clinical Studies (decision number: 21.03). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
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Abstract

Aim: It is difficult to maintain the necessary depth of sedation during bronchoscopy, and hypoxemia, hypoventilation, and undesirable cardiovascular effects are often encountered. Transcutaneous carbon dioxide monitoring is a reliable means of detecting hypoventilation. The aim of this study was to determine the effects of transcutaneous carbon dioxide ($tPCO_2$) monitoring on the amount of propofol required for sedation and examine sedation-induced hypoventilation and other adverse events requiring intervention, such as stopping the procedure to ventilate during flexible bronchoscopy.

Methods: This prospective observational study included 60 patients undergoing bronchoscopy who were administered propofol. Of these, 30 patients were observed with transcutaneous carbon dioxide, and 30 were observed without. Propofol was used for sedation in all patients and the amount of propofol was compared between the groups monitored and not monitored transcutaneously for carbon dioxide. The sedation level was determined with the subjective sedation scale of the group that was not monitored.

Results: No significant differences were found between the groups in terms of propofol consumption or the number of patients who required airway interventions during the procedure (P>0.05 for both). In this observational study, the partial carbon dioxide pressure in arterial blood was measured with a transcutaneous carbon dioxide monitor, which is a non-invasive method, and the maximum carbon dioxide value measured in prolonged interventions was 85 mmHg. Hypoxia was not observed in patients who developed hypoventilation.

Conclusions: Hypoventilation is inevitable during bronchoscopy. Transcutaneous carbon dioxide monitoring may be important for high-risk cardiovascular patients.

Keywords: Bronchoscopy, Transcutaneous carbon dioxide, Hypoventilation, Propofol, Moderate sedation

Öz

Amaç: Bronkoskopi sırasında gerekli sedasyon derinliğini korumak zordur, hipoksemi, hipoventilasyon ve sedasyon sırasında sıklıkla istenmeyen kardiyovasküler etkilerle karşılaşılır. Transkutanöz karbondioksit monitorizasyonu, hipoventilasyonun saptanması için güvenilir bir yoldur. Bu çalışmanın amacı, transkütanöz karbondioksit ($tPCO_2$) takibinin sedasyon için gereken propofol miktarı üzerindeki etkilerini belirlemek ve Sedasyona bağlı hipoventilasyon ve fleksibl bronkoskopi sırasında ventilasyon için işlemi durdurmayı gerektiren istenmeyen müdahale edilmesini gerektiren diğer olumsuz olayları incelemektir.

Yöntemler: Prospektif gözlemsel çalışmaya bronkoskopi yapılan ve propofol titrasyonu uygulanan 60 hasta dahil edildi. 30 hastaya transkütanöz karbondioksit monitörizasyonu uygulandı ve 30 hasta transkütanöz karbondioksit monitörizasyonu olmaksızın gözlendi. Tüm hastalarda sedasyon amacıyla propofol kullanıldı ve propofol miktarı transkutanöz karbondioksit ile izlenen ve izlenmeyen gruplar arasında karşılaştırıldı. Sedasyon seviyesi transkütanöz karbondioksit monitörizasyonu ile izlenmeyen grupta subjektif sedasyon skalası ile belirlendi.

Bulgular: Gruplar arasında propofol tüketiminde anlamlı fark bulunmadı. Ayrıca işlem sırasında hava yolu müdahalesi gerektiren hasta sayısı arasında anlamlı bir fark bulunmadı (P>0.05). Bu gözlemsel çalışmada arterial kan gazındaki parsiyel karbondioksit basıncı invaziv olmayan transkütanöz karbondioksit monitörü ile yapıldı ve maksimum karbondioksit değerinin 85 mmHg olduğu gözlendi. Hipoventilasyon gelişen hastalarda hipoksi görülmedi.

Sonuç: Bronkoskopi sırasında hipoventilasyon kaçınılmazdır. Transkutanöz karbondioksit monitorizasyonu, yüksek riskli hastalar için önemli olabilir.

Anahtar kelimeler: Bronkoskopi, Transkütanöz karbondioksit, Hipoventilasyon, Propofol, Orta düzeyde sedasyon

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Introduction

Flexible bronchoscopy (FB) is a procedure performed by respiratory physicians and has become a gold standard technique to directly visualize and access the airway for diagnostic and therapeutic intervention [1]. Unfortunately, patients frequently suffer from pain, coughing, and the sensation of asphyxiation during the procedure. Thus, this procedure is performed by bronchologists with the patient under sedation to facilitate the examination of the tracheobronchial tree and improve the patient's safety and comfort [2,3].

Sedation during bronchoscopy is frequently recommended. Moderate sedation, also referred to as conscious sedation, maintains the patient's purposeful response to verbal and tactile stimuli and adequate spontaneous breathing, but this target level of sedation is difficult to achieve in practice [4]. Serious complications, including respiratory depression in the form of hypoxia or hypercapnia and cardiovascular instability, may occur during flexible bronchoscopy under moderate sedation. Propofol (2,6-diisopropylphenol) is a moderate sedation drug that is ideal for use in flexible bronchoscopy because it provides rapid recovery due to its pharmacokinetic properties, such as rapid clearance [5].

End tidal carbon dioxide monitoring during bronchoscopy procedure cannot provide accurate measurements. Transcutaneous carbon dioxide ($TcCO_2$) monitoring is a non-invasive alternative to arterial blood sampling. Transcutaneous partial carbon dioxide pressure gives results close to those measured by arterial blood gas. We planned this study with the thought that it may be useful to detect patients in cardiovascular risk groups early and prevent over-sedation.

This prospective randomized controlled study was designed to determine the effect of transcutaneous carbon dioxide ($tPCO_2$) monitoring on propofol consumption and examine sedation-induced hypoventilation as well as adverse events requiring intervention during flexible bronchoscopy.

Materials and methods

This study obtained approval (decision number 21.03) from the Kırıkkale University Ethical Committee of Clinical Studies. All participants signed the required consent form. Only patients scheduled to undergo flexible bronchoscopy (Karl Storz 11001 BN1) under local anesthesia with sedation were included in the study. Exclusion criteria for the study included patients under 18 years of age, those who refused to participate, those with psychiatric disorders, and those who were allergic to anesthetic drugs such as propofol, midazolam, and fentanyl. Patients with a tracheostomy or endotracheal tube, and peripheral vascular disease were excluded because it may have affected transcutaneous measurement.

Bronchoscopy procedure

Local anesthesia was provided by applying 2% lidocaine to the patient's oropharynx at the beginning of the procedure. The sedation protocol began with 0.02 mg kg^{-1} midazolam and 0.5 mcg kg^{-1} fentanyl. Anesthesia was maintained with intermittent boluses of 20–50 mg propofol dependent on clinical judgement and Ramsay Sedation Scale (RSS) scores (Table 1) [6]. The target score was 3–4 to maintain light or moderate sedation. Standard monitorizations, such as non-invasive blood pressure, electrocardiography, and pulse oximetry, were performed. A computer randomly divided patients into two groups and closed envelopes were prepared by an independent anesthesiologist not associated with the study. The envelopes were subsequently opened by the anesthesiologist who prepared and administered the medicines during the procedure. In the control group (group C, n=30), only standard monitorization was applied. In the transcutaneously monitored group (group TM), continuous $tPCO_2$ monitoring was performed ($TCM4^{TM}$, Radiometer Copenhagen, Denmark) through a probe placed on the patient's upper left chest using a solution as per the manufacturer's instructions. After applying the transcutaneous probe, the staff anesthesiologist and thoracic surgeon waited to begin the procedure until the sensor completed calibrating. Data collected included the patient's demographics, indication for the bronchoscopy, non-invasive blood pressure measurement values, electrocardiography, pulse oximetry, propofol consumption, transcutaneous carbon dioxide, RSS score, duration of the procedure, and whether interventions were necessary for hypoventilation or respiratory arrest. For this study, we defined hypoventilation as $tPCO_2$ ≥55 mmHg and hypoxia as SpO_2 <90% (>2 min). All interventions that required stopping the procedure, such as endotracheal intubation or manual mask ventilation, were recorded.

Table 1: Ramsay sedation score system

	Score Definition
1	Patient is anxious and agitated or restless, or both
2	Patient is co-operative, oriented, and tranquil
3	Patient responds to commands only
4	Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
5	Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus
6	Patient exhibits no response

Adapted from Ramsay et al. [6]

Statistical analysis

Statistical Package for the Social Sciences (SPSS) version 21 (SPSS Inc., Chicago, Illinois, United States) was used for statistical analysis. The demographic data were provided as mean (standard deviation (SD)) or median with minimum (min) and maximum (max), as appropriate. Independent samples *t* tests were used to compare the variables with normal distribution, and the Mann–Whitney test was used to compare the nonparametric variables. Pearson correlation was used to identify the correlation between the independent variables. $P<0.05$ was considered statistically significant.

Results

Demographic data, propofol consumption, duration of procedure, continuous positive airway pressure (CPAP) and mask-ventilation values of the patients and indication for the procedure are shown in Table 2. Age, gender, indication for the procedure, dose of propofol, mask ventilation, continuous positive airway pressure (CPAP) application, systolic blood pressure (SBP), mean arterial pressure (MAP), and oxygen measurements were not significantly different between the two groups. The distributions of heart rate, mean arterial pressure, pulse oximetry and Ramsay Sedation scores of the patients according to the groups are presented in Table 3.

The patients were divided into two groups as "biopsy" and lavage" according to the indication, and the two groups were found to significantly differ with respect to the following

parameters: The patients undergoing biopsy were older than those who were undergoing the procedure for lavage, their American Society of Anesthesiologist classification (ASA) scores were higher, the procedure duration was longer, and the diastolic blood pressure (DBP) and MAP values were lower. Among 60 patients, the procedure had to be interrupted for mask ventilation in 15 patients and CPAP ventilation in 5 patients.

Table 2: The demographic data, propofol consumption, duration of procedure, and CPAP and mask-ventilation values of the patients according to the groups

Variable		Control Mean (SD) / Median (min-max) / n (%)	TM Mean (SD) / Median (min-max) / n (%)	t / Z	*P*-value
Age (year)		63.50 (23-85)	60.50 (27-84)	-1.176	0.239
Gender	Female	4 (6.7%)	9 (15.0%)	-1.554	0.120
	Male	26 (43.3%)	21 (35%)		
Indication	Biopsy	9 (15.0%)	15 (25.0%)	-1.568	0.117
	Lavage	21 (35.0%)	15 (25.0%)		
ASA	2	13 (21.7%)	12 (20.0%)	-0.260	0.795
	3	17 (28.3%)	18 (30.0%)		
Weight (kg)		76.50 (60-103)	68 (50-135)	-3.204	0.001
Height (cm)		170.13(4.68)	168.53(7.62)	0.980	0.331
BMI (kg/m^2)		26.38 (20.90-36.49)	22.92 (18.42-41.67)	-2.558	0.011
Duration (minute)	15	6 (10.0%)	2 (3.3%)	-2.452	0.014
	20	12 (20.0%)	8 (13.3%)		
	25	9 (15.0%)	11 (18.3%)		
	30	3 (5.0%)	9 (15.0%)		
Propofol (mg)		153.17(36.49)	160.17(57.30)	-0.564	0.575
CPAP	No	29 (48.3%)	26 (43.3%)	-1.390	0.165
	Yes	1 (1.7%)	4 (6.7%)		
Mask ventilation	No	25 (41.7%)	20 (33.3%)	-1.478	0.139
	Yes	5 (8.3%)	10 (16.7%)		

Independent samples t test, Mann–Whitney U test

Table 3: The distribution of heart rate, mean arterial pressure, pulse oximetry and Ramsay Sedation score of the patients according to the groups and indication for the procedure

Variable	Control Mean (SD) / Median (min-max)	TM Mean (SD) / Median (min-max)	*P*-value
HR0	86.20(11.98)	83.57(13.06)	0.419
HR5	83.67(11.86)	90.13(15.28)	0.072
HR10	81.63(12.59)	89.33(13.02)	0.023
HR15	80.30(11.62)	87.00(12.19)	0.033
HR20	79.48(11.34)	87.50(13.33)	0.023
HR25	74.69(12.09)	87.25(12.36)	0.007
HR30	69.33(16.56)	78.30(10.25)	0.267
MAP0	95.60(13.65)	91.43(16.68)	0.294
MAP5	88.67(11.84)	91.93(18.25)	0.414
MAP10	92.17(14.21)	87.00(14.92)	0.175
MAP15	85.27(16.22)	84.47(16.20)	0.849
MAP20	81.44(12.19)	79.32(18.06)	0.623
MAP25	79.31(14.50)	79.55(20.86)	0.971
MAP30	76.00(16.09)	74.67(21.31)	0.924
Oxygen0	96.24(1.62)	95.53(2.97)	0.262
Oxygen5	93.90(1.84)	94.10(4.83)	0.833
Oxygen10	92.76(2.71)	91.07(7.06)	0.232
Oxygen15	93.45(3.48)	93.50(4.31)	0.960
Oxygen20	93.65(1.55)	92.82(6.96)	0.578
Oxygen25	94.42(1.73)	95.00(3.81)	0.621
Oxygen30	94.33(2.08)	96.22(2.86)	0.323
RSS0	2 (2-2)	2 (2-2)	1.000
RSS5	3 (3-5)	3 (2-5)	0.312
RSS10	4 (3-5)	4 (3-6)	0.908
RSS15	4 (3-5)	4 (2-5)	0.012
RSS20	4 (3-5)	4 (3-6)	0.105
RSS25	4 (3-5)	4 (3-6)	0.434
RSS30	4 (3-4)	4 (3-5)	0.466

Independent samples t test, Mann–Whitney U test

Correlation analysis

No correlation was found between gender, ASA, BMI, required dose of propofol, mask ventilation and CPAP requirement between the groups. The results suggest that older patients who underwent biopsy could have higher ASA scores and the duration of the procedure could be longer. In addition, DBP and MAP should be measured more frequently in patients undergoing lavage. A correlation was found between duration and RSS at the 10th (pc=0.300, P=0.020), 15th (pc=0.524, P<0.001), and 20th minutes (pc=0.463, P=0.001), and the amount of propofol used (pc=0.380, P=0.001). There was a positive correlation between duration and mask ventilation (pc=0.398, P=0.002), as well as the need for CPAP (pc=0.406, P=0.001). The results suggest that propofol dose, RSS values, mask ventilation rate of these patients, and the need for CPAP increased. The maximum carbon dioxide value measured in prolonged interventions, such as those in which CPAP or mask ventilation was required, was 85 mmHg (Table 4).

Table 4: The maximum levels of transcutaneous carbon dioxide

Group	Variable	n	Minimum	Maximum	Mean	SD
Control	transcutaneous0	-	-	-	-	-
	transcutaneous5	-	-	-	-	-
	transcutaneous10	-	-	-	-	-
	transcutaneous15	-	-	-	-	-
	transcutaneous20	-	-	-	-	-
	transcutaneous25	-	-	-	-	-
	transcutaneous30	-	-	-	-	-
TM	transcutaneous0	30	30.00	47.00	36.57	4.46
	transcutaneous5	30	32.00	57.00	42.73	6.81
	transcutaneous10	30	34.00	68.00	47.53	7.94
	transcutaneous15	30	35.00	77.00	50.97	9.63
	transcutaneous20	27	24.00	85.00	51.67	12.18
	transcutaneous25	20	35.00	74.00	54.00	10.05
	transcutaneous30	9	47.00	63.00	56.44	6.17

Discussion

End-tidal CO_2 monitoring during FB can be performed continuously by sampling with a device placed in the mouth of the patient. However, this randomized controlled study used transcutaneous CO_2 measurement to provide more accurate results, since there may be difficulties in end tidal sampling during bronchoscopy.

Previous studies have reported a correlation between end tidal CO_2 and $tPCO_2$ in volunteers and in spontaneously breathing patients in the intensive care unit [7,8]. A study showed the superiority of $tPCO_2$ to end tidal CO_2 and suggested that upper airway muscle weakness due to propofol is the reason that end tidal CO_2 monitoring is not useful [9]. Another study reported that false apnea alarms occurred 83 times in 185 patients monitored by end-tidal CO_2 capnography [7]. The current study aimed to reach the optimum sedation level necessary for the bronchoscopist to complete the procedure successfully. Propofol titration during sedation, clinical observation and patient response, and suppression of reflexes were used to keep the sedation score at 4. Deep hypoventilation without hypoxemia was seen in patients with high CO_2 levels when the duration of the bronchoscopy procedure exceeded 15 minutes. Although there was no statistically significant difference between the groups according to the variable parameters, hypoventilation was inevitable. It occurred despite a prolonged treatment time without hypoxemia and although the dose of propofol was well titrated to the appropriate transcutaneous CO_2 values to complete the procedure. Another study showed that propofol-associated complications were more likely to occur during prolonged or complex procedures [10].

Results of the present study suggest that patients monitored by pulse oximetry, which is the standard monitorization in clinical practice, are at cardiovascular risk. This study showed that $tPCO_2$ monitoring has no effect on propofol dose titration in determining sedation levels. Although acute hypercapnia had no effect on myocardial contractility and relaxation in the physiological system, it led to arrhythmia by causing repolarization abnormalities reflected by an increase in QT dispersion. Hypercapnia also causes pulmonary vasoconstriction in humans [11]. In our study, hypercapnia did not cause arrythmia, but it is crucial to monitor $tPCO_2$ in patients with arrythmia and pulmonary hypertension. Most of the patients

undergoing bronchoscopy are elderly, which increases the likelihood of cardiac arrest due to arrhythmias or cardiac ischemia during bronchoscopy [12]. The heart has rich innervation from the parasympathetic and sympathetic limbs of the autonomic nervous system, and autonomic nervous imbalance is believed to be a crucial factor in these cardiac events [13]. A bronchoscopy can trigger spasms and plaque disruption in the coronary arteries due to an increase in sympathetic activity caused by tension and anxiety. Bronchoscopy under sedation allows for the suppression of anxiety and stress-induced sympathetic activity in patients, while simultaneously allowing the effects of hypoxia and hypercarbia [14]. Monitoring the sedation level becomes important, and titration of the propofol dose is difficult to achieve for the completion of the bronchoscopy procedure, ensuring the comfort of the bronchoscopist and the patient.

Carbon dioxide monitoring during a bronchoscopy under sedation can identify increases in the partial carbon dioxide pressure of the arterial blood early in the procedure, which may occur depending on the central effect of the sedative drugs used or the process itself and cause a ventilation-perfusion mismatch. In a study similar to ours which showed a rise in $tPCO_2$ reflecting hypoventilation without hypoxia, sedation was achieved with intermittent boluses of intravenous midazolam and 5 mg of hydrocodone [15]. In our study, propofol administered for sedation with intermittent boluses was monitored using RSS, which is commonly used as a subjective sedation scale.

Another study compared propofol with midazolam + alfentanil used for sedation in bronchoscopies and found that carbon dioxide tension values were significantly higher in the midazolam + alfentanil group than in the propofol group at 5 and 10 minutes following the procedure with transcutaneous carbon dioxide monitoring. They also found that significantly more patients in the midazolam + alfentanil group needed oxygen supplementation or airway support. They concluded that propofol is safer than the combination of midazolam + alfentanil [16]. In our study, sedation protocol was started with 0.02 mg kg^{-1} midazolam and 0.5 mcg kg^{-1} fentanyl, then maintained with intermittent boluses of 20–50 mg of propofol according to clinical judgement and the patient's score on the RSS in the control group. In the $tPCO_2$ group, the titration of propofol was determined by monitoring and the response of the patient. The duration of the bronchoscopy and the indication correlated with higher carbon dioxide levels. Transcutaneous carbon dioxide pressure was higher in patients who underwent bronchoscopy for biopsy. Another study determined the maximum value of $tPCO_2$ as 59.25 mmHg by examining 22 bronchoscopy patients. The maximum value measured in our study was 85 mmHg, and we found the processing times to be longer. The fact that we did not perform cerebral monitoring, such as bispectral indexing, in our study indicates the lack of objective data on sedation levels. Although it is a short-term intervention, sedation depth measurement with bispectral index monitoring may be more effective in reducing propofol consumption and preventing hypoventilation. One study demonstrated that Bispectral Index (BIS)-guided propofol infusion is feasible, safe, easily tolerated, and provides a fast recovery for patients undergoing FB [17,18]. In their study, carbon dioxide monitorization was not used, and hypoventilation was not assessed.

A previous study showed that bronchoscopists used propofol 50% of the time, capnography was used in 10% of patients, and transcutaneous CO_2 monitoring was used 1% of the time and only in specialized centers [19]. This suggests that the use of transcutaneous carbon dioxide monitoring is not a cost-effective method for short duration procedures such as bronchoscopy. Although it has the advantage of being a non-invasive method, in clinical practice, calibration takes almost as much time as the procedure itself. However, transcutaneous carbon dioxide monitoring may be appropriate in high-risk cardiovascular patients.

Another undesirable effect during bronchoscopy is the cough reflex. The activation of the cough center results in the contraction of the respiratory muscles. The contraction of the bronchial muscles causes bronchoconstriction, which leads to hypoventilation. The limitation of this study is that patient satisfaction was not evaluated.

Different agents are used for sedation to ensure patient comfort during bronchoscopy. Propofol was the only agent used for sedation in this study. Studies with different sedation drugs, such as dexmedetomidine, are needed.

Conclusion

Hypoventilation without desaturation is inevitable during bronchoscopy, and transcutaneous carbon dioxide monitoring should be used in patients with arrhythmia, cardiovascular disease, or higher ASA physical status.

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Microsurgical anatomy of the anterior commissure through the anterior interhemispheric transcallosal approach to the third ventricle: An anatomical and morphological study

Üçüncü ventriküle anterior interhemisferik transkallozal yaklaşım yoluyla anterior komissürün mikrocerrahi anatomisi: Anatomik ve morfolojik bir çalışma

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Abstract

Aim: The third ventricle is a funnel-shaped cavity located deep in the brain and difficult to access with surgical approach. The anterior commissure is an anatomical structure located on the anterior wall of the third ventricle. This study aimed to demonstrate the use of the anterior interhemispheric transcallosal approaches to access the third ventricle, evaluate the microsurgical anatomy of the anterior commissure and investigate the morphological features of this region.

Methods: Eleven cadaveric brain specimens were dissected using microsurgical tools. Different anterior interhemispheric routes to the third ventricle were demonstrated, and stepwise dissections were performed to expose the limbs of the anterior commissure. Morphological measurements of the anterior commissure and the third ventricle were carried out.

Results: The anterior limb of the anterior commissure extends towards the anterior perforating substance, olfactory bulb, anterior olfactory nucleus and the orbitofrontal cortex. The posterior limb extends from the basal part of the caudate nucleus, passes below the substantia innominata and courses through the basal part of the putamen. It constitutes the major component of the anterior commissure and is composed of temporal and occipital fibers. The mean length of the anterior commissure body was 16.2 ± 4.2 (range 9.7–24.2) mm, while the mean width was 4.3 ± 0.7 (range 2.8–5.1) mm.

Conclusion: A better understanding of the microsurgical anatomy and morphometric features of the third ventricle and anterior commissure increases the success of surgical interventions and prevents possible complications in this region.

Keywords: Third ventricle, Anterior interhemispheric transcallosal approach, Anterior commissure, Microsurgical anatomy

Öz

Amaç: Üçüncü ventrikül, huni şeklinde derin yerleşimli bir beyin boşluğudur ve cerrahi yaklaşımlarla ulaşılması güçtür. Anterior komissür üçüncü ventrikülün anterior duvarında lokalize anatomik bir yapıdır. Bu çalışmada, üçüncü ventriküle ulaşmak için uygulanan anterior interhemisferik transkallozal yaklaşımların gösterilmesi, anterior komissürün mikrocerrahi anatomisinin incelenmesi ve bu bölgenin morfolojik özelliklerini incelenmesi amaçlanmıştır.

Yöntemler: 11 kadaverik beyin spesimeni mikrocerrahi aletlar kullanılarak diseke edildi. Üçüncü ventriküle ulaşmak için farklı anterior interhemisferik yollar gösterildi ve anterior komissürün bacaklarını ortaya koymak için kademeli diseksiyonlar yapıldı. Anterior komissür ve üçüncü ventrikülün morfolojik hesaplamaları yapıldı.

Bulgular: Anterior komissürün anterior bacağı, anterior perforan maddeye, olfaktör bulba, anterior olfaktör nükleusa ve orbitofrontal kortekse doğru uzanmaktadır. Posterior bacağı ise, kaudat nükleusun bazal kısmından uzanarak substansiya innominatanın altından geçmekte ve putamenin bazal kısmına doğru seyretmektedir. Anterior komissürün posterior bacağı, anterior komissürün majör komponentini oluşturmaktadır, ve temporal ve oksipital loblara giden liflerden oluşmaktadır. Anterior komissür gövdesinin ortalama uzunluğu 16,2 ± 4,2 (Aralık 9,7-24,2) mm, ve ortalama eni ise 4,3 ± 0,7 (Aralık 2,8-5,1) mm idi.

Sonuç: Üçüncü ventrikülün ve anterior komissürün mikrocerrahi anatomisi ve morfometrik özelliklerinin daha iyi anlaşılması bu bölgeye yapılacak cerrahi girişimlerde başarılı olmayı sağlar ve olası komplikasyonları önler.

Anahtar kelimeler: Üçüncü ventrikül, Anterior interhemisferik transkallozal yaklaşım, Anterior komissür, Mikrocerrahi anatomi

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Introduction

Accessing the third ventricle of the brain often proves to be quite challenging due to its deep location and the functional importance of the adjacent anatomical structures [1]. The success of surgical interventions involving this region depends on a clear understanding of its microsurgical anatomy and principles.

The anterior interhemispheric transcallosal approach (AITA) is the most common method used to access lesions involving the third ventricle and can be used in combination with the transforaminal, interforniceal, subchoroidal, and transchoroidal routes [2,3].

The anterior commissure represents a key interhemispheric connecting structure that needs to be protected when approaching lesions affecting the anterior wall of the third ventricle. This study aims to demonstrate the use of an AITA to access the third ventricle, evaluate the microsurgical anatomy of the anterior commissure and investigates the morphological features of this region.

Materials and methods

Eleven cadaveric human brain specimens that kept in 10% formalin solution for at least 3 months were used. The arachnoid, pia mater and vascular structures were removed in the anatomy laboratory, and all dissections were performed using a surgical microscope (magnification 4–40x) and appropriate microsurgical tools. The specimens were stored in 75% alcohol solution between dissections.

First, the cingulate gyri were exposed using the interhemispheric space. Then, retractors were advanced towards the corpus callosum. A callosal incision, 1.5–2 cm in length, was created at a point approximately 2.5 cm posterior to the genu of the corpus callosum, depending on the access angle of the foramen of Monro, which was used as the central point of incision for all hemispheres. Thereafter, the third ventricle was accessed via the right lateral ventricle in all specimens.

The relationship between the anterior commissure and the approaches used were also demonstrated. Morphometric calculations were made using an electronic caliper between the anterior commissure and various anatomical landmarks.

This study was approved by the Research Ethics Committee of Istanbul University–Cerrahpasa, Cerrahpasa Medical Faculty (Number: 83045809/32140; Date: 9/3/2014).

Results

Although the anterior transcallosal pathway represents a common surgical corridor for accessing third ventricular lesions, various modifications can be made based on the location of the lesion. The modifications demonstrated in this study are listed below:

Transforaminal approach

This is the most common approach used to access tumors located in the anterior part of the third ventricle. The current study demonstrates access to the third ventricle from the foramen of Monro, followed by exposure of its anterior section by lifting the roof using dissection (Figure 1).

Interforniceal approach

This approach is typically suggested for accessing lesions in the anterior and middle sections of the third ventricle. Once adequate interforniceal exposure has been achieved, the velum interpositum can be opened and both internal cerebral veins may be retracted to expose the third ventricle floor (Figure 2).

Subchoroidal approach

The subchoroidal approach consists of opening the choroidal fissure by leaving the choroid plexus on the fornix side. However, this approach has almost been abandoned now as it typically requires sacrificing the thalamostriate vein which leads to serious complications due to venous hypertension (Figure 3).

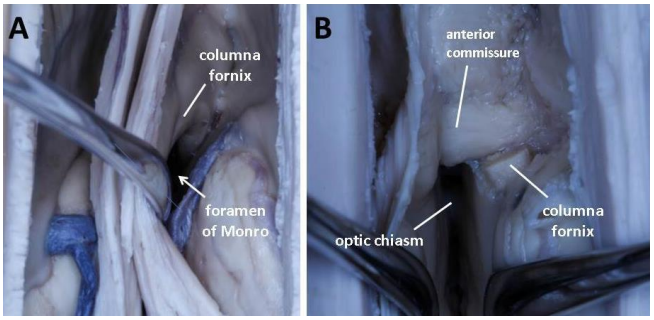

Figure 1: Transforaminal approach. A. Superior view of the foramen of Monro of the right lateral ventricle. The foramen of Monro was exposed more widely by retracting the upper border of the foramen of Monro and columna fornix. B. The anterior commissure is clearly exposed by cutting the right columna fornix.

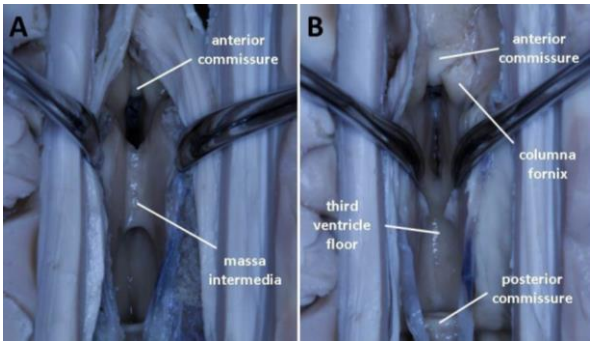

Figure 2: Interforniceal approach. A. Supeior view of the third ventricle after opening the septum pellucidum and corpus fornix in the midline. B. After the massa intermedia incision, the third ventricle floor was seen with bilateral retraction. The right columna fornix was cutted for a better view of the anterior commissure body.

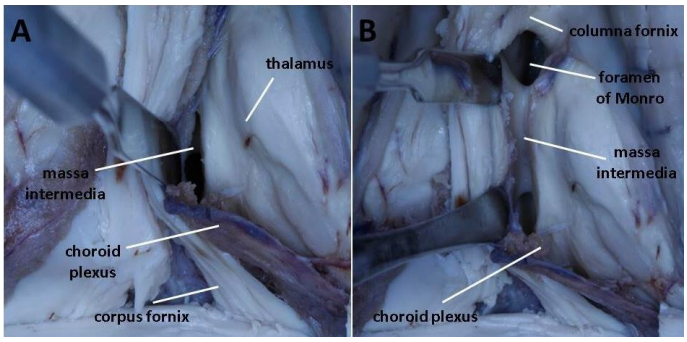

Figure 3: Subchoroidal approach. A. After the right choroid plexus was medialized with a retractor, access to the third ventricle was demonstrated. B. Third ventricle exposure was achieved with a double retractor. A large massa intermedia and columna fornix are seen.

Transchoroidal approach

The transchoroidal approach includes opening of the choroidal fissure along the tenia fornicis by starting at the posterior edge of the foramen of Monro and displacing the fornix medially and the choroid plexus to the opposite side to expose the deep third ventricle structures. Once the choroidal fissure has been opened and the fornix is retracted medially, the anatomical structures of the third ventricle were exposed (Figure 4).

Microanatomy of anterior commissure

The anterior leg of the anterior commissure includes axonal connections that enter the anterior perforating substance, coursing to the olfactory bulb, anterior olfactory nucleus and the orbitofrontal cortex. The posterior leg of the anterior commissure runs to the basal part of the caudate nucleus in a medio-lateral direction and then courses right behind the substantia innominata to a point below the anterior section of the globus pallidus. Most of the fibers go through the basal section of the putamen to its lateral border and then enter the white matter of the temporal lobe to the middle and inferotemporal region, with some fibers advancing further up to the occipital lobe [4] (Figure 5).

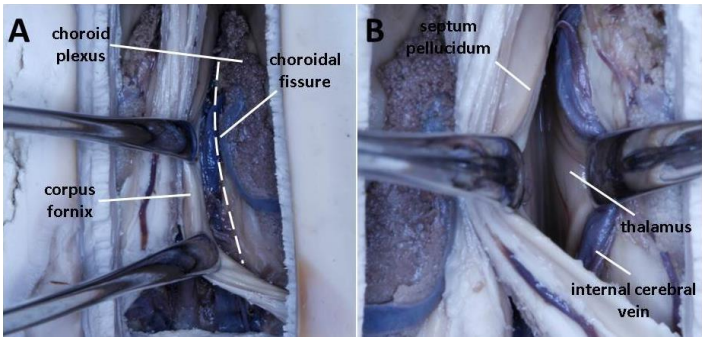

Figure 4: Transchoroidal approach. A. Superior view of the choroid plexus after the right corpus fornix is medialized. Choroidal fissure is shown in dashed lines. B. After the choroidal fissure was opened, the third ventricle was exposed.

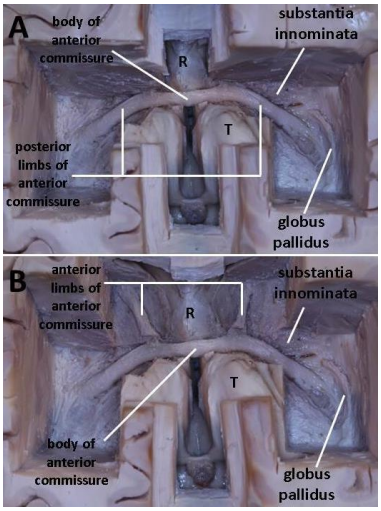

Figure 5: A. Anterior commissure body and bilateral posterior limb of the anterior commissure are seen from superior. The relationship between posterior limb and basal ganglia is also demonstrated. B. Anterior limb of the anterior commissure is exposed in superior view. R=Rostrum, T=Thalamus.

Morphological assessment

Important landmarks of the anterior commissure and third ventricle, including the cortical interhemispheric entry point where the anterior transcallosal approach was applied and the entry point to the third ventricle through which the corpus callosum was passed, were measured in the sagittal and axial planes (Figure 6). The mean, range and standard deviation values were calculated and are presented in Table 1.

The mean lengths from the entry point to the corpus callosum (EP-CC) and from the corpus callosum to the foramen of Monro (CC-FM) were 34.9 ± 3.1 (range 29.5–39.7) mm and 15.3 ± 4.8 (range 9.1–24.5) mm, respectively. The mean length of the anterior commissure body (ACL) was 16.2 ± 4.2 (range 9.7–24.2) mm, while the mean width (ACW) was 4.3 ± 0.7 (range 2.8–5.1) mm.

Approximately 90.9% (10/11) of the specimens in this study had a Massa intermedia, with only one specimen lacking it.

Table 1: Morphometric values of the third ventricle with anterior interhemispheric transcallosal approach focusing on the anterior commissure

Parameters	Mean and SD values (mm)	Range values (mm)
ACL	16.2 ± 4.2	9.7–24.2
ACW	4.3 ± 0.7	2.8–5.1
AC-FM	7.1 ± 0.8	5.5–8.4
AC-PC	24.9 ± 1.4	22.6–27.2
AC-R	17.5 ± 2.7	14.3–21.3
MIW	8.1 ± 2.8	3.7–12.2
MI-AC	9.3 ± 2.8	6.1-14.9
MI-PC	11.7 ± 1.9	8.1–14.1
Aq-AC	27.6 ± 3.6	22.1–32.1
Aq-FM	25.1 ± 3.4	20.1–29.8
FM-PC	23.1 ± 1.4	21.4–25.1
OC-AC	9.3 ± 0.9	7.4–10.1
OC-FM	14.5 ± 0.8	13.2–16.1
OC-PC	24.9 ± 1.3	22.7–26.9
EP-CC	34.9 ± 3.1	29.5–39.7
CC-FM	15.3 ± 4.8	9.1–24.5

SD: standard deviation, mm: millimeter, AC: anterior commissure, ACL: anterior commissure length, ACW: anterior commissure width, FM: foramen of Monro, PC: posterior commissure, R: rostrum, MI: Massa intermedia, MIW: Massa intermedia width, Aq: aquaduct, OC: optic chiasm, EP: entry point, CC: corpus callosum

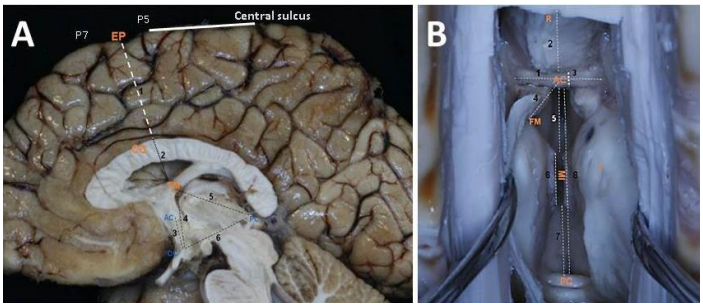

Figure 6: A. In order to determine the interhemispheric entry point in the sagittal plane, two points are determined 5 cm and 7 cm in front of the central sulcus. These are P5 and P7. The anterior transcallosal approach is made through this opening. This place is designated as Entry Point (EP). 1. The distance between the entry point and the corpus callosum (EP-CC), 2. The distance between corpus callosum and foramen of Monro (CC-FM), 3. The distance between the optic chiasm and the anterior commissure (OC-AC), 4. The distance between the optic chiasm and the foramen of Monro (OC-FM), 5. The distance between the Foramen of Monro and the posterior commissure (FM-PC), 6. The distance between the optic chiasm and the posterior commissure (OC-PC). B. Morphometric parameters of the third ventricle in the axial plane. 1. Anterior commissure length (ACL), 2. The distance between anterior commissure and rostrum (AC-R), 3. Anterior commissure width (ACW), 4. The distance between anterior commissure and foramen of Monro (AC-FM), 5. The distance between anterior commissure and massa intermedia (AC-MI), 6.Massa intermedia width (MIW), 7.The distance between massa intermedia and posterior commissure (MI-PC), 8.The distance between anterior commissure and posterior commissure (AC-PC).

Discussion

The third ventricle is a narrow funnel-shaped cavity and is located deep in the central nervous system, which is difficult to access. The transforaminal route is the most commonly used AITA to reach the third ventricle, mainly because colloid cysts, which typically originate from the anterior wall of the third ventricle, tend to constitute the majority of pathologies affecting this region [5,6]. Therefore, the current study focused on the anterior commissure, which is one of the most important structures located in the anterior wall of the third ventricle.

The anterior commissure is a paleopallial connection pathway developed in the embryological period from the telencephalon, and connects the two amygdaloid nuclei at the mesial temporal region. It is also an important anatomical landmark of the rhinencephalon and serves as a functional pathway between the two hemispheres [7].

There are limited studies on the detailed morphometry of the anterior commissure. Ozer et al. [8] measured the antero-posterior width and height of the anterior commissure and its distance from the pineal gland. Erturk et al. [9] investigated the morphometry of the anterior third ventricle using the subfrontal translaminaterminalis approach and reported FM-OC, AC-OC, OC-PC and ACW values similar to those seen in the current study. However, their ACL values were lower than those seen in the current study (3.89 ± 0.79 mm), and this could be attributed

to the different approaches used. This suggests that the part of the anterior commissure encountered during the anterior transcallosal approach may be wider than that accessed using the subfrontal trans-lamina terminalis approach.

The Massa intermedia is a grey matter structure connecting the both thalamus from the midline, and little is known about its functions [10]. Previous studies have reported that approximately 24%–30% of people do not have a Massa intermedia [11,12], and only one out of 11 brain hemisphere samples examined in the current study did not have one.

The interhemispheric approach to the third ventricle requires crossing the commissural fibers which, if damaged, may lead to disconnection syndromes associated with major neurosurgical problems such as aphasia, left ideomotor apraxia, amnesia, and neglect [13-15]. Although the exact mechanism of disconnection syndromes is still unclear [16], the pathologies observed typically focus on two structurally important interhemispheric connection pathways, the corpus callosum and the anterior commissure.

Alternative pathways, particularly those involving the anterior commissure, play an important role in patients whose motor, language, cognitive and behavioral functions remain unaffected following incision of the corpus callosum [17,18]. The anterior commissure is also potentially associated with diffuse axonal injury, schizophrenia and cerebral tumor spread [19-21]. Fisher et al. [22] reported that anterior commissure hypertrophy develops due to re-routing in patients with corpus callosum agenesis. Also, DTI studies have shown that the anterior commissure may play a role more important than previously thought [18,23].

Patients with anterior commissure damage during surgery suffer from a delay in recognition, loss in ability to perform arithmetic calculations, problems with interpretation of abstract thoughts, and short-term memory loss [7,24,25]. Anterior commissurotomy decreases emotional awareness, social connectedness and interpersonal relationships, and can also lead to neurological disorders such as alexithymia [26,27]. However, direct stimulation of the anterior commissure during awake surgeries does not appear to produce any neurological findings, and partial excision along with the pathological lesion being treated has been shown to have no complications [28]. It is still unknown whether complete sacrifice of the anterior commissure with incision of the corpus callosum will lead to any neurological disorders. However, in their study involving monkeys, O'Reilly et al. [29] found that incision of the anterior commissure with the corpus callosum led to complete loss of the interhemispheric connection, as seen in the functional MRI, suggesting that special attention should be paid to preservation of the anterior commissure during surgeries requiring incision of the corpus callosum. In our opinion, this can only be achieved by developing a clear understanding of the anatomy of this region.

Limitations

This study had several limitations. Firstly, formalin fixation may have resulted in some shrinkage of the neural tissue and alteration of the ventricular system morphometry. However, a previous morphometric study comparing formalin-fixed brain samples to fresh ones reported no significant differences [30]. Secondly, this study only measured the anterior commissure body and not the anterior and posterior limbs as the aim was to focus on the part of the anterior commissure encountered during AITA and located in the anterior wall of the third ventricle.

Conclusion

The findings of this study emphasize the need to preserve neuronal pathways and critical neuro-anatomical structures during surgical interventions involving the third ventricle. Morphometric measurements of this region play a major role in the planning and success of surgical interventions, and the surgeon should have a clear understanding of the anatomy of the anterior commissure when using the anterior transcallosal approaches so as to avoid damaging it.

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Comparison of long-stemmed cementless hemiarthroplasty with proximal femur nail in unstable intertrochanteric femur fractures over 85 years of age

85 yaş üstü instabil intertrokanterik femur kırıklarında uzun stemli sementsiz hemiartroplasti ile proksimal femur çivisinin karşılaştırılması

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Ethics Committee Approval: The study was approved by the Clinical Research Ethics Committee of Maltepe University Faculty of Medicine on 5/22/2020 (Number: 2020/900/36). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
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Abstract

Aim: The most appropriate treatment option for intertrochanteric femoral fractures is still controversial. While there are articles showing that proximal femoral nails are superior to partial prostheses, other studies claim that partial prostheses result in better patient outcomes. We aimed to compare long-stemmed cementless hemiarthroplasty (LFS-BPH) and proximal femur nail (PFN), which are the treatment options applied in unstable intertrochanteric hip fractures in patients over 85 years of age.

Methods: The records of 64 patients with unstable intertrochanteric femur fractures who were operated between May 2016 and December 2018 in the Orthopedics and Traumatology Clinic of Maltepe University Medical Faculty Hospital were evaluated. A retrospective cohort study was conducted and 42 patients who met the inclusion criteria were included in the study. The patients were divided into 2 groups as the proximal nail group and the prosthesis group, and evaluated in terms of total hospitalization time, operation time, amount of blood transfusion, time until the patient walked independently, postoperative complications, and Harris hip scores.

Results: There were statistically significant differences in favor of the PP group in terms of total length of stay, fully independent mobilization time, deep vein thrombosis and decubitus development in the postoperative period. There was no difference between LFS-BPH and PFN in terms of total hospitalization time, blood transfusion amount, and Harris hip scores in unstable intertrochanteric hip fractures occurring above 85 years of age.

Conclusion: LFS-BPH was superior to PFN in terms of operation time, early independent mobilization, reduction of deep vein thrombosis and decubitus development rate in the postoperative period.

Keywords: Intertrochanteric fractures, Intramedullary nailing, Hip prosthesis, Geriatric

Öz

Amaç: İntertrokanterik femur kırıkları için en uygun tedavi seçeneği halen tartışmalıdır. Proksimal femoral tırnakların parsiyel protezlerden üstün olduğunu gösteren makaleler varken, diğer çalışmalar kısmi protezlerin daha iyi hasta sonuçları verdiğini iddia etmektedir. Mayıs 2016 ile Aralık 2018 tarihleri arasında Maltepe Üniversitesi Tıp Fakültesi Hastanesi Ortopedi ve Travmatoloji Kliniğinde opere edilen 85 yaş üstü instabil intertrokanterik kalça kırığı vakalarında uygulanan tedavi seçeneklerinden uzun stemli sementsiz hemiartroplasti (UFS-BPH) ile proksimal femur çivisinin(PFN)karşılaştırılması amaçlandı.

Yöntemler: 64 AO/OTA 31-A2.3 instabil intertrokanterik femur kırığı hastasının kayıtları retrospektif olarak değerlendirildi. Dâhil edilme kriterlerine uyan 42 hasta çalışmaya alınıp 2 homojen gruba ayrıldı. Gruplar toplam yatış süresi, operasyon süresi, kan transfüzyon miktarı, hastanın tek başına bağımsız olarak yürümesine kadar geçen süre, postoperatif dönemde gelişebilecek derin ven trombozu ve dekübitüs yara gelişimi ve Harris kalça skorları açısından değerlendirildi.

Bulgular: Gruplar arasında toplam yatış süresi, tam bağımsız mobilizasyon süresi ve postoperatif dönemde derin ven trombozu ve dekübitüs gelişimi açısından PP grubu lehine istatistiksel olarak anlamlı fark saptanmıştır. Yapılan çalışma sonucunda 85 yaş üstü instabil intertrokanterik kalça kırığı vakalarında toplam yatış süresi, kan transfüzyon miktarı ve Harris kalça skorları açısından UFS-BPH ile PFN arasında bir farka rastlanmadı.

Sonuç: Ameliyat süresi, erken bağımsız mobilizasyon ve postoperatif dönemde gelişebilecek derin ven trombozu ve dekübitüs yara gelişim oranının azaltılması açısından UFS-BPH nin PFN ne göre daha üstün olduğu görüldü.

Anahtar kelimeler: İntertrokanterik kırık, İntramedüller çivileme, Kalça protezleri, Geriatri

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Introduction

Hip fracture surgery is one of the most common operations in orthopedic surgery [1–4]. The worldwide incidence of hip fractures is 2.3% per year [5]. Surgical indications for femoral neck fractures (CFF) are clearer than those for intertrochanteric femoral fractures (ITF) [6]. If the rate of fracture union is high in CFF, osteosynthesis is preferred, otherwise, arthroplasty is the procedure of choice [6]. However, ITFs have higher fracture union rates compared to CFFs. Despite this union rate, hemiarthroplasty is performed by many surgeons [7]. ITF surgery is still controversial, especially in older patients [8].

In order to contribute to the discussion about the indications for ITF surgery, we compared long femoral stemless bipolar hemiarthroplasty (LFS-BPH) and proximal femoral nail (PFN) outcomes in terms of total hospitalization time, operation time, amount of blood transfusion, time until the patient walks independently, postoperative complications and Harris hip scores.

Materials and methods

This retrospective cohort study was conducted in Maltepe University Hospital. There were 64 patients with unstable ITF who were operated between 2016 and 2019. Data were collected from hospital files, operating room, and polyclinic records.

Inclusion criteria included having unstable ITF and being over 85 years of age, coming to outpatient clinic controls in the first 6 postoperative months, and not having had a revision surgery due to implant failure or infection in the postoperative period.

The study was started with 42 patients who met the inclusion criteria. All patients were selected according to the AO classification, according to which 12 patients were A2.2, 8 patients were A2.3, 8 patients were A3.1,6 patients were A3.2 and 8 patients were A3.3. Preoperative anesthesia evaluation was performed: According to the ASA (American Society of Anesthesiologists) classification, 37 patients included in the study were ASA4 and 5 patients were ASA3.

The patients were divided into 2 groups as those who underwent LFS-BPH and PFN. The groups were evaluated in terms of total hospitalization time, operation time, amount of blood transfusion, time until the patient walked independently, presence of deep vein thrombosis in the postoperative period, development of decubitus wounds, and Harris hip scores [8]. Deep vein thrombosis was evaluated with Doppler USG, decubitus ulcers were clinically diagnosed, and the hip scores of both groups were calculated using the Harris hip score at the 6th postoperative month.

Surgical technique

All patients who underwent PFN were placed supine on the traction table. Under fluoroscopy, traction, adduction, and internal rotation were applied gradually, and reduction was absolutely controlled in the anterior and lateral planes. PFN was adapted to the femoral medulla with fluoroscopy after raemerization over the K-wire. PFN was locked with 2 dynamic screws locking each other on the femoral neck and 1 dynamic screw on the femur shaft (SMITH NEPHEW trigene intertan, Cordova, USA) (Figure 1).

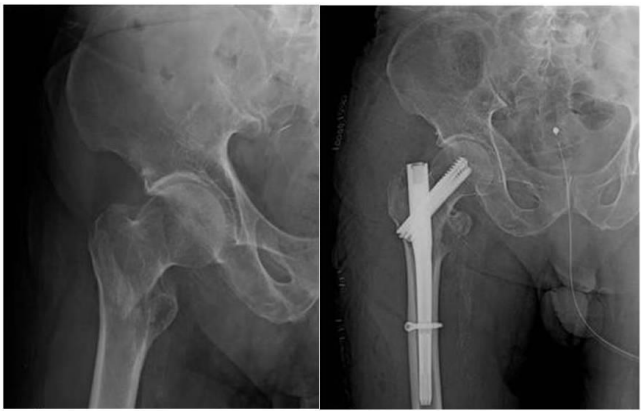

Figure 1: Preoperative and postoperative radiographs of the patient in whom intramedullary nail was applied for intertrochanteric femur fracture

All patients in the UFS-BPH group were placed in lateral supine position. Following a 12 cm skin incision with a posterior hip approach, the subcutaneous tissues were incised and the short rotator muscles were cut with a sling suture. T incision was performed to the hip joint capsule. The fractured femoral neck was exposed, and the femoral capsule was opened. The fractured femoral head and neck were removed from the fracture line at the femoral neck. After the femoral medulla was prepared, an appropriately sized uncemented femoral stem was adapted to the femur medulla with a femoral bipolar head (T2, Tıpsan, Izmir, Turkey) (Figure 2).

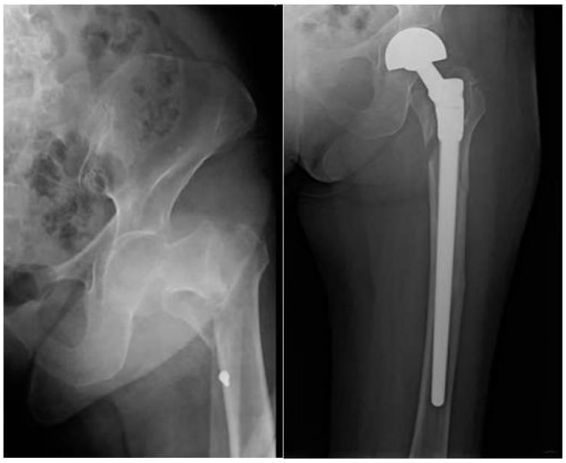

Figure 2: Preoperative and postoperative radiographs of the patient in whom intramedullary nail was applied for intertrochanteric femur fracture

All patients were put on anti-embolic stockings from the first day of hospitalization to the 30th postoperative day and anticoagulant prophylaxis was performed. On the 1st postoperative day, both groups of patients started in-bed exercise, on the 2nd day, patients were mobilized with help.

Statistical analysis

SPSS 25.0 program was used for analysis. Frequency analysis was performed for demographic data. For comparison, parametric data were analyzed with the Chi-square, Student t and ANOVA tests, while non-parametric data were analyzed with Mann Whitney U and Kruskal Wallis tests. *P*-value <0.05 was considered statistically significant.

Results

Among the patients participating in the study, there were 19 males and 23 females. The mean age of all patients was 89.6 (86-99) years. Mean follow-up time was 26.4 weeks (24-29

weeks). Twenty-three patients were in the UFS-BPH group and 19 were in the PFN group (Table 1).

UFS-BPH group was superior to the group with PFN in terms of total hospital stay, total operation time and independent mobilization time (P=0.29, P=0.02 and P<0.001, respectively). However, no difference was found in terms of the number of erythrocyte suspensions used during and after surgery, and the 6th Month Harris Hip Scores (P=0.74 and P=0.65, respectively) (Table 2).

When compared in terms of postoperative complications, the rate of decubitus ulcer in the UFS-BPH group was insignificantly lower than the group with PFN (P=0.23). The rate of DVT in the UFS-BPH group was significantly lower than the group with PFN (P=0.03) (Table 3).

Table 1: Distribution of demographic data by groups

	Groups		*P*-value
Demographic Information	LFS-BPH	PFN	
Number of patients (n)	23	19	
Average age (min.-max.)	88.7 (86-94)	90.6 (86-99)	0.16
Gender (F / M)	11/12	12/7	0.09
Average follow-up time (min.-max.)	24.6 (24-28)	27.1 (24-29)	0.89

LFS-BPH: Bipolar partial hemiarthroplasty with long femoral stems, PFN: Proximal femoral nail, min: Minimum, max: Maximum, F: Female, M: Male

Table 2: Comparison of independent variables according to the implants used

Independent variables, mean (SD)	LFS-BPH	PFN	*P*-value *
Average length of stay in hospital	5.39 (0.7)	4.58 (0.9)	0.29
Operation times (min)	60.9 (9.8)	106.3 (13.9)	0.02
Duration until independent mobilization	3 (1.2)	32.5 (6.9)	<0.001
Erythrocyte Suspension number	1.7 (0.68)	1.7 (0.65)	0.74
Harris Hip Scores	77.1 (9.1)	77.0 (9.2)	0.65

LFS-BPH: Bipolar partial hemiarthroplasty with long femoral stem, PFN: Proximal femoral nail, SD: standard deviation, min: minutes, * Independent Sample Test

Table 3: Distribution of postoperative complications by groups

Postoperative complications, mean (%*)	LFS-BPH	PFN	*P*-value §
DVT	3 (13%)	8 (42.1%)	0.03
Decubitus ulcer	4 (17.4%)	6 (31.6%)	0.23

LFS-BPH: Long femoral stem bipolar partial hemiarthroplasty, PFN: Proximal femoral nail, DVT: Deep vein thrombosis, * Percentage within implant groups, § Pearson Chi-Square Test

Discussion

In our study, it was observed that UFS-PBH was superior to PFN due to the shorter independent mobilization time, less postoperative complications such as deep vein thrombosis and decubitus wounds, and short operative time.

Hip fractures constitute an important public health problem in the world. They progress with high mortality in old age patient groups. Conservative treatment has a limited place; the main treatment for hip fractures is surgery [10]. ITFs are observed 3 times more than CFFs [11]. The surgical approach to CFFs has gained clarity in the literature [12], while surgical indication in ITFs is still controversial [13]. While many surgeons always prefer osteosynthesis in ITF, many surgical teams prefer hemiarthroplasty [14].

In the literature, there are comparative studies with different views for surgical indication in old age ITFs. In their meta-analysis in 2019, Bao et al. [15] examined 1067 patients and published results in favor of early weight-bearing and low-complication hemiarthroplasty, while surgical time, length of stay, blood loss and Harris scores were similar for hemiarthroplasty and PFN. In this study, both cemented and non-cemented hemiarthroplasty were performed and patients over 65 years of age were selected. Nie et al. [16] emphasized that PFN was superior to hemiarthroplasty due to its high Harris scores, low blood loss and short operation time in the meta-analysis of 1239 patients in 2017. In their series of 1239 patients, Nie et al. [16] reported no clear data about the time until independent mobilization in patients with ITF. This meta-analysis was performed between 1980 and 2016 with patients over 60 years of age. The results are not similar, even with recent, very large series of patients. The retrospective selection of patients over the age of 85 years and the creation of two homogeneous groups were the highlights of our study.

In our study, we found that the surgical durations of our patients with UFS-BPH were considerably shorter than that of our patients with PFN. On the contrary to our study, Korkmaz et al. [17] found the duration of surgery to be shorter in the group with PFN. In the studies of Korkmaz et al, there is no clear data on whether the time for positioning the patient is added or not. The difference in our study is that the time elapsed until closed reduction is achieved in PFN surgery during the operation. In addition, the use of cementless stem shortens the operation time in LFS-BPH. Exposure to anesthesia is less in LFS-BPH surgery compared to PFN surgery. In the literature, it has been observed that the use of cementless stem decreases the operation time [18]. Li et al. [19] compiled 1577 hip hemiarthroplasty surgeries, and it was observed that the durations of non-cemented hemiarthroplasty were consistent with those in our study.

While there are authors in the literature claiming that blood loss is not related to surgical technique and is caused by fracture [19], there are publications that support the need for less transfusion in PFN compared to LFS-PBH [20]. In the meta-analysis of Bao et al. [15] the need for blood transfusion was less than that in PFN, but there was no difference in blood loss between these two groups during the entire hospitalization period. In our study, not only the peroperative needs of the patients were calculated, but the transfusions performed during the entire hospitalization period were examined as well. The transfusion needs of UFS-PBH and PFN patients were equal.

They found that the length of stay was equal in LFS-PBH and PFN in Nie et al.'s series of 1239 patients and Bao et al.'s series of 1067 patients [15,16]. On the other hand, Jian-Bin [21] reported that the length of stay in hemiarthroplasty was short. In our study, no significant difference was found between the two groups in terms of length of stay. Being over the age of 85 years and having advanced ASA scores were more effective on hospitalization periods.

In the series of Bao et al. [15], the incidence of deep vein thrombosis was higher in the group with PFN, while Jian-Bin Dong et al. [21] published equal results in both groups in their 2015 study. In our study, they found a significant difference in DVT between 2 groups. Although all patients with unstable ITF were given anticoagulant prophylaxis from the first day of hospitalization and anticoagulant maintenance and anti-embolic stockings were used for 30 days after discharge, deep vein thrombosis was more common in the group undergoing PFN surgery. Studies in the literature that show that prolonged immobilization increases deep vein thrombosis support our results [22].

In a meta-analysis of 8871 patients conducted in April 2020, Galivanche et al. [23] associated decubitus wounds with the patient's preoperative skin condition or any postoperative complications. According to this meta-analysis, the surgical technique was not important. In the study of Jian-Bin et al., they found that decubitus wounds were less in patients who

underwent PFN compared to hemiarthroplasty. In our study, although we encountered more decubitus ulcers in the PFN group, no statistical differences were found.

In the literature, it has been reported that patients who underwent hemiarthroplasty were mobilized earlier than those who underwent PFN [24]. While there are studies in which cemented hemiarthroplasty was performed and patients were mobilized early [25], some other studies regarding uncemented hemiarthroplasty have also been conducted[26]. Wang et al. [27] published a research about the need to load weight on the operated extremity for independent mobilization, due to atrophy and arthrosis in the upper extremities of geriatric patients. In our study, in accordance with the literature, it was observed that patients who underwent LFS-PBH were mobilized earlier than those in the PFN group.

In the study of Jian-Bin et al. [21], Harris scores were high in the group with hemiarthroplasty, while in a similar meta-analysis, Nie et al. [16] presented the Harris scores as high in the group with PFN. Although it was observed that Harris scores were high in PFN at the end of the 4th week, it was reported that they were equal in the 12th week [28]. Jonnes et al. [29] found no significant difference between the 3-month Harris results of PFN and LFS-PBD in their comparative study. In our study, when we compared the 6-month hip Harris scores of the LFS-PBH and PFN groups, no significant differences were found.

Limitations and strengths of the study

One of the limitations in our study was that age-related skeletal system problems and cognitive functions were ignored while calculating the time until the patient could walk independently. The other limitation was the lack of comparison with the pre-transfusion control group, as the need for transfusion of geriatric patients may be higher than the normal population.

The strength of our study was that all patients were over the age of 85 years and all fractures were unstable. In the literature, while a comparison has been made with a large case series over 60 and 65 years of age, regardless of the fracture type, there is no comparative study with patients with unstable fractures over 85 years of age.

Conclusion

In unstable intertrochanteric fractures over the age of 85 years, PFN and UFS-PBH surgery did not show superiority to each other in terms of hospital stay, amount of blood transfusion and Harris hip scores. LFS-PKD was superior to PFN due to shorter time until independent mobilization, fewer complications such as deep vein thrombosis and decubitus wounds in the postoperative period, and short operation time.

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Evaluation of perinatal arterial ischemic stroke patients: A single center experience

Perinatal arteriyel iskemik inme hastalarının değerlendirilmesi: Tek merkez deneyimi

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Abstract

Aim: Perinatal arterial ischemic stroke (PAIS) is the one of the frequent causes of morbidity and neurologic disability, such as unilateral cerebral palsy (UCP), epilepsy and neurodevelopmental deficiencies. The aim of this study is to determine the clinical characteristics, risk factors and long term outcomes of PAIS patients.

Methods: This retrospective cohort study was conducted with 49 PAIS patients who were followed up in the Pediatric Neurology Department between January 2009 and September 2015. Clinical data including demographic features, gestational history, age at diagnosis, initial clinical presentation, brain MRI features, perinatal risk factors and long-term outcome were collected from patient files.

Results: The study group comprised 30 females and 19 males with a mean age of 6.3 (4.5) years. Twin pregnancy (6.1%), intrauterine growth retardation (IUGR) (8.2%), peripartum asphyxia (8.2%) and presentation abnormality (6.1%) were the most common maternal / neonatal risk factors. The most common prothrombotic risk factors were MTHFR mutations (42.85%), followed by FVL mutations (16.32%). The epilepsy rate was 73.3%, 6.4% of which had refractory epilepsy. All patients had UCP.

Conclusions: Risk factors and their roles in development of PAIS have not been fully established. According to this study, most of the PAIS patients have at least one or more maternal, neonatal or prothrombotic risk factors, and all patients have motor and cognitive impairment related with PAIS. Multi-center prospective studies with more cases are needed to fully enlighten the causes of this disease and to develop preventive measures.

Keywords: Perinatal, Neonatal, Ischemic, Stroke, Epilepsy

Öz

Amaç: Perinatal arteriyel iskemik strok (PAIS), unilateral serebral palsi (UCP), epilepsi ve nörogelişimsel bozukluklar gibi morbidite ve nörolojik hastalığın sık nedenlerinden biridir. Bu çalışmanın amacı, PAIS hastalarının klinik özelliklerini, risk faktörlerini ve uzun vadeli sonuçlarını belirlemektir.

Yöntemler: Bu retrospektif kohort çalışma, Ocak 2009-Eylül 2015 tarihleri arasında Çocuk Nörolojisi Bölümünde takip edilen 49 PAIS hastası ile yapılmıştır. Demografik özellikler, gebelik öyküsü, tanı yaşı, ilk klinik bulgu, beyin MRG bulguları, perinatal risk faktörlerini ve uzun vadeli sonuçları hasta dosyalarından toplandı.

Bulgular: Çalışma grubu yaş ortalaması 6,3 (4,5) yıl olan, 30 kadın ve 19 erkekten oluşmuştur. İkiz gebelik (%6,1), intrauterin büyüme geriliği (IUGR) (%8,2), perpartum asfiksi (%8,2) ve prezentasyon anormallikleri (%6,1) en sık görülen maternal / neonatal risk faktörleri idi. En yaygın protrombotik risk faktörleri ise MTHFR mutasyonları (%42,85) ve FVL mutasyonlarıydı (%16,32). Hastalardaki epilepsi oranı %73,3 olarak saptandı ve bu hastaların % 6,4'ünde dirençli epilepsi vardı. Tüm hastalar unilateral serebral palsi tanısı ile izleniyordu.

Sonuç: PAIS risk faktörleri ve bu risk faktörlerinin PAIS gelişimindeki rolleri tam olarak belirlenmemiştir. Bu çalışmaya göre, PAIS hastalarının çoğunda en az bir veya daha fazla maternal, neonatal veya protrombotik risk faktörü bulunmaktadır. Ve tüm hastalarda PAIS ile ilgili motor ve bilişsel bozukluk vardır. Bu hastalığın nedenlerini tam olarak aydınlatmak ve önleyici tedbirler geliştirebilmek için daha fazla vaka içeren çok merkezli prospektif çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Perinatal, Yenidoğan, İskemik, İnme, Epilepsi

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Introduction

Perinatal arterial ischemic stroke (PAIS) is an important cause of chronic neurological morbidity such as cerebral palsy (CP), epilepsy, cognitive dysfunction, language and behavioral problems [1]. PAIS occurs in an estimated 1:2300-4000 term births [1,2]. PAIS may cause no symptoms or subtle or nonspecific symptoms, therefore the age of diagnosis of PAIS varies. It is divided into 3 groups according to the age of diagnosis. Fetal stroke is diagnosed before birth by fetal imaging methods or in stillbirths on the basis of neuropathological examination, neonatal stroke is diagnosed after birth and on or before the 28th postnatal day, presumed perinatal stroke is diagnosed in infants >28 days of age but in whom the event is presumed to have taken place between the 20th week of gestation and the 28th postnatal day [3,4]. In the newborn period, PAIS mostly presents with seizures. There may also be signs and symptoms of neonatal encephalopathy such as lethargy, hypotonia, feeding difficulties, or apnea. Presumed PAIS is diagnosed when children present with a focal hand weakness (or early handedness), seizures or global developmental delay [3,5].

The etiology of PAIS remains unclear. Various maternal and neonatal risk factors have been identified in previous studies such as preeclampsia, maternal fever, small for gestational age, oligohydramnios, birth asphyxia, hypoglycemia, chorioamnionitis, twin pregnancy, congenital heart diseases, low Apgar score and peripartum asphyxia [5-7]. Genetic disorders may play a role in the pathogenesis of PAIS. Prothrombotic risk factors including MTHFR and factor V Leiden mutation, elevated lipoprotein (a), prothrombin gene mutation, and protein C deficiencies can be associated with PAIS [8,9].

This study focuses on neonatal and presumed perinatal arterial ischemic stroke. The aim of this study was to identify risk factors, clinical presentations, and neurodevelopmental outcomes of PAIS.

Materials and methods

This study was performed retrospectively on 49 perinatal arterial ischemic stroke patients who were diagnosed and followed at Eskisehir Osmangazi University Hospital, Department of Pediatric Neurology between January 2009, and September 2015. The principles of the Declaration of Helsinki were abided. Written informed consent was obtained from each of the parents and/or legal representatives before the patient's inclusion in the study.

This study included neonatal and presumed PAIS patients. The diagnoses of neonatal and presumed PS were based on clinical features, neurological examinations, and cranial magnetic resonance imaging (MRI) findings. Inclusion criteria were term birth, PS confirmed with neuroimaging (magnetic resonance imaging (MRI)) and a follow-up of more than 12 months. Exclusion criteria included cortical dysplasia, congenital cerebral anomaly, brain tumor, sequela of hypoxic ischemic encephalopathy, central nerve system infection, cerebrovascular disorders, or trauma.

The patients' following data were obtained by evaluating hospital files retrospectively using a standard form: Consanguineous marriage, number of pregnancies, age of pregnancy, detailed prenatal and natal history, perinatal stroke types, age of first symptoms, age at the time of diagnosis, maternal-fetal risk factors, neuroimaging findings and clinical features.

Among the laboratory data, the following thrombophilic screening tests were obtained from the patient files retrospectively: Protein C and S, antithrombin III (ATIII), lipoprotein (a), homocysteine, factor VIII levels, anticardiolipin antibodies and lupus anticoagulant, methylenetetrahydrofolate reductase (MTHFR) mutations (C677T and/or A1298C), factor V Leiden mutation(FVL) and prothrombin G20210A mutation.

Cranial MRI examinations were performed on admission at 1.5 Tesla at different institutions using T1- and T2-weighted spin-echo, and inversion recovery sequences in the axial, sagittal and coronal planes.

Results

A total of 49 patients were enrolled in the study (61.2% females, 38.8% males). The mean age of the patients was 6.36 (4.5) years, with a range of 1-17 years. Thirty-two patients (65.3%) were presumed to have perinatal stroke, and 17 patients (34.7%) were diagnosed with neonatal perinatal stroke. Thirty-three (67.3%) patients had right, and 16 (32.7%) patients had left hemiplegia. The average duration of follow-up was 4.2 years (range: 1–15 years).

Consanguineous marriage was present in 18.4% of parents. About 10.2% of the pregnant women were under 20 years of age, 12.2% were over 35 years of age and 40.8% had the first pregnancy. Among all, 63.3% patients were born with spontaneous vaginal delivery and 37.7% with caesarian section. One mother (2%) had chronic hypertension and one had multiple sclerosis (2%). Twin pregnancy was present in 6.1% of patients and 41.5% were the first pregnancy. Other maternal/fetal risk factors were as follows: Intrauterine growth retardation (IUGR) (8.2%), gestational diabetes, peripartum asphyxia (8.2%), presentation abnormality (6.1%), preeclampsia (4.1%), abnormal vaginal bleeding (4.1%), fetal heart rate abnormality (4.1%), and emergency cesarean delivery (4.1%). Prothrombotic risk factors were detected in 73.5% of the patients. The most common prothrombotic risk factors were MTHFR mutations (42.85%), followed by FVL mutations (16.32%). Co-existence of MTHFR and FVL mutations were detected in 8.2% of patients and 26.5% of patients had no prothrombotic risk factors (Table 1).

Table 1: Prothrombotic risk factors of patients

Prothrombotic risk factors	n	%
MTHFR mutation		42.85
C677T	7	
A1298C	8	
C677T+A1298C	2	
C677T+FVL	4	
FVL mutation	4	16.32
FVL+MTHFR(C677T)	4	
Elevated Lp(a)	4	8.16
Prothrombin G20210A mutation	2	4.08
PC deficiency	1	2.04

All patients' echocardiography results were normal. None had family histories of cerebrovascular disorders and stroke recurrence was not observed in any of the patients.

Patients had different presentations before receiving the diagnosis of PAIS. Around 59.1% presented with early handedness, 22.4% with seizures, 10.2% with hypotonia, 6.1% with apnea, 29.4% with hypotonia, and 2.2% with

encephalopathy. The epilepsy rate among patients was 73.3%, 6.4% of which had refractory epilepsy. All patients had different impairments in motor or cognitive functions. All the patients had unilateral cerebral palsy (UCP). Speech problems were present 34.2% of patients and 21.2% had behavioral problems.

On brain MRI investigations, 67.3% of patients had chronic encephalomalacia at frontotemporoparietal region supplied by the left middle cerebral artery, and 32.7% had chronic encephalomalacia at frontotemporoparietal region supplied by the right middle cerebral artery. Among all, 14.3% had cortical lesions.

Discussion

Perinatal arterial ischemic stroke is the most frequent type of pediatric stroke. It has been increasingly recognized with the availability and safe use of MRI in newborns in recent years. However, the etiopathogenesis of PAIS is not yet clear. PAIS has an extremely low recurrence rate, which suggests that pregnancy and perinatal state may have important roles in pathophysiology [10,11]. The majority of PAIS is most likely caused by thromboembolism passing from the placenta through the patent neonatal foramen ovale [12,13]. The left middle cerebral artery (MCA) is the most common vessel involved, with the left cerebral hemisphere being the most common region affected [14,15]. The emboli may pass through a patent foramen ovale or patent ductus arteriosus directly into the left common carotid artery and then to the left MCA [15]. Chorioamnionitis, congenital heart disease, twin pregnancy, bacterial meningitis, traumatic birth injury and peripartum asphyxia are the other main causes and risk factors of PAIS [6,12,15]. In accordance with the literature, peripartum asphyxia and twin pregnancy were the most common risk factors in our study.

Prothrombotic risk factors may be important causes of PAIS, and they were reported at different rates in previous studies. Kocaman et al. [8] stated that at least one of thrombophilia risk factors was present in 69% of the cases. Another study reported that thromboembolic risk factors were found in 68% of PAIS patients, compared with 24% of normal controls [17]. Curry et al. [18] found MTHFR mutations in 68% of PAIS patients. Kocaman et al. [8] reported that MTHFR mutation was the most frequent thrombophilic factor (57%), which was followed by FVL mutation (20%), like our study. In this study, 73.5% of patients had at least one of the prothrombotic risk factors.

PAIS may cause no or nonspecific symptoms, which may result in diagnostic delay. In the neonatal period, PAIS may present with focal and systemic symptoms including seizures, apnea, hypotonia, encephalopathy, feeding difficulties, fever, and irritability [19,20,21]. A delayed presentation after the age of 2 months was observed in 40% to 65% of PAIS in previous studies [19,21,22]. Presumed PAIS patients are generally referred to the pediatric neurology department because of handedness, seizure or neurodevelopmental delay. In this study, 50.9% of presumed PAIS patients presented with early handedness, 18.1% with seizure and 30% with neurodevelopmental delay.

PAIS is the one of the frequent causes of morbidity. Almost all PAIS patients present with UCP [23]. Children with PAIS who have cortical involvement carry a higher risk for epilepsy, cognitive impairment and learning disabilities [5,24]. Frequency of epilepsy is highly variable, ranging from 24.6% to 54%, among children with PAIS [24-27]. In this study, all patients presented with UCP and 73.3% had epilepsy, among which 6.4% had refractory epilepsy and all had cortical lesions on brain MRI. Speech problems were present 34.2% of patients and 21.2% had behavioral problems.

Limitation

The main limitation of this study is its retrospective nature. Additionally, there was no healthy control group in this study. To understand the role of prothrombotic risk factors in stroke mechanism, it would be more meaningful to compare the frequency of prothrombotic risk factors in PAIS patients with the healthy population.

Conclusion

PAIS is an important cause of neurologic and cognitive dysfunctions. However, the pathophysiology and causes of PAIS are not fully established. We determined that prothrombotic and maternal risk factors are important in the development of PAIS, in accordance with the literature. Risk factors' interdependence and role in the causal pathway of PAIS are still poorly understood. Multicenter prospective studies involving control groups are needed to determine the role of risk factors in the pathophysiology of PAIS.

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General characteristics of otorhinolaryngology consultations: 3-year analysis

Kulak burun boğaz hastalıkları konsültasyonlarının genel özellikleri: 3 yıllık analiz

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Abstract

Aim: Nowadays, with the rapid development and change of knowledge in the scientific field, the number of specialty branches in medicine has increased. Therefore, the rate of consultation requests in different specialties during the patient evaluation process gradually escalates. This study aims to evaluate the characteristics of the diagnostic and therapeutic consultations requested from the Otorhinolaryngology (ENT) branch in a university hospital.

Methods: In this cross-sectional study, the data of patients consulted to the ENT clinic of Kütahya University of Health Sciences Evliya Çelebi Training and Research Hospital between January 1st, 2017 and December 31st, 2019 were retrospectively scanned. Apart from demographic findings such as age and gender, departments requesting the consultation, post-consultation diagnoses and surgical treatments performed by an ENT physician were noted.

Results: The total number of patients with an ENT consultation was 2340. The mean age of the patients was 45.95 (25.09) years. Most consultation requests were made from the emergency department (n=877, 37.5%), which was followed by 278 requests (11.9%) by the neurology and neurology ICU departments, and 193 (8.2%) requests by the anesthesiology and intensive care unit (ICU) departments. Although varying among age groups, epistaxis (10%) and vertigo (dizziness) (10%) were the most common diagnoses. A total of 146 patients received surgical treatment. The most common surgical operations were tracheotomy and nasal bone fracture reduction.

Conclusion: Determining the characteristics of patients for whom ENT consultation is required will be beneficial in shaping the training programs for other clinics, reducing unnecessary consultation requests, thus reducing the workload of ENT physicians.

Keywords: Consultation, Otorhinolaryngology, University hospital

Öz

Amaç: Günümüzde bilimsel alanda bilginin çok hızlı bir şekilde gelişimi ve değişimi ile birlikte tıpta uzmanlık dallarının sayısı artmıştır. Bu nedenle hasta değerlendirme sürecinde farklı uzmanlık dallarından konsültasyon istenme oranları giderek artmaktadır. Bu çalışmanın amacı bir üniversite hastanesinde kulak burun boğaz hastalıkları (KBB) branşından tanısal ve tedavi amaçlı istenilen konsültasyonların özelliklerinin değerlendirilmesidir.

Yöntemler: Bu kesitsel çalışmada 01.01.2017 - 31.12.2019 tarihleri arasında Kütahya Sağlık Bilimleri Üniversitesi Evliya Çelebi Eğitim ve Araştırma Hastanesi KBB Hastalıkları kliniğine konsültasyonla yönlendirilen hastaların dosyaları retrospektif olarak tarandı. KBB hastalıkları konsültasyonu istenen olguların yaş, cinsiyet gibi demografik bulgularının dışında; konsültasyon istenen branş, konsültasyon sonrası konulan tanıları ve KBB hekimi tarafından yapılan cerrahi tedavileri not edildi.

Bulgular: 3 yıl içinde KBB hastalıklarına konsültasyon istemi yapılan toplam hasta sayısı 2340'dır. Hastaların yaş ortalamaları 45,95 (25,09)'dir. En çok konsültasyon istemi 877 (%37,5) hasta ile acil servis bölümünden olmuştur. Acil servis bölümünü 278 (%11,9) hasta ile nöroloji ve yoğun bakım ünitesi (YBÜ), 193 (%8,2) hasta ile anestezi ve YBÜ takip etmiştir. Hastalara konsültasyon sonrası yaş gruplarına göre değişmekle birlikte toplamda en sık epistaksis (%10) ve baş dönmesi (%10) tanıları konulduğu görülmüştür. 146 hastaya konsültasyon sonrası cerrahi girişim uygulanmıştır. En sık yapılan cerrahi girişimler trakeotomi açılması ve nazal fraktür onarımı olarak bulunmuştur.

Sonuç: KBB konsültasyonu istenilen hastaların özelliklerinin belirlenmesi, diğer branşların eğitim programlarının şekillenmesinde faydalı olacak, gereksiz konsültasyon istemlerinin azalmasını sağlayacak böylece KBB hekimlerinin iş yükünü azaltacaktır.

Anahtar kelimeler: Konsültasyon, Kulak burun boğaz hastalıkları, Üniversite hastanesi

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Introduction

Scientific and technological advances in medicine have enabled the diversification and specialization of different medical branches. The specialization of physicians in certain branches has increased the effectiveness and efficiency in the relevant field, however, it has led to the need for multiple physicians in patients with multiple organ complications or systematic diseases. The practice of consultation, in which more than one physician participates in the diagnosis and treatment process, is an important health service in approaching the patient [1].

Consultation can be defined as a request of help or counseling by the primary responsible physician to a physician in another clinic, sharing all the information gathered during the diagnosis, treatment, and follow-up process about the patient. Thus, physicians in different clinics participate in the diagnosis and treatment process of the same patient, and the quality of healthcare service increases by ensuring that the patient is provided with the most appropriate healthcare service. Numerous studies are examining the consultation requests in many branches, which include consultations requested especially by the emergency service. There are also studies on internal medicine, general surgery, thoracic surgery, chest diseases and dermatology, as well [2-6]. However, studies examining the ENT section are very limited. The main purpose of this study is to make a three-year retrospective analysis of patients who were referred to the ENT department from other clinics in a university hospital.

Materials and methods

This study was conducted after approval was obtained from Kütahya University of Health Sciences (KUHS) Institutional Ethics Committee for Non-Invasive Research, with the reference number 10/21/2020- 2020/15-06.

In this study, the files of patients, who were referred with a consultation to the ENT department of the KUHS Evliya Çelebi Training and Research Hospital between January 01, 2017, and December 31st, 2019 (included), were retrospectively scanned. Apart from demographic findings such as age and gender, the departments requesting the consultation, post-consultation diagnoses and surgical treatments performed by an otorhinolaryngologist were noted. The data of patients whose consultation requests are not finalized by ENT physicians were not included in this study. Patients who received surgical treatment by an otolaryngologist and consulted for emergency services due to postoperative complications were also excluded.

Statistical analysis

The data obtained from the study were evaluated using open source software 'Jamovi' (version 1.1.9). During the statistical evaluation of the data obtained from the study, categorical data were summarized in frequency (n) and percentage (%).

Results

The total number of patients for whom consultation was requested from ENT diseases between 01.01.2017 and 31.12.2019 was 2340. The mean age of the patients was 45.95 (25.09) years. Among the patients included in the study, there were 1368 (58.5%) males and 971 (41.5%) females. A total of 394 of these patients were within the pediatric age range and 667 were geriatric patients over 65 years of age. The demographic findings of the patients are summarized in Table 1.

Table 1: The demographic findings of the patients

Number of patients	2340
2017	953 (40.7%)
2018	817 (35%)
2019	569 (24.3%)
Mean Age	45.95 (25.09)
Distribution of patients by age	
Ages 0 – 17	394 (16.8%)
Ages 18 – 64	1279 (54.7%)
Ages > 65	667 (28.5%)
Gender	
Male	1368 (58.5%)
Female	971 (41.5%)
Number of outpatients / inpatients	839 (35.8%) / 1501 (64.2%)

Most of the consultations were from the emergency department with 877 (37.5%) patients. The emergency department was followed by 278 requests (11.9%) from the neurology and neurology ICU departments and 193 requests (8.2%) from the anesthesiology department and the ICU. The distribution of the departments requesting an ENT consultation is summarized in Figure 1.

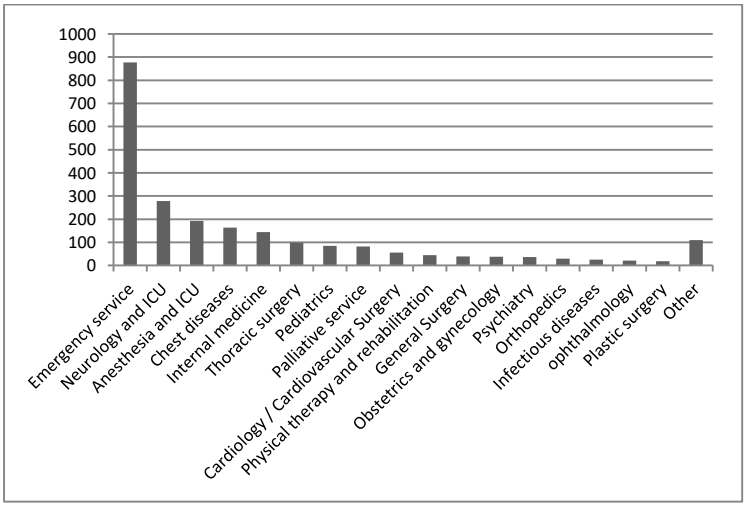

Figure 1: Distribution of departments requesting an ENT consultation

It was observed that the most common diagnoses made by the ENT department during a consultation were epistaxis (10%) and vertigo (dizziness) (10%). Epistaxis (98 patients), foreign body in the nose (69 patients), and nasal bone fracture (62 patients) were the most common reasons for consultation requests from the emergency department. The distribution of diagnoses of the consultations requested from the ENT diseases is summarized in Table 2.

The most common reason for consultation request was foreign body in the nose (18%), foreign body in the ear (11.4%), and nasal bone fracture (8.9%). In the 18-65-year age group, the most frequent cause of consultation was vertigo (dizziness) (12.6%), epistaxis (10.2%) and upper respiratory tract infection (9.5%). In geriatric patients, the most common causes were tracheotomy/tracheostomy and related complaints (13.9%), epistaxis (12.6%), and dizziness (9.1%).

Following ENT consultations, 66 patients were treated for tracheotomy, 65 patients for nasal bone fracture reduction, 5 patients for nasal bleeding, 4 patients for foreign body removal from the external auditory canal, 2 patients for neck exploration due to falling from a height, 2 patients for foreign body removal

from the nose, 1 patient for endoscopic sinus surgery due to firearm injury, and 1 patient received tracheotomy for foreign body aspiration and foreign body removal from the larynx.

It was observed that a detailed and thorough reason for the consultation request was written in the Hospital Information Management System (HIMS) in 1205 (51.5%) of the requests, while insufficient information was provided in 1135 (48.5%) patients.

Table 2: Distribution of diagnoses of consultations in ENT disease

	0-17 age	18-64 age	>65 age	Total
Otology				
Dizziness (vertigo)	10	162	61	233
Cerumen impaction	10	74	35	119
External and Middle ear infections (acute otitis media, acute serous otitis media)	30	46	13	89
Foreign body in the outer ear canal	45	25	6	76
Hearing loss	3	25	22	50
Chronic otitis media	12	22	9	43
Facial nerve paralysis	5	18	18	41
Tinnitus	2	10	1	13
Otorrhea	2	9	2	13
Traumatic eardrum perforation	2	10	-	12
Temporomandibular joint diseases	-	6	6	12
Sudden hearing loss	-	3	3	6
Superficial injury of the ear	1	-	3	4
Head and Neck Surgery				
Acute tonsillitis	11	54	1	66
Benign soft tissue masses	18	21	18	57
Intraoral / Tongue / lip diseases	2	12	16	30
Head and Neck trauma	10	3	1	14
Acute lymphadenitis	1	7	6	14
Foreign body in the mouth	3	5	2	10
Salivary gland diseases	-	5	5	10
Adenoid hypertrophy	9	-	-	9
Malign soft tissue masses	-	8	1	9
Oral candidiasis	-	2	6	8
Myalgia	1	3	2	6
Foreign body in the neck	2	-	-	2
Choanal atresia	1	-	-	1
Laryngology				
Tracheostomy/tracheotomy and related diseases	3	83	93	179
Dysphagia	3	7	24	34
Foreign body in the larynx	10	21	3	34
Voice disorder	1	16	12	29
Laryngeal malignancies	-	15	14	29
Vocal cord paralysis	-	9	3	12
Gastroesophageal reflux	1	5	5	11
Laryngomalacia	1	-	-	1
Rhinology				
Epistaxis	19	131	84	234
Upper respiratory tract infection (acute pharyngitis nasopharyngitis)	5	122	14	141
Nasal bone fracture	35	71	5	111
Foreign body in the nasal passage	71	-	-	71
Nasal septum deviation	5	-	30	35
Allergic rhinitis	7	19	9	35
Acute sinusitis	2	20	4	26
Superficial injuries of the nose	4	5	1	10
Nasopharyngeal / paranasal sinus malignancies	-	1	6	7
Headache	-	5	1	6
Sleep apnea	-	3	3	6
Traffic accident / work accident	9	36	3	48
Assault / gunshot injury	7	21	3	31
Dropping	5	8	4	17
Others	26	151	109	286
Total	394	1279	667	2340

Discussion

Aygencel et al. [2] found the rate of consultation requests by the emergency service to be between 20-40% in Turkey. In the same study, the most frequently consultation-requested departments were internal medicine, cardiology, and chest diseases, while the most consulted surgical branch was general surgery. Bali et al. [7] examined the distribution of one-year consultation requests in the context of the requester and requested departments, and found that among 6113 requests, the department which made the most requests was the emergency department with 991 (16.2%) requests, the department which received the most requests was the infectious diseases department, with 2047 (33.5%) requests. The same study reveals consultation requests made by the ENT department as 19 (0.03%) whereas consultation requests to the ENT department were 85 (1.4%). There is no other study in the literature that provides a request rate about ENT diseases. In the institution where the study was conducted, an average of 87,000 consultation requests were made in the last three years throughout the hospital. Of all consultation requests, 2340 (0.9%) were made to the ENT department. In this study, we found that the rate of consultation requests made to the ENT department is about 30 times higher, compared to the results provided by Bali et al.

In Turkey, studies reveal that the most frequent age group that is consulted in the emergency department is middle age (40-65 years) [8,9]. Parallel to this, the mean age of patients for whom ENT consultation request was made was 45.95 (25.09) years in our study. Reasons of consultation requests differ according to age groups. In the pediatric age group, the most common reason for consultation was a foreign body (18%) in the nose. Among the 18-64 age group, the most common reason for admission was vertigo (dizziness) (12.6%). In geriatric patients, the most common complaints regarded tracheotomy/tracheostomy (13.9%). There is no study in the literature examining the rates of consultation requests based on age groups. For this reason, epidemiological studies to be carried out in larger populations will play an important role in the planning of health services and the development of preventive health services.

In present study, the rate of consultation requests from ENT diseases was 780 patients per year. Bali et al. [7] determined this rate as 85 patients per year. There is no other study in the literature that includes such data in the field of ENT. In the study on general surgery, 221 consultation requests for patients were made in six months, whereas in the thoracic surgery 388 requests were made annually [3,4]. The number of consultation requests from the emergency department to internal medicine is 546, within only two months. [2] These rates may of course vary according to patient density, regional and seasonal differences. Nevertheless, in line with this information, our rate of requesting consultation in surgical clinics is high and lower than that of internal medicine.

In this study, consultations requested from the ENT department of a university hospital were examined. There are similar studies in many branches in the literature. A study reported that 50.51% of the consultations requested from thoracic surgery were by the emergency department [4]. In another study conducted by the chest diseases department, it was found that the most frequent consultation request was made by the emergency department (28.9%) [5]. The only study on ENT was conducted by Kayabaşı et al. [10] and they found this rate as 80.6%. In this study, it is observed that most outpatient consultation requests were made by the emergency department (37.5%). When the qualities of the requests are examined, we found that most diseases do not require emergency surgical intervention and can be treated with a simple intervention or medical treatment. Obviously, special training in these circumstances for emergency room physicians will contribute to eliminating such deficiencies and reduce the consultation requests. However, especially due to the high circulation of

physicians working in the emergency room in our country, hospital-based training will not deliver a definite solution.

Kayabaşı et al. [10] found sore throat (acute tonsillitis) (22.33%), vertigo (dizziness) (14.88%), and epistaxis (14.88%) as the most common reasons for seeking a consultation by the emergency department. In this study, the most common diagnoses after ENT evaluation were epistaxis (10%) and vertigo (dizziness) (10%). Epistaxis occurs in 60% of the population [11]. An epidemiological study concluded that 20–30% of adults experience dizziness at least once in their lifetime, and the prevalence increases further with age [12]. Epistaxis and dizziness are diseases that need to be considered seriously because they affect a significant portion of the society, deteriorate quality of life, cause loss of workforce, and sometimes are a symptom of potentially life-threatening diseases.

In the present study, the number of outpatient consultation requests was 839. The number of outpatient consultation requests outside the emergency department was only 182. Most outpatient consultations were requested by the anesthesia department with 78 patients. Unfortunately, this data does not reflect actual practice. This was thought to be due to outpatient referrals not via HIMS, but in the form of a memo or with verbal directions such as "make an appointment to the ENT department and get examined by an ENT physician". Our clinical experience is that outpatient consultation requests are much higher.

Kayabaşı et al. [10] reported the surgical intervention rate after consultation as 1%. This rate was reported as 33% in the general surgery department [3]. In this study, the number of patients who underwent surgery within 3 years after a consultation was 146 (6.2%). The plastic surgery department deals with maxillofacial traumas in the institution we work in. Therefore, our rate of intervention due to trauma is very low.

In present study, the most common surgical intervention after a consultation was a tracheotomy operation. Patient follow-up rates in ICU have increased with the development of medical treatment techniques. Temporary tracheostomy is more beneficial for patients who may require long-term ventilator support in ICU or palliative care unit wards for various reasons [13]. The procedure of tracheotomy by percutaneous dilatation method by anesthesiologists is increasing day by day, and consultation is requested from ENT physicians only in complicated cases. For this reason, tracheotomy operation is thought to be at higher rates than we found in this study.

It has been shown that the rate of consultation requests has increased gradually over the years [14]. Although the consultation is an important application in the diagnosis and treatment of patients, it also causes negative results such as extending the duration of patient stay in the hospital, sometimes requiring extra laboratory tests and imaging, in parallel, increasing the cost of diagnosis and treatment, and escalation in patient density, especially in departments receiving outpatients. Furthermore, during the consultation process, request being made, disruptions in reaching the consultant physician, and related slowdowns in health services tend to increase violence in patients and their relatives, which result in unwanted incidents. Therefore, when requesting a consultation, physicians should be more selective and should stay away from the defensive medicine approach. In present study, it was found that the consultation requests decreased over the years (40.7%, 35%, 24.3%). It was thought that the main reason for the decreasing number of requests over the years was to make requests in the form of verbal or paper writing instead of making requests through the hospital information management system (HIMS).

It is very important to fill in the consultation forms with the necessary information to make the correct diagnosis and treatment of the patients. Insufficient communication between physicians may hinder the provision of a safe health service. In this study, it was found that almost half (48.5%) of the sections requesting consultation did not write anything meaningful in the explanations section. Generally, the physician who requests a consultation informs the consultant physician verbally (face to face or by phone) or by hand with a consultation paper. However, consultations that are not officially registered on HIMS play essential roles, both in terms of keeping records and medicolegal issues.

Limitations

Since the current study is based on retrospective file scanning, it has some limitations. Firstly, it is a single-center study. Neurology consultations may be higher than other health institutions due to the presence of a neurology ICU in our institution. Again, the number of patients hospitalized for physical therapy and rehabilitation due to the separate physical therapy and rehabilitation hospital affiliated to our institution is quite high. This increases the number of consultations in the physical therapy and rehabilitation department. It should be considered normal to see differences in consultation requests due to these differences in the specific health institution. Due to this and similar reasons, this study may not represent the whole country. A multi-center study will be useful in obtaining more detailed information. Another important limitation is that outpatient consultations are not conducted on HIMS, but by writing a memo or verbal reference. Therefore, consultation requests from non-emergency departments were not received at the expected rate. Our experience is that the consultation rates of pediatric, anesthesia, neurology, and chest disease departments are higher than the rates found in our study.

Conclusion

This is the first study to examine the consultations requested from the ENT department in the Aegean region. Only one study has been conducted on this subject in our country. The patient profile may vary due to regional differences. For this reason, similar studies to be carried out in different regions of our country will contribute to understanding the characteristics of the consultations other departments request from the ENT department. Thus, the reasons for requesting consultation will be better understood and the workload of ENT physicians will be reduced by providing training on some issues that can be concluded without an ENT physician in other related clinics.

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Evaluation of the prognostic factors for candidemia in a medical intensive care unit

Medikal yoğun bakım ünitesinde kandidemi ile ilişkili prognostik faktörlerin değerlendirilmesi

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Abstract

Aim: Infections with *Candida species* are an important cause of morbidity and mortality in intensive care units (ICUs). The studies about the prognostic factors related with candidemia in ICU patients are limited and lacking in our country. The aim of this study is to evaluate the epidemiology and prognostic factors for candidemia in adult patients admitted to a medical ICU.

Methods: This is a retrospective cohort study. A total of 693 patients who were followed for more than 48 hours in our 16-bedded medical ICU between 2016 October-2019 March were evaluated retrospectively and 60 candidemia patients were included in the study. The patients were divided into two groups according to ICU mortality (survivor vs. non-survivor) and compared to determine possible prognostic factors among Candida infection risk factors.

Results: The total incidence of candidemia was 46 per 1000 admissions. The most common fungal isolate was *Candida albicans* (57.5%). The 30-day mortality was 71.7% and ICU-mortality was 78.3%. There was no difference for age, gender, co-morbid diseases, SOFA and APACHE II scores, Glasgow Coma Score, immunosuppressive treatments (steroid or chemotherapy), septic shock, neutropenia, acute hepatic or renal failure, need for vasopressors, hemodialysis, erythrocyte transfusion and total parenteral nutrition between groups. No relationship was found between the time of initiation of antifungal therapy and mortality (P=0.268). Survivors had shorter ICU stay and hospital stay before ICU, and lower Charlson Comorbidity Index scores than non-survivors (P=0.039, P=0.008, P=0.02, respectively). Length of hospital stay before ICU, need for invasive mechanical ventilation and hypoalbuminemia were the prognostic factors for ICU mortality of candidemia patients (P=0.034, P=0.013, P=0.029, respectively).

Conclusion: We reported the highest incidence rate of candidemia and one of the highest mortality rates in critically ill patients with candidemia. Confirming to most of the previous reports, *Candida albicans* (57.5%) was the most common isolate in our study. We evaluated reported risk factors for invasive candidiasis as a prognostic indicator for candidemia in ICU patients, and found that the length of hospital stay, invasive mechanical ventilation and hypoalbuminemia were prognostic indicators.

Keywords: Candidemia, Mortality, Critical care, Prognostic factors

Öz

Amaç: *Candida türleri* ile enfeksiyonlar, yoğun bakım ünitelerinde (YBÜ) önemli bir morbidite ve mortalite nedenidir. YBÜ hastalarında kandidemi ile ilişkili prognostik faktörlerle ilgili çalışmalar sınırlı sayıdadır ve ayrıca ülkemizde YBÜ'lerde kandidemi ile ilgili yeterli klinik çalışma bulunmamaktadır. Bu çalışmanın amacı, medikal bir YBÜ'ye kabul edilen yetişkin hastalarda kandideminin epidemiyolojisi ve prognostik faktörlerini değerlendirmektir.

Yöntemler: Bu çalışma retrospektif kohort bir çalışmadır. 2016 Ekim-2019 Mart tarihleri arasında 16 yataklı yoğun bakım ünitemizde 48 saatten fazla takip edilen 693 hasta retrospektif olarak değerlendirildi ve 60 kandidemili hasta çalışmaya dahil edildi. Hastalar YBÜ mortalitesine göre (sağ kalan ve ölen) iki gruba ayrıldı ve Candida enfeksiyon risk faktörleri arasından olası prognostik faktörleri belirlemek için karşılaştırıldı.

Bulgular: Toplam kandidemi insidansı 46 hasta/1000 başvuru olarak bulundu. En sık görülen mantar izolatı *Candida albicans*'tı (%57,5). Hastaların 30 günlük mortalitesi %71,7 ve YBÜ mortalitesi %78,3 olarak bulundu. Yaş, cinsiyet, eşlik eden hastalıklar, SOFA ve APACHE II skorları, Glasgow koma skoru, immünsüpresif tedaviler (steroid veya kemoterapi), septik şok, nötropeni, akut karaciğer veya böbrek yetmezliği, vazopresör ihtiyacı, hemodiyaliz, eritrosit transfüzyonu ve total parenteral beslenme bakımından gruplar arasında fark yoktu. Antifungal tedaviye başlama zamanı ile mortalite arasında ilişki bulunamadı (P=0.268). Sağ kalanlar YBÜ öncesinde daha kısa YBÜ yatış ve hastanede kalış süresine sahipti ve hayatta kalmayanlara göre Charlson Komorbidite İndeksi puanları daha düşüktü (sırasıyla P=0,039, P=0,008, P=0,02). Kandidemi hastalarının YBÜ mortalitesi için prognostik faktörler olarak YBÜ öncesi hastanede kalış süresi, invazif mekanik ventilasyon ihtiyacı ve hipoalbüminemi saptandı (sırasıyla P=0,034, P=0,013, P=0,029).

Sonuç: Kandidemili kritik hastalarda en yüksek kandidemi insidans oranını ve en yüksek ölüm oranlarından birini bildirdik. Daha önceki raporların çoğunu doğrular şekilde çalışmamızda en sık *Candida albicans* (%57,5) izolatı saptandı. YBÜ hastalarında kandidemi için prognostik bir gösterge olarak invaziv kandidiyaz için bildirilen risk faktörlerini değerlendirdik. Bunlardan hastanede kalış süresi, invazif mekanik ventilasyon ve hipoalbüminemi prognostik birer gösterge olarak bulundu.

Anahtar kelimeler: Kandidemi, Mortalite, Yoğun bakım, Prognostik faktörler

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Introduction

Candidemia is the fourth of the nosocomial bloodstream infection in intensive care units (ICUs). Although the rate of candidemia in ICUs varies between 3.5 and 34.3 per 1000 ICU admissions, it is gradually increasing [1-4]. In different studies in Turkey, candidemia is reported between 1.76 and 12.3 per 1000 individuals [3, 5]. Diagnosis and treatment are often delayed in patients with candidemia, leading to high mortality [6]. Reported candidemia mortality ranges from 30% to 72% [7-9]. While *Candida albicans* is the most frequently isolated *Candida species* in blood cultures, the frequency of non-albicans species has also been increasing in recent studies [10]. Identifying the risk factors of this infection with high mortality is important to prevent its development, detect patients at risk at its onset and start treatment early [1]. There are many studies on risk factors for candidemia in ICU patients, some of which report different results [3,5,11-14]. In these studies, long ICU stay, mechanical ventilation, total parenteral nutrition administration, broad spectrum antibiotic use, presence of diabetes mellitus, immunosuppression, steroid use, central venous catheter interventions, abdominal surgery, hemodialysis, sepsis or septic shock, high SOFA and APACHE II scores, and multiple site *Candida* isolations have been reported as possible risk factors for candidemia. However, the studies about the prognostic factors related with candidemia in ICU patients are limited [2,4,9,15-17].

As in all other ICUs, candidemia is an important cause of mortality in our ICU. In this study, we aimed to evaluate the epidemiology of candidemia cases and determine the effects of *Candida* risk factors on prognosis in patients with candidemia in our ICU.

Materials and methods

In this retrospective cohort study, we evaluated all patients followed between October 2016 and March 2019, in a 16-bedded ICU of a tertiary care hospital, Ondokuz Mayıs University, Faculty of Medicine. All patients ≥18 years-old, who were followed-up for more than 48 hours in the ICU and diagnosed with candidemia were included.

The age, gender, concomitant diseases, hospitalization before and after admission to the ICU, mortality, albumin levels, treatments (vasopressors, total parenteral nutrition, broad spectrum antimicrobial agents, antifungal treatments, erythrocyte transfusion, steroid use, chemotherapy in the last three months), and invasive procedures (invasive mechanical ventilation, central venous catheterization and hemodialysis) of the patients were noted from the hospital registry. Charlson Comorbidity Index, Glasgow Coma Score (GCS), disease severity scores by Acute Physiology and Chronic Health Evaluation II (APACHE II), and Sequential Organ Failure Assessment (SOFA) were also evaluated. Candidemia was defined as having signs and symptoms of infection and sepsis or septic shock, and at least one positive blood culture for Candida species. The patients were divided into two groups according to ICU mortality (survivor vs. non-survivor) and compared with regards to the effects of *Candida* infection risk factors on prognosis.

This study was performed in line with the principles of the Declaration of Helsinki and approved by the Ethics Committee of Ondokuz Mayıs University (2020/115).

Statistical analysis

Statistical Package for Social Sciences (SPSS), Version 25.0 was used for statistical analysis. The categorical parameters were given as frequency and percentages and compared by a Chi-square test. Parametric data were presented as mean (standard deviation) and independent samples t test was used for the comparison of two groups. Non-parametric data were given as median (interquartile range) and Mann-Whitney U test was used for the comparison of two groups. Logistic regression analysis (with backward elimination method) was used including variables, which were significant in bivariate analysis for mortality. The odds ratios (ORs) and their 95% confidence intervals (95% CIs) are presented. A *P*-value of <0.05 is considered significant.

Results

A total of 286 *Candida* isolates were recovered from 204 (29.4%) of 693 patients. Candidemia was present in 60 (8.7%). The total incidence rate of candidemia was 46 per 1000 admissions. The most common fungal isolate was *Candida albicans*, with 57.5% of the patients. The distribution of *Candida spp.* is shown in Table 1. *Candida* growth was first detected in the blood in 28 (46.7%) of the patients, in the urine in 22 (36.7%) patients, in the tracheal aspirate in 3 (5%) patients, in the central venous catheter in 12 (20%) patients, and in the body fluids in 2 (3.3%) patients.

Table 1: Comparison of isolated *Candida spp*

	All patients (n:60) n (%)	Survivors (n:13) n (%)	Non-Survivors (n:47) n (%)	*P*-value**
Candida albicans	42 (57.5)	10 (76.9)	32 (68.1)	0.538
Candida glabrata	8 (11.0)	2 (15.4)	6 (12.8)	0.806
Candida parapsilosis	7 (9.6)	1 (7.7)	6 (12.8)	0.614
Candida tropicalis	7 (9.6)	1 (7.7)	6 (12.8)	0.614
Candida keyfr	3 (4.1)	0	3 (6.4)	0.35
Candida krusei	2 (2.7)	0	2	0.449
Candida lusiteniae	2 (2.7)	0	2	0.449
Unknown spp*	2 (2.7)	0	2	0.449

* Two samples could not be specified. ** Pearson chi-square test for the comparison of categorized data was used.

The 30-day mortality rate was 71.7% (43 patients). When the mortality status of the patients was evaluated according to the status of discharge from the ICU, the mortality rate was 78.3% (47 patients). Evaluation of prognostic factors in patients was made according to ICU mortality. After positive cultures of *Candida*, 14 (29.8%) died in the first 7 days, 26 (55.3%) died within 7-30 days and 7 (14.9%) died after 30 days.

The comparison of survivor and non-survivor candidemia patients for demographic and medical factors and illness severity were shown in Tables 2 and 3. There were no differences in terms of age, gender, co-morbid diseases, SOFA, GCS and APACHE II scores, immunosuppressive treatments (steroid or chemotherapy), septic shock, neutropenia, acute hepatic or renal failure, need for vasopressors, hemodialysis, erythrocyte transfusion and total parenteral nutrition between groups. Survivors had shorter ICU and hospital stay before ICU, and lower Charlson Comorbidity Index scores than non-survivors (*P*=0.039, *P*=0.008, *P*=0.02, respectively). Colistin was the only antimicrobial agent which its previous use was

significantly associated with mortality in our study cohort (P=0.041).

Table 2: Age and the factors related with illness severity of the patients

Variables	All patients (n:60)	Survivors (n:13)	Non-Survivors (n:47)	*P*-value
Age (years)	65.3 (16)	62.2 (16.1)	66.2 (16.0)	0.423[a]
Length of ICU stay (days)	19 (23)	10 (18)	21 (22)	0.039[b]
Length of hospital stay before ICU (days)	13 (27)	3 (10)	17 (27)	0.008[b]
SOFA score	9.6 (3.1)	9.1 (4)	9.8 (2.8)	0.476[a]
APACHE II Score	24.8 (7.1)	21.9 (6.5)	25.6 (7.1)	0.098[a]
Glasgow Coma Score	9 (7)	12 (5)	8 (7)	0.06[b]
Charlson Comorbidity Index Score	3 (4)	2 (2)	3 (4)	0.02[b]
Time to start antifungal therapy after culture (days)	2 (1)	1 (1)	2 (1)	0.271[b]

ICU: Intensive care unit, SOFA: Sequential Organ Failure Assessment, APACHE II: Acute Physiology and Chronic Health Evaluation II. In parametric distribution, the data was given as mean (standard deviation) and independent samples t test [a] was used for the comparison of two groups. In non-parametric distribution, the data was given as median (interquartile range) and Mann-Whitney U test [b] was used for the comparison of two groups.

Table 3: Baseline characteristics and risk factors for mortality of patients with candidemia

Variables	All patients (n:60) n (%)	Survivors (n:13) n (%)	Non-Survivors (n:47) n (%)	*P*-value
Demographics				
Gender (Female)	32 (53.3)	9 (69.2)	23 (48.9)	0.194
Age≥ 65 years	33 (55)	7 (53.8)	26 (55.3)	0.925
Medical history				
Diabetes mellitus	14 (23.3)	2 (15.4)	12 (25.5)	0.444
Chronic pulmonary disease	4 (6.7)	0	4 (8.5)	0.276
Chronic renal disease	11 (18.3)	3 (23.1)	8 (17.0)	0.617
Chronic hepatic disease	2 (3.3)	0	2 (4.3)	0.611
Malignancy	33 (55)	7 (53.8)	26 (55.3)	0.925
Hematological	13 (21.7)	5 (38.5)	8 (17.0)	0.097
Solid tumor	20 (33.3)	2 (15.4)	18 (38.3)	0.121
Solid organ transplantation	3 (5)	1 (7.7)	2 (4.3)	0.615
Prior drug exposure				
Immunosuppressive therapy				
Steroid treatment	13 (21.7)	2 (15.4)	11 (23.4)	0.534
Chemotherapy	22 (36.7)	5 (38.5)	17 (36.2)	0.879
Broad-spectrum antimicrobial agents	60 (100)	13 (100)	47 (100)	-
Third generation cephalosporins	16 (26.7)	5 (38.5)	11 (23.4)	0.277
Beta lactam+beta lactamase inhibitors	36 (60.0)	6 (46.2)	30 (63.8)	0.250
Carbapenems	49 (81.7)	9 (69.2)	40 (85.1)	0.190
Glycopeptides	36 (60)	10 (76.9)	26 (55.3)	0.159
Quinolones	9 (15.0)	2 (15.4)	7 (14.9)	0.965
Aminoglycosides	10 (16.7)	1 (7.7)	9 (19.1)	0.436
Colistin	24 (40)	2 (15.4)	22 (46.8)	0.041
Antifungal treatment	55 (91.7)	13 (100)	42 (89.4)	0.219
Empirical	27 (45.0)	8 (61.5)	19 (40.4)	
After signal for culture positivity	28 (46.7)	5 (38.5)	23 (48.9)	0.268
None	5 (8.3)	0	5 (10.6)	
Antifungal agents				
Fluconazole	13 (21.7)	4 (30.8)	9 (19.1)	0.364
Echinocandin	42 (70.0)	9 (69.2)	33 (70.2)	
Other factors				
Septic shock	46 (76.7)	8 (61.5)	38 (80.9)	0.145
Neutropenia	11 (18.3)	4 (30.8)	7 (14.9)	0.190
Acute hepatic failure	5 (8.3)	1 (7.7)	4 (8.5)	0.925
Acute renal failure	33 (55)	8 (61.5)	25 (53.2)	0.592
Hemodialysis	29 (49.2)	5 (41.7)	24 (51.1)	0.561
Invasive mechanical ventilation	42 (70.0)	5 (38.5)	37 (78.7)	0.005
Need for vasopressors	46 (76.7)	8 (61.5)	38 (80.9)	0.145
Total parenteral nutrition	49 (81.7)	9 (69.2)	40 (85.1)	0.190
Hypoalbuminemia (albumin < 2.0 g/dL)	26 (43.3)	2 (15.4)	24 (51.1)	0.022
Central venous catheter	46 (76.7)	10 (76.9)	36 (76.6)	0.980
Erythrocyte transfusion	54 (90)	13 (100)	41 (87.2)	0.174
Multiple-site colonization with Candida spp	45 (75)	11 (84.6)	34 (72.3)	0.366
Tracheotomy	4 (6.7)	0	4 (8.5)	0.276

Examination of antifungal treatment revealed that five (8.3%) patients were not given any antifungal treatment, 27 (45%) patients were empirically treated after culture collection and 28 (46.7%) patients were administered antifungal treatment after yeast signal or growth in culture. No relationship was found between the time of initiation of antifungal therapy and mortality (P=0.268). Average antifungal treatment initiation time was 1.9 (1.4) days from the day of culture collection. It was observed that 13 (21.7%) of 55 patients who were given antifungal treatment were given fluconazole and 42 (70.0%) were given echinocandin.

All patients had previous use of broad-spectrum antimicrobial agents, a urinary catheter and gastric acid suppression before *Candida* growth, therefore, these factors could not be evaluated between the groups.

In Table 4, we evaluated the prognostic factors associated with ICU mortality for candidemia patients. In bivariate logistic regression analysis, backward elimination method was used and the variables included in the first step were length of hospital stay before ICU, length of ICU stay, APACHE II, SOFA and Charlson Comorbidity Index scores, previous use of Colistin, need for invasive mechanical ventilation and hypoalbuminemia. The results for variables retained in the final multivariable model are presented (Nagelkerke R^2=0.488). Length of hospital stay before ICU, need for invasive mechanical ventilation and hypoalbuminemia were the prognostic factors for ICU mortality of candidemia patients (P=0.034, P=0.013, P=0.029, respectively).

Table 4: Binary logistic regression analyses of prognostic factors associated with ICU mortality for candidemia patients.

Variables	Odds Ratio	95% CI	*P*-value
Length of hospital stay before ICU (days)	1.119	1.008-1.241	0.034
Need for invasive mechanical ventilation	7.887	1.541-40.358	0.013
Hypoalbuminemia (albumin <2.0 g/dL)	9.465	1.265-70.815	0.029

CI: Confidence Interval, ICU: Intensive care unit, SOFA: Sequential Organ Failure Assessment, APACHE II: Acute Physiology and Chronic Health Evaluation II.
Logistic Regression analysis backward elimination method was used and the variables included in the first step were length of hospital stay before ICU (days), length of ICU stay (days), APACHE II Score, SOFA Score, Charlson Comorbidity Index Score, previous use of Colistin, need for invasive mechanical ventilation and hypoalbuminemia (albumin <2.0 g/dL). Results for variables retained in the final multivariable model are presented (Nagelkerke R^2=0.488).

Discussion

In our study, the incidence of candidemia was 46 per 1000 admissions and this is the highest reported rate. The incidence rate of candidemia in ICUs varies between 3.5 and 34.3 per 1000 ICU admissions [1-4]. This high rate of candidemia may be due to backgrounds of our patients. The rate of malignancy was remarkably high, and all had previously used antimicrobial agents. We all know that alterations in host defense can result in an overgrowth of Candida, which is termed colonization. Antibiotic usage can provoke colonization by suppressing normal intestinal bacterial micro-flora, and allowing the proliferation of *Candida spp.*

The incidence of *Candida albicans* is around 50-60% in many studies [3,9,15,16,18]. Consistent with the literature, the most common *Candida species* in our patient cohort was *Candida albicans* (57.5%). However, there are studies in which *non-albicans Candida species* were reported more frequently. For example, *Candida tropicalis* in North India [19] and *Candida parapsilosis* in Thailand [20] and in China [2] were more common.

The 30-day mortality rate was 71.7% and ICU mortality rate was 78.3% in our study. This mortality rate is higher than most of the previous studies, in which it ranged from 30% to 72% [5,7-9,21]. Increased mortality was also reported in case of the need for mechanical ventilation [22]. We suggest that the possible reasons for the high mortality rate were the presence of severely ill patients with high APACHE II (24.8 (IQR:7.1)) and

SOFA (9.6 (IQR:3.1)) scores and very high malignancy rate (55%) in our study cohort. In addition, the hospitalization periods of our patients before ICU were long (13 days-interquartile range=27) and the rate of invasive mechanical ventilation (70%), which we found as a prognostic factor in mortality, was high in our patients.

In some studies, the mortality rate was higher in C*andida albicans* related candidemia than with non-*albicans Candida* spp [*4*]. In our study, the distribution of *Candida spp.* was not different between the groups. So, there was no difference between Candida spp. regarding mortality rate in our study, like some previous studies [9,16,23,24].

The risk factors associated with invasive candidiasis were well established [9,25] and the *Candida* score is a tool used widely for the diagnosis of invasive candidiasis [26]. We evaluated the effect of all previously reported risk factors on mortality. All patients had previous use of broad-spectrum antimicrobial agents, a urinary catheter and gastric acid suppression before *Candida* growth, therefore, these factors could not be evaluated between the groups. Candida score includes total parenteral nutrition, multifocal *Candida spp.* colonization and severe sepsis. In our study, no relationship was found between all these factors and mortality. Increased mortality in the presence of septic shock is an expected finding, and there are studies confirming this in patients with candidemia [17,27]. Although the rate of septic shock was higher in the non-survivor group (80.9% vs. 61.5%) in our study, this difference may not have reached the level of significance due to the small number of patients.

When chronic diseases were evaluated, Charlson Comorbidity Index, which is a chronic disease score, was significantly higher in non-survivors, although no effect of each chronic disease on mortality was detected. For the evaluation of the severity of illness we used SOFA and APACHE II scores and GCS. Although it was not significant, survivors had higher GCS and lower SOFA and APACHE II scores than non-survivors.

All our patients had a history of antimicrobial agent usage. Colistin was the only one that was significantly associated with mortality in our study cohort. This may be because of drug toxic effects and the resistant pathogens requiring Colistin use. There are different findings about the effect of steroid use on prognosis in patients with candidemia. There are studies reporting that it increases [2,13] or decreases mortality [17]. In our study, we could not detect any effect of the patient's prior steroid treatment or chemotherapy on mortality. In our study, there was no significant difference in the mortality rates of patients in terms of starting antifungal treatment earlier or receiving fluconazole or echinocandin treatments similar to previous studies [2,28].

The effect of hypoalbuminemia on mortality was evaluated in only one study [9] and no association was found in candidemia patients. However, we found that low albumin levels are associated with high mortality. We suggest that this may be related to both the fact that albumin is a negative acute phase reactant and the poor nutrition status of the patient.

As we mentioned before, the number of studies evaluating the factors affecting mortality in patients with candidemia is limited and the results are controversial. In an Italian multi-center study [17], risk factors associated with mortality were evaluated in internal medicine wards. They found the presence of septic shock and concomitant chronic kidney failure as risk factors associated with mortality in candidemia patients. Basetti et al. [27] evaluated the incidence and outcome of invasive candidiasis in ICUs in Europe and found that age, SOFA score, severe hepatic failure and septic shock were associated with increased mortality. Ala-Houhala et al. [28] reported that the severity of underlying illnesses, ICU stay at the onset of candidemia and older age (>65 years) were independent risk factors of mortality in candidemia. However, Gonzalez de Molina et al. [4] found that only APACHEII score was a predictor of mortality. In a study conducted with ICU patients in Japan [9], 25 patients with candidemia were divided into two groups as survivors and non-survivors, and the effect of candidemia risk factors on patient prognosis was evaluated. It was concluded that none of the 15 risk factors identified were associated with mortality, but the cumulative increase in the total number of risk factors was the most useful marker on prognosis.

In the comparison of groups according to mortality, length of ICU stay, hospital stay before ICU, Charlson Comorbidity Index score, concomitant Colistin use, need for invasive mechanical ventilation, and hypoalbuminemia were significantly associated with mortality. However, some of the variables did not retain significance at multivariable analysis. In logistic regression analysis, only three factors were associated with mortality, which included the length of hospital stay before ICU, need for invasive mechanical ventilation and hypoalbuminemia.

Limitations

The main limitations of our study included its retrospective and single-center nature, and lack of information regarding laboratory parameters such as beta-d-glucan. Patients were followed until discharge from the ICU. Despite this, we evaluated the effects of many risk factors on mortality in our study.

Conclusions

We reported the highest incidence rate and one of the highest mortality rates in critically ill patients with candidemia. The most common species was *Candida albicans*, concordant with most of the previous studies. We evaluated each risk factor reported for invasive candidiasis in terms of prognostic value for candidemia in ICU patients and found that only three (length of hospital stay, mechanical ventilation and hypoalbuminemia) could be considered prognostic indicators.

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A new biological marker in inflammatory bowel disease: Pentraxin 3

İnflamatuvar barsak hastalığında yeni biyolojik göstergeç: Pentraxin 3

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Ethics Committee Approval: The approval was obtained from the Ethics Committee of Prof. Dr. Cemil Taşcıoğlu City Hospital (4/16/2019, 1175). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
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Abstract

Aim: Pentraxin 3 is known to show inflammation, however, few related studies with contradictory results have been conducted in Inflammatory Bowel Disease patients. We aimed to investigate whether PTX3 can be used in the discrimination between Crohn's disease and Ulcerative Colitis (UC) patients and the correlation of PTX3 with disease activity, involved intestinal segments and their length.

Methods: Ethical committee approval was obtained for this prospective case-control study. IBD patients who were older than 18 years of age, not pregnant, and did not have any malignancies, acute/chronic infections or inflammatory diseases were included. Healthy volunteers were included in the control group. PTX3 levels were measured in the blood. The results were statistically analyzed with the NCSS 2007 program.

Results: The median age of 56 male and 42 female participants was 37 years (25 CD, 43 UK and 30 controls). In the UC group, PTX3, which was not related to the Trulove Witts or Mayo scores, was significantly higher in patients with pancolitis (P<0.05 and P=0.046, respectively). There was no relationship between PTX3 levels and involvement, behavior pattern, CDAI scores and activity of the disease in the CD group (P<0.05 for all).

Conclusion: PTX3 is not an appropriate biomarker for monitoring the activation of IBD and it can't distinguish two subtypes from each other. PTX3 is insufficient to indicate both the behavior pattern and the location of involvement in CD patients. Until the control endoscopy times of the patients with UC, it can be monitored whether the disease affects the entire colon by following PTX3 levels.

Keywords: PTX3, IBD, Crohn, Ulcerative colitis, Inflammation

Öz

Amaç: Pentraxin **3**, inflamasyonu gösterdiği bilinen, ancak İBH hastalarında güncel literatürde birbirleri ile çelişkili ve az sayıda çalışma yapılan moleküldür. Bizde bu çalışmamız da PTX3'ün İBH hastalarında Crohn ve Ülseratif kolit hastalarının ayırımında kullanılıp kullanılamayacağını, PTX3 ile hastalığın aktivitesi, tutulan barsak segmenti ve uzunluğu ile korelasyonu olup olmadığını araştırmayı amaçladık.

Yöntemler: Etik kurul onayı bu prospektif vaka kontrol çalışması için alındı. 18 yaşından büyük, gebeliği, malignitesi, akut/kronik enfeksiyöz veya inflamatuvar hastalığı olmayan İBH tanılı hastalar alındı. Kontrol grubu olarak ta sağlıklı gönüllüler çalışmaya dahil edildi. Kanda PTX3 seviyesi bakıldı. Sonuçlar NCSS 2007 programı ile istatistiksel olarak analiz edildi.

Bulgular: 56 kadın, 42 erkek katılımcının ortalama yaşı 37 idi (25 CH, 43 ÜK, 30 kontrol). Ülseratif kolit grubunda Trulove Witts skoru, Mayo skoru ile ilişkiye sahip olmayan PTX3, pankolit tutulumlu hastalarda istatistiksel olarak anlamlı daha yüksekti (P<0.05, P=0.046 sırasıyla). Crohn hastalığı grubunda tutulum yeri, davranış paterni, CDAI skoru ve aktivite ile PTX3 arasında istatistiksel bir ilişki saptanmadı (P<0.05).

Sonuç: PTX3 İBH aktivasyonunun takibinde uygun bir biomarker değildir ve iki alt tipi birbirinden ayıramaz. Crohn hastalarında gerek davranış paterni gerekse tutulum yerini belirtmede yetersizdir. Ancak Ülseratif kolit hastalarının takibinde endoskopik inceleme olmadan tutulan kolon alanının yaygınlığını gösterebilir, dolayısıyla Ülseratif kolit hastalarının kontrol endoskopi zamanları gelene kadar ki ara dönemde PTX3 düzeyleri takip edilerek tutulan barsak alanının tüm kolonu etkileyip etkilemediği izlenebilir.

Anahtar kelimeler: PTX3, İBH, Crohn, Ülseratif kolit, İnflamasyon

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Introduction

Crohn's disease and ulcerative colitis are the subclasses of inflammatory bowel diseases and can affect the digestive system to result in diarrhea, constipation, rectal bleeding, abdominal pain, and malnutrition. Today, the diagnosis is made with the combination of anamnesis, physical examination, laboratory data, and radiology, endoscopy and biopsy results [1].

Histological diagnosis of ulcerative colitis is made by incessant epithelial damage, crypt abscess, and detection of goblet cell decline. Although neutrophils play a significant role in pathogenesis, there is still no treatment in which they are targeted [2-4].

Pentraxin-3 (PTX3) is from the same pentraxin family with short pentraxins such as CRP and serum amyloid A, but it is a long pentraxin. As a multimeric inflammation mediator, it is an acute phase reactant secreted especially from neutrophils [5-7].

Unlike short pentraxins released from the liver, PTX3 is released by the stimulation of cytokines such as IL-1B from different cell types such as mononuclear phagocytes, dendritic cells, endothelial cells, and smooth muscle cells. Unlike CRP, its blood level rises in response to inflammation and returns to normal in a shorter time [8,9].

As neutrophils play a central role in the pathogenesis of Crohn's disease and Ulcerative colitis, we aimed to determine if PTX3 increases at different levels in the blood according to the subtypes of these diseases, their activity status, and their involvement.

Materials and methods

This prospective case-control study was conducted after the Prof. Dr. Cemil Taşcıoğlu City Hospital Ethics Committee's approval (4/16/2019, 1175) was obtained. Blood samples were taken after obtaining the informed consent of the patients who were older than 18 years of age and previously followed up by the gastroenterology outpatient clinic with the diagnosis of inflammatory bowel diseases based on endoscopic evaluations and biopsies. PTX3 levels were measured by the ELISA method. The criteria for exclusion from the study were being under the age of 18, presence of an acute or chronic infection, having any other inflammatory disease that would raise the acute phase reactants, pregnancy, malignancy, inability to participate in the study, chronic or acute kidney failure, or chronic liver disease. The patient group was divided into two as ulcerative colitis and Crohn's disease groups. Smoking history of the patients was also recorded. In all patients, simultaneously with PTX levels, ESR and CRP values were also recorded.

In the ulcerative colitis group, the patients were divided into 4 groups according to the disease location (proctitis, distal colon involvement, left colon involvement and pancolitis). Ulcerative colitis disease activity was defined according to Truelove Witts, endoscopic activity index and Mayo scoring.

In the Crohn's disease group, patients were evaluated according to involvement (ileal, ileocolonic, colonic involvement) and behavior (non-penetrating, stricturing, penetrating) of the disease, and clinical activities were assessed with Crohn's disease activity index (CDAI). Those with CDAI <150 were classified as having mild disease, and those >150 were classified as severe.

Healthy volunteers with no history of disease or medication were included as the control group in the study.

Statistical analysis

Power analysis was performed with the G*power (version 3.1.9.7) program. The minimum calculated sample size was 29 (effect size 0.87, alpha error 0.05, power 0.95).

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, and percentage, minimum, maximum) were used when evaluating the study data. The suitability of quantitative data for normal distribution was tested by Shapiro-Wilk test and graphical examinations. Mann-Whitney U test was used to compare the quantitative variables between the two groups that did not show normal distribution. Kruskal Wallis test was used for comparisons of three or more groups that did not show normal distribution, and Bonferroni-Dunn test was used for binary comparisons. Spearman correlation analysis was used to evaluate the relationships between quantitative variables. Statistical significance was set at $P<0.05$.

Results

This study was carried out on 68 patients who volunteered to participate and were under follow-up with the diagnosis of inflammatory bowel disease by the gastroenterology outpatient clinic and 30 healthy volunteers. Among the participants, 57.1% (n=56) were female and 42.9% (n=42) were male; their ages ranged between 18 and 69 years, with a mean age of 37.2 (11.9) years. While 30.6% (n=30) of the cases were in the healthy control group, 43.9% (n=43) were in ulcerative colitis group, 25.5% (n=25) were in Crohn's disease group. PTX3 measurements ranged from 91 to 1691, with a mean of 408.56 (87.03). The rate of smokers was 43.0% (n=37) (Table 1).

There was no statistically significant difference regarding age, gender distribution and smoking rates between the groups ($P=0.198$, $P=0.096$, $P=0.129$). There was a statistically significant difference regarding the PTX3 measurements between the groups ($P=0.021$). The binary comparisons made to determine which group the significant difference originated from yielded that Crohn's disease group's measurements were lower than that of the control group's ($P=0.028$). No statistically significant difference was found in other binary comparisons ($P>0.05$).

Sedimentation and CRP levels were significantly higher in the Crohn's disease group than the ulcerative colitis group ($P<0.05$).

In the ulcerative colitis group, colonic involvement was reported as proctitis in 18.6% (n=8), distal colon in 16.3% (n=7), left colon in 25.6% (n=11) and pancolitis in 39.5% (n=17) of the patients. According to Truelove Witts scoring, 27.9% (n=12) were in remission, 20.9% (n=9) had mildly active, 18.6% (n=8) had moderately active and 32.6% (n=14) had severely active disease. In addition, as patients were analyzed according to the Truelove-Witts clinical activity index, while 27.9% (n=12) of the cases were in remission, 72.1% (n=31) were in their active period. The Mayo score was zero in 25.6% (n=11), one in 11.6%

(n=5), two in 14.0% (n=6), and three in 48.8% (n=21) of the patients.

In the Crohn's disease group, the involvement was ileal in 20.0% (n=5), ileocolonic in 60.0% (n=15) and colonic in 20.0% (n=5) of the patients. The disease was non-penetrating (B1) in 60.0% (n=15), structuring (B2) in 16.0% (n=4) and penetrating (B3) in 24.0% (n=6). According to the CDAI index, 20.0% (n=5) of the cases were in remission while 80.0% (n=20) were in their active period. CDAI measurements ranged from 62 to 511 with a mean of 295.44 (136.21); the disease was mild in 32.0% (n=8) and severe in 68.0% (n=17). Disease duration of all IBD patients varied between 0.01 and 260 months, with a mean of 37.50 (60.29) months. ESR measurements ranged from 2 to 92 with a mean of 33.66 (22.15), and CRP measurements ranged from 1.2 to 446, with a mean of 36.03 (70.87) (Table 2).

There was a statistically significant difference regarding PTX3 measurements between ulcerative colitis, Crohn's disease and control groups (P=0.021). The binary comparisons made to determine which group the significant difference originated from showed that Crohn's disease group's measurements were significantly lower than that of the control group's (P=0.028). No statistically significant difference was found in other binary comparisons (P>0.05) (Table 3).

Table 1: Demographic data

		Control (n=30)	Ulcerative Colitis (n=43)	Crohn's Disease (n=25)	*P*-value
Age (years)	Min-Max (Median)	19-60 (31.5)	18-69 (40)	20-55 (32)	[a]0.198
	Mean (SD)	37.29 (13.64)	39.33 (12.20)	34.04 (9.19)	
Gender	Female	22 (73.3)	22 (51.2)	12 (48.0)	[b]0.096
	Male	8 (26.7)	21 (48.8)	13 (52.0)	
PTX3	Min-Max (Median)	111-848 (453)	142-1138 (296)	91-1691 (245)	[a]0.020*
	Mean (SD)	485.03 (241.90)	378.93 (265.73)	367.76 (357.90)	
Sedimentation	Min-Max (Median)	-	2-92 (25)	6-84 (46)	[c]0.049*
	Mean (SD)	-	28.60 (18.25)	42.36 (25.72)	
CRP	Min-Max (Median)	-	1.16-446 (6.12)	2.1-320 (25)	[c]0.024*
	Mean (SD)	-	29.34 (70.72)	47.52 (71.07)	
Smoking	No	15 (62.5)	25 (64.1)	9 (39.1)	[b]0.129
	Yes	9 (37.5)	14 (35.9)	14 (60.9)	

[a] Kruskal Wallis Test, [b] Pearson Chi-Square test, [c] Mann Whitney U test, * P<0.05

Table 2: The features of Ulcerative Colitis and Crohn's disease groups

*The features of Ulcerative Colitis group (n=43)		
Involvement; n (%)	Proctitis	8 (18.6)
	Distal	7 (16.3)
	Left colon	11 (25.6)
	Pancolitis	17 (39.5)
True love Witts; n (%)	Remission	12 (27.9)
	Mild-active	9 (20.9)
	Moderate-active	8 (18.6)
	Severe-active	14 (32.6)
Activity; n (%)	Remission	12 (27.9)
	Active	31 (72.1)
Mayo; n (%)	0	11 (25.6)
	1	5 (11.6)
	2	6 (14.0)
	3	21 (48.8)
* The features of Crohn's disease group (n=25)		
Involvement; n (%)	İleal	5 (20.0)
	İleocolonic	15 (60.0)
	Colonic	5 (20.0)
Behavior; n (%)	B1 Non-penetrating	15 (60.0)
	B2 Stricturing	4 (16.0)
	B3 Penetrating	6 (24.0)
Activity; n (%)	Remission	5 (20.0)
	Active	20 (80.0)
CDAI; n (%)	Min-Max (Median)	62-511 (313)
	Mean(SD)	295.44 (136.21)
	Mild	8 (32.0)
	Severe	17 (68.0)

Table 3: Evaluation of PTX3 Measurements by Groups

	PTX3			*P*-value
	n	Min-Max (Median)	Mean (SD)	
Control group	30	111-848 (453)	485.03 (241.90)	[a]0.020*
Ulcerative colitis group	43	142-1138 (296)	378.93 (265.73)	
Crohn's disease group	25	91-1691 (245)	367.76 (357.90)	

[a] Kruskal Wallis Test, * P<0.05

In the ulcerative colitis group, a significant relationship was detected between involvement and PTX3 measurements (P=0.049). Binary comparisons to determine which group the significance originated from showed that the PTX3 value of the pancolitis group was higher than the distal involvement group (P=0.046). No statistically significant difference was found in other binary comparisons (P>0.05). There was no statistically significant relationship between Truelove Witts activity or Mayo score and PTX3 measurements (P>0.05).

There was no significant relationship between involvement, behavior, activity and CDAI level and PTX3 measurements in the Crohn's Disease group (P>0.05). PTX3 measurements did not show statistically significant differences among any IBD groups with regards to smoking status (P>0.05) (Table 4).

There was no significant relationship between ESR, CRP levels and PTX3 measurements in the whole IBD group (P>0.05) (Table 5).

There was no statistically significant difference between PTX3 measurements with regards to CDAI levels (P=0.682) (Table 6).

Table 4: Evaluation of PTX3 Measurements According to Descriptive Features

			PTX3		*P*-value
		n	Min-Max (Median)	Mean (SD)	
Smoking status (n=86)	No	49	111-1135 (296)	408.94 (267.69)	[b]0.547
	Yes	37	117-1691 (322)	431.35 (325.64)	
*The features of Ulcerative Colitis group (n=43)					
Involvement; n (%)	Proctitis	8	142-449 (232)	260.50 (111.03)	[a]0.049*
	Distal	7	142-678 (194)	248.14 (191.68)	
	Left colon	11	194-1138 (296)	391.09 (283.9)	
	Pancolitis	17	142-1135 (398)	480.65 (300.37)	
True love Witts	Remission	12	142-678 (296)	344.58 (170.28)	[a]0.568
	Mild-active	9	194-1138 (322)	471.67 (320.56)	
	Moderate-active	8	142-1135 (245)	372 (331.32)	
	Severe-active	14	142-882 (232)	352.71 (271)	
True love Witts Activity	Remission	12	142-678 (296)	344.58 (170.28)	[b]0.800
	Active	31	142-1138 (245)	392.23 (295.92)	
Mayo	0	11	142-678 (296)	363 (165.58)	[a]0.204
	1	5	194-1138 (219)	398 (414.21)	
	2	6	219-1135 (602)	580.17 (345.42)	
	3	21	142-882 (245)	325.24 (234.58)	
* The features of Crohn's disease group (n=25)					
Involvement; n (%)	İleal	5	117-1009 (373)	438.6(347.36)	[a]0.745
	Ileocolonic	15	91-1691 (245)	349.6 (390.68)	
	Colonic	5	168-932 (219)	351.4 (325.32)	
Behavior; n (%)	B1 Non-penetrating	15	142-1009 (270)	384.07 (264.47)	[a]0.204
	B2 Stricturing	4	91-347 (219)	219 (104.51)	
	B3 Penetrating	6	117-1691 (155)	426.17 (624.38)	
Activity	Remission	5	219-475 (270)	316.4 (106.18)	[b]0.375
	Active	20	91-1691 (219)	380.6 (398.2)	
CDAI	Mild	8	142-475 (257.5)	286.25 (106.01)	[b]0.682
	Severe	17	91-1691 (219)	406.12 (427.01)	

[a] Kruskal Wallis Test, [b] Mann Whitney U Test, * P<0.05

Table 5: Relationship between ESR and CRP and PTX3 levels

		PTX3
ESR	r	-0.181
	P-value	0.139
CRP	R	-0.128
	P-value	0.299

r: Spearman's Correlation Coefficient, * $P<0.05$

Table 6: Evaluation of PTX3 Measurements by CDAI Levels

		PTX3			*P*-value
		n	Min-Max (Median)	Mean (SD)	
CDAI	Mild	8	142-475 (257.5)	286.25 (106.01)	[a]0.682*
	Severe	17	91-1691 (219)	406.12 (427.01)	

[a] Mann Whitney U test

Discussion

PTX3 is an indicator which increases in inflammatory events. Previous studies have shown that plasma PTX3 levels increase in acute myocardial infarction, sepsis, acute pancreatitis, and autoimmune diseases such as rheumatoid arthritis, psoriasis, Churg-Strauss syndrome, Wegener granulomatosis, and microscopic polyangiitis. Unlike CRP, which is another inflammation indicator produced from the liver through IL-6, PTX3 is produced from the inflamed tissue through IL-1, IL-8, TNF-alpha and LPS. It reaches peak and decreases to normal levels in a brief time. PTX3 is normally produced from the lamina propria of colon cells and its secretion from inflammatory tissue increases in intestinal inflammation.

Although there are many studies showing the relationship of PTX3 with inflammation, the number of studies conducted with IBD in the literature is very few and their results are contradictory. In their in vitro studies, Savchenko et al. [9] showed the relationship between neutrophil activation and PTX3 levels in colon tissues of ulcerative colitis patients. Contrary to the results of this study, Chen et al. [1] reported that PTX3 was superior to CRP in showing disease activity in Crohn's disease patients, although they could not detect any relationship between ulcerative colitis and PTX3, like us. In the study of Kato et al. [10], the presence of PTX3 in cryptic abscesses containing neutrophils was also shown. They also found that PTX3 levels correlated with CRP and were associated with the activation of the disease. However, in our study, there was no relationship between PTX3 and neither CRP and ESR nor the activity of ulcerative colitis. In our Crohn's disease group, we think that the reason for lower PTX3 levels was the immunosuppressive treatment our patients received. There was a statistically significant relationship between PTX3 levels only when ulcerative colitis manifested as pancolitis.

Limitation

This study has two potential limitations, one being the small number of patients. The second one is that it is based on data from a single center. Multicenter studies with more IBD patients could yield more valid results.

Conclusions

In the light of all these studies, which are very few in the IBD patient group with PTX3 and contradict with our study, PTX3 blood level is not more sensitive, more specific, or effective in determining the type of disease, and not strong in understanding the disease activity in existing IBD patients. Therefore, PTX3 is not suitable for use in the IBD patient group except for follow-up of ulcerative colitis patients with pancolitis in daily practice, without studies and meta-analyses involving more patients.

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Comparative outcomes of thyroid surgery in elderly patients: A retrospective cohort study

Yaşlı hastalarda tiroid cerrahisinin karşılaştırmalı sonuçları: Retrospektif bir kohort çalışması

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Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Ankara Numune Training and Research Hospital (Date: 07/02/2019, No: E-19-2474). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
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Abstract

Aim: The prevalence of benign and malignant thyroid diseases increases with age. Since the population continues to age, the necessity and feasibility of thyroid surgery in the elderly has become more questionable. The aim of this study is to evaluate thyroid surgery and determine whether thyroidectomy is a safe option in the elderly population, by comparing with younger counterparts.

Methods: The data of 471 consecutive patients (370 females, 101 males) with benign or malignant thyroid disorders who underwent thyroid surgery between June 2016 and May 2018 were evaluated retrospectively. The patients were divided into two groups, as younger (age <65) and elderly group (age ≥65). Both groups were compared in terms of indications, post-surgical complications, and histopathological results. All statistical tests were performed using SPSS, version 18.0, software (SPSS Inc., Chicago, IL).

Results: Thyroid surgery in the elderly patients showed similarities compared to younger patients in terms of indications and most of the postoperative complications (P>0.05 for each). However, some differences were seen such as increased postoperative hemorrhage and length of hospital stay in favor of the elderly (P=0.035 and P<0.001, respectively).The incidence of malignant disease was found to be slightly higher in the younger group compared to the elderly (42.96% vs. 31.81%, respectively, P=0.095). Surgery-related death was not observed.

Conclusion: Our experience confirms that successful results can be achieved with low morbidity in experienced hands if careful and close monitoring of co-morbid conditions is provided in elderly patients.

Keywords: Thyroidectomy, Elderly, Thyroid surgery, Complication, Geriatric

Öz

Amaç: Benign ve malign tiroid hastalıklarının prevalansı yaşla birlikte artar. Nüfus yaşlanmaya devam ettiğinden, yaşlılarda tiroid cerrahisinin gerekliliği ve uygulanabilirliği daha tartışmalı hale gelmiştir. Bu çalışmanın amacı, yaşlı hastalarda tiroid cerrahisini değerlendirmek ve genç hastalarla karşılaştırıldığında tiroidektominin yaşlı popülasyonda güvenli bir seçenek olup olmadığını belirlemektir.

Yöntemler: Haziran 2016-Mayıs 2018 tarihleri arasında benign veya malign tiroid hastalığı olan ve tiroid cerrahisi geçiren 471 ardışık hastanın (370 kadın, 101 erkek) verileri retrospektif olarak incelendi. Hastalar genç grup (yaş <65) ve yaşlı grup (yaş ≥65) olmak üzere iki gruba ayrıldı. Her iki grup endikasyonlar, cerrahi sonrası komplikasyonlar ve histopatolojik sonuçlar açısından karşılaştırıldı. Tüm istatistiksel testler SPSS, sürüm 18,0, yazılım (SPSS Inc., Chicago, IL) kullanılarak yapıldı.

Bulgular: Yaşlı hastalarda tiroid cerrahisi, endikasyon ve postoperatif komplikasyonların çoğu açısından genç hastalara göre benzerlikler gösterdi (P>0,05). Bununla birlikte, artmış postoperatif kanama ve hastanede kalış süresi gibi yaşlılar lehine bazı farklılıklar görüldü (sırasıyla P=0,035 ve P<0,001). Malign hastalık insidansı genç grupta yaşlılara göre biraz daha yüksek bulundu (sırasıyla %42,96 ve %31,81, P=0,095). Cerrahi ile ilişkili ölüm gözlenmedi.

Sonuç: Deneyimlerimiz, yaşlı hastalarda ko-morbid durumların dikkatli ve yakından izlenmesi durumunda, deneyimli ellerde düşük morbidite ile başarılı sonuçların elde edilebileceğini doğrulamaktadır.

Anahtar kelimeler: Tiroidektomi, Yaşlı, Tiroid cerrahisi, Komplikasyon, Geriatrik

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Introduction

As people get older, the frequency of benign and malignant thyroid disease increases [1]. In almost 50% of patients over the age of 65, nodules can be shown on ultrasound scanning. Ninety percent of women over 60 years of age and 60% of men over 80 years of age refer to the physician with symptoms caused by thyroid nodules, and of these, %5 have malignant nodules [2]. Due to the increased incidence of malignancy, nodules require a more careful examination in elderly patients. Furthermore, it has been reported many times in the literature that the course of malignant cases tends to be more aggressive in elderly patients. Some subtypes of malignant thyroid diseases, such as anaplastic thyroid cancer and primary thyroid lymphoma, occur particularly over the age of 60 years [3,4]. Also, some authors reported that patients over 60 years of age who present with hyperfunctional thyroid nodules are at risk for developing osteoporosis and severe cardiac arrhythmia [5]. However, when it comes to the treatment of thyroid diseases in elderly patients, there is a general belief that surgical treatment will be risky due to advanced age and co-morbidities. Therefore, patients are often followed up with conservative treatment methods such as medical therapy or radioactive iodine. But because of long-term medical treatment, delays in surgical procedures may expose elderly patients to undesired risks such as compression-related respiratory distress, hyperthyroidism-related arrhythmias, bone loss, and metastasis in malignant cases.

The aim of this study is to evaluate thyroid surgery in elderly patients in terms of indications for surgery, post-surgical complications, and histopathological results and to determine whether thyroidectomy is a safe option in the elderly population by comparing with younger counterparts.

Materials and methods

The data of 471 consecutive patients (370 female, 101 male) with benign or malignant thyroid disorders who underwent thyroid surgery between June 2016 and May 2018 at the endocrine surgery department of a single tertiary level referral center were retrospectively evaluated. The study protocol was approved by the Ethics Committee of Ankara Numune Training and Research Hospital (Date: 07/02/2019, No: E-19-2474). Informed consent form was obtained from patients at the time of registry. The study was conducted in accordance with the Declaration of Helsinki. All patients were evaluated by an endocrinologist and an anesthesiologist before surgery. If necessary, patients with co-morbidities were consulted from the relevant clinics, and their treatment was rearranged before surgery. Patients who had preoperative recurrent laryngeal nerve (RLN) palsy and/or parathyroid disorder were excluded from the study. Patients were divided into two groups. The first group included 405 patients under the age of 65 years (85.98%), named as the younger group. The second group included 66 patients (14.02%), who were 65 years and over, and defined as the elderly group. Both groups were compared in terms of gender, body mass index, initial complaints, family history, previous thyroid surgery, preoperative indications, co-morbid diseases, surgical procedures, length of post-operative hospital stay, post-operative complications (laryngeal nerve injury, hypocalcemia, hemorrhage, seroma, wound infection and systemic complications) and final histopathological results.

All operations were performed by surgeons who had experience in thyroid surgery (more than 50 surgeries per year). In the postoperative period, all patients received prophylactic calcium supplementation therapy consisting of oral calcium combined and, if needed, vitamin D. In the follow-up period, patients were evaluated in the 3rd and 6th months after thyroidectomy. Postoperative hypocalcemia is diagnosed in the presence of hypocalcemia (serum calcium < 8.0 mg/dL) with an inadequate parathyroid hormone (PTH) concentration (below 15 ng/L) which persists 12 months after cervical surgical procedure. All patients were examined with an indirect laryngoscope to evaluate vocal cord mobility in the pre and postoperative period. The RLN palsy is considered "temporary", if the motility of the vocal cords is normal within 6 months. If RLN palsy lasts longer than this period, it is considered "permanent". Surgery-related mortality was defined as death occurring within 30 days postoperatively.

Statistical analysis

All statistical tests were performed using SPSS, version 18.0, software (SPSS Inc., Chicago, IL). Descriptive analyses were presented as number/percentage for categorical variables, and mean (standard deviation (SD)), percentages, minimum and maximum values for continuous variables. One-way analysis of variance (ANOVA) was used to compare continuous variables. The difference between the ratios was compared using the Pearson Chi-square test. Differences were calculated for their statistical significance using the Fisher exact test. A *P*-value <0.05 was considered statistically significant.

Results

Of the 471 patients undergoing thyroid surgery, 405 were younger, and 66 were elderly. The mean age was 45 (11) years in the younger group and 71 (6) years in the elderly group (P<0.001). Among the complaints of the patients, especially in the elderly group, compressive symptoms were more common than the younger group (28.78% vs. 12.09%) (P<0.001). The indication of thyroidectomy in the younger group was suspicious or malignant nodule in 53 (13.08%). In the elderly group, 7 (10.6%) of the patients had malignancy diagnosed preoperatively by fine needle aspiration biopsy (Table 1). One or more co-morbidities were observed in 37.03% of the patients in the younger group and 74.24% of the patients in the elderly group (P<0.001). In both groups, hypertension and diabetes were the most common co-morbid diseases. The distribution of co-morbidities is presented in Table 2. Total thyroidectomy (TT) was the most common operation in both younger (96.8%) and elderly groups (97%). However, neck dissections were performed in 40 (9.88%) patients in the younger group and 5 (7.5%) in the elderly group. The mean operation time was 68.5 (13.09) minutes in the younger group and 75.44 (9.55) minutes in the elderly group, and the difference was not statistically significant (P=0.14). When postoperative complications were evaluated, the rates in groups were similar. In younger and elderly groups, permanent hypocalcemia was observed in 2.46% and 3%, permanent vocal cord paralysis, in 1.23% and 1.52%,

seroma, in 0.74% and 1.51%, and wound infection, in 1.23% and 1.51%, respectively.

Table 1: Comparison of demographics and other characteristics of patients

Variables	Younger Group Age <65 years (n=405)	Elderly Group Age ≥65 years (n=66)	*P*-value
Age (years)	45 (11)	71 (6)	<0.001
Sex			
-Male	86 (21.23)	15 (22.72)	0.795
-Female	319 (78.77)	51 (77.28)	
Body mass index (kg/m^2)	28.73 (4.08)	28.07 (5.31)	0.507
Preoperative complaint			
-Asymptomatic	105 (25.92)	19 (28.78)	0.71
-Neck swelling and pain	162 (40)	15 (22.73)	0.22
-Compressive symptoms	49 (12.09)	19 (28.78)	0.001
-Hyperthyroidism	64 (15.81)	12 (18.19)	0.52
-Hypothyroidism	25 (6.18)	1 (1.52)	0.024
Family history			
-No	396 (97.8)	65 (98.48)	0.684
-Yes	9 (2.2)	1 (1.52)	
Previous thyroid surgery			
-No	384 (94.81)	61 (92.42)	0.889
-Yes	21 (5.19)	5 (7.58)	
Indications for thyroidectomy			
-MNG	270 (66.67)	42 (63.64)	
-Toxic goiter	82 (20.25)	17 (25.76)	0.316
-Suspicious & malignant nodule	53 (13.08)	7 (10.60)	

MNG: Multinodular goiter, values in parentheses are percentages, the data are used as the mean (standard deviation) for age and body mass index.

Table 2: Comparison of co-morbidities between groups

Co-morbidities	Younger Group Age<65 (n=405)	Elderly Group Age ≥65 (n=66)	*P*-value
-None	255 (62.96)	17 (25.75)	
-Hypertension	37 (9.14)	19 (28.79)	
-Diabetes Mellitus	48 (11.85)	10 (15.16)	
-Cardiovascular disease	9 (2.23)	6 (9.09)	
-Pulmonary disease	7 (1.72)	4 (6.07)	
-Dyslipidemia	10 (2.46)	3 (4.54)	
-Renal failure	4 (0.98)	1 (1.52)	
-History of cancer	9 (2.23)	3 (4.54)	
-Other diseases	26 (6.43)	3 (4.54)	
Total number of patients with co-morbidities	150 (37.03)	49 (74.24)	<0.001

Values in parentheses are percentages.

The postoperative hemorrhage rate was higher in the elderly group (4.54% vs. 1.72%), and this difference was statistically significant (*P*=0.035). Tracheostomy was performed in 3 patients in the younger group and 1 in the elderly group due to respiratory distress after bilateral vocal cord paralysis. Due to postoperative hemorrhage and hematoma, 2 patients from the younger group and 1 patient in the elderly group required re-surgery. Hematoma, in other cases, was reabsorbed spontaneously. Wound infections were successfully treated with abscess drainage and antibiotics in 5 (1.23%) patients in the younger group and 1 (1.51%) in the elderly group. In the younger group, 2 male patients aged 49 and 64 years were followed up in the postoperative intensive care unit due to postoperative angina pectoris, one 52-year-old female due to pneumonia (patient with tracheostomy), and 2 other patients due to resistant hypertension. In the elderly group, a 74-year-old male patient with ischemic heart disease and arrhythmia and another patient who was re-operated due to a postoperative hematoma were also followed up in the postoperative intensive care unit. Postoperative length of hospital stay was 1.7 (0.91) and 2.2 (0.34) days for younger and old groups, respectively (*P*<0.001). Surgical procedures, postoperative complications, and length of hospital stay between groups are presented in Table 3.

Final pathology results revealed malignancy in 174 (42.96%) cases in the younger group and 21 (31.81%) in the elderly group. However, in both groups, micro-papillary cancers accounted for the majority of malignant cases. While all 4 follicular cancer cases were observed in the younger group, the single anaplastic cancer case was detected in an 80-year-old male patient. Although the malignancy rates were similar between the groups (*P*=0.095), the distribution of histological subtypes differed statistically (*P*<0.001) (Table 4). However, the tumor size, bilaterality, multifocality, extra-capsular invasion and lymph node involvement were similar. Distant metastasis was not detected in any of the patients. The mean follow-up time after surgery was 18.62 (7.79) months (4-33 months), and death associated with thyroid disease occurred in one case. The patient diagnosed with anaplastic cancer died in the 4th postoperative month.

Table 3: Surgical procedures, postoperative complications and length of hospital stay between groups

Variables	Younger Group Age<65 (n=405)	Elderly Group Age ≥65 (n=66)	*P*-value
Type of thyroidectomy			
-Lobectomy	8 (1.97)	0 (0)	0.435
-Total	392 (96.8)	64 (97)	
-Complementary	5 (1.23)	2 (3)	
Neck dissection			
-No	365 (90.12)	61 (92.5)	0.773
-Yes	40 (9.88)	5 (7.5)	
-Central	24 (5.92)	4 (6.0)	
-Lateral	16 (3.96)	1 (1.5)	
Operation time (min)	68.5 (13.09)	75.44 (9.55)	0.14
Hypocalcemia			
-Transient	29 (7.16)	7 (11)	0.412
-Permanent	10 (2.46)	2 (3)	
RLN injury			
-Transient	17 (4.19)	4 (6.06)	0.22
-Permanent	5 (1.23)	1 (1.52)	
Seroma	3 (0.74)	1 (1.51)	0.314
Post-operative hemorrhage	7 (1.72)	3 (4.54)	0.035
Wound infection	5 (1.23)	1 (1.51)	0.374
Tracheostomy	3 (0.74)	1 (1.51)	0.071
Systemic complications	5 (1.23)	2 (3.03)	0.068
Post-operative length of hospital stay (day)	1.7 (0.91)	2.2 (0.34)	<0.001

RLN: Recurrent laryngeal nerve. Values in parentheses are percentages. The data are presented as mean (standard deviation) for the duration of surgery and hospital stay.

Table 4: Histopathological results

Variables	Younger Group Age <65 (n=405)	Elderly Group Age ≥65 (n=66)	*P*-value
Final Pathology			
-Benign	231 (57.04)	45 (68.19)	0.095
-Malignant	174 (42.96)	21 (31.81)	
Histological type of malignancies			
PTMC	92 (52.87)	9 (42.85)	<0.001
PTC	66 (37.93)	7 (33.35)	
FTC	4 (2.31)	0 (0)	
MTC	1 (0.57)	4 (19.04)	
ATC	0 (0)	1 (4.76)	
Others	11(6.32)	0 (0)	
Tumor size (mm)	10 (1-77)	8 (2-105)	0.922
Bilaterality	59 (10)	6 (9)	0.739
Multifocality	91 (38)	9 (43)	0.645
Extracapsular Invasion	35 (15)	4 (19)	0.576
LN involvement			
No	151 (86.78)	19 (90.47)	0.88
Yes	23 (13.21)	2 (9.53)	

PTMC: Papillary thyroid microcarcinoma, PTC: Papillary thyroid carcinoma, FTC: Follicular thyroid carcinoma, MTC: Medullary thyroid carcinoma, ATC: Anaplastic thyroid carcinoma, LN: Lymph node. Values in parentheses are percentages.

Discussion

Since the population continues to age, it is further questioned whether thyroidectomy is a safe option in the treatment of thyroid diseases in the elderly. The definition of the elderly differs between studies. Usually, patients between the ages of 16 and 64 years are classified as younger, those 65 to 79 years old are classified as elderly, and those 80+ years old are classified as super-elderly [6,7]. Since the number of patients over 80 was insufficient in our series, we designed our study in 2 groups. There are many single-center studies evaluating thyroidectomy in many aspects among younger and elderly patients [5,8]. In these studies, indications for thyroid surgery in elderly patients are reported as benign enlargements with compressive symptoms, medical treatment-resistant thyrotoxicosis, and malignancy or suspicious diagnoses. In the

present study, although the compressive symptoms were at the forefront in elderly patients as in Tartaglia's study [8], there was no significant difference between the groups in terms of surgical indications. Contrary to the study of Passler et al. [9], it was noteworthy that the indication for malignancy was higher in the younger group. This situation has been associated with an increase in the detection of micro cancer as a result of advanced diagnostic imaging methods and ultrasound-guided needle biopsies. The safety of thyroidectomy in elderly patients is still a controversial issue in the literature. Although there is no consensus on this issue, surgery is rarely recommended due to increased operative risks in elderly [10]. The common approach among surgeons has long been avoiding elective surgery in the elderly, due to high co-morbidity rates. Even Passler et al. [9] and Miccoli et al. [11] suggested the surgery in elderly patients only when absolutely necessary. However, some authors have also reported that mortality is related to biological age and co-morbidities rather than chronological age [8]. Tartaglia et al. [8] reported a 2.45% postoperative mortality in 448 patients aged 65+ due to co-morbidities unrelated to thyroidectomy. In our study, in the elderly group, 75% of the patients had a minimum of one co-morbidity, and hypertension was the most common. In different series that report high mortality, cardiovascular diseases (such as coronary arteriosclerosis or cardiac arrhythmia) are most frequently reported as co-morbidities [8]. Although age is not a determining factor for the radicality of the surgery to be chosen, TT is the preferred surgical method in our clinic to minimize the recurrence of the disease and decrease the morbidity due to re-intervention, especially in elderly patients. Two of 66 elderly patients in our study underwent complementary thyroidectomy, and 64 underwent TT. Our postoperative mortality rate was 0 as Seybt et al. [12] and two other studies [9-11]. Although postoperative complication rates were slightly higher in the elderly group, statistical significance was found only in terms of postoperative hemorrhage. All elderly patients who developed hematoma were hypertensive and had a history of cardiac stents requiring anti-coagulation medication. Recently, a meta-analysis of thyroidectomy for thyroid cancer (TC) in elderly patients reported increased mortality rates [Hazard Ratio 1.95] and risk of complications [Odds Ratio 1.82] following thyroidectomy compared to younger patients [13]. In another study, Echanique et al. [1] reported that the incidence of RLN injury increased in patients with age >65 while hypoparathyroidism decreased with age>65 but <85 years. However, in the current study, similar complication rates were observed in younger and elderly groups. Permanent RLN damage rate was 1.23% vs. 1.52%, while permanent hypocalcemia rates were 2.46% and 3%, respectively. As in Tartaglia [8] and Seybt's [12] studies, we did not find a statistically significant difference between the groups in terms of these two primary complications. In accordance with the literature [1,14], our study showed that the length of hospital stay increases with patient age. This finding can be associated with co-morbidities that may predispose the patients to increased complications, which may result in a prolonged hospital stay.

In contrast to some articles in the literature [9,12], we found that malignancy rates were significantly higher in the younger group (42.96% vs. 31.81%). Almost all undifferentiated cancers were detected in patients 65 years and older, as expected. It is a general belief that TC in elderly patients may be more aggressive with a poor prognosis due to the fact that undifferentiated types are more common and diagnosed at an advanced stage. Moreover, several authors concluded that TC in elderly patients was associated with larger tumors and higher rates of extrathyroidal extension than that in younger patients [4, 7]. However, we found no significant difference between the younger and elderly groups in terms of tumor size, bilaterality, multifocality, extra-capsular invasion, or lymph node involvement.

Limitations

The most important limitations of this study are insufficient sample size of elderly patients and retrospective nature as it has an inherent selection bias for the surgical patient. Even so, the current study presents a unique evaluation of thyroid surgery performed in both the younger and elderly patients by demonstrating trends in surgical outcomes.

Conclusion

Thyroid surgery in elderly patients are similar to younger patients in terms of indications, surgical procedures, and postoperative complications; however, some differences were seen, such as increased postoperative hemorrhage and length of hospital stay. In addition, an increase in favor of the elderly was not found in terms of malignancy rates, but it was confirmed that almost all undifferentiated tumors were seen at 65 years and older. Therefore, an aggressive surgical approach may be required for elderly patients due to the worse prognosis of malignancies and to avoid recurrence and reinterventions, particularly in the case of toxic diseases. In light of the results obtained from this study (similar complication rates and no surgery-related mortality), it can be said that thyroidectomy in elderly patients is not more dangerous than in younger patients. Our experience confirms that successful results can be achieved with low morbidity in experienced hands if careful and close monitoring of co-morbid conditions is provided in elderly patients.

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Research article
Araştırma makalesi

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Comparison of quantitative computed tomography and dual-energy X-ray absorptiometry in elderly patients with vertebral and nonvertebral fractures: Preliminary results

Vertebral ve vertebra dışı fraktürü olan yaşlı olgularda dual–enerji X-ışını absorbsiyometri ve kantitatif bilgisayarlı tomografi karşılaştırması: Preliminar sonuçlar

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Abstract

Aim: Dual-energy X-ray absorptiometry (DXA) and quantitative computed tomography (QCT) are methods used today to evaluate bone mass and structure and determine the risk of fractures. In this study, spinal and femoral bone density results measured by DXA and QCT in elderly patients with vertebral and non-vertebral fractures were compared to identify the most effective method in determining the risk of osteoporosis and fractures.

Methods: In this retrospective cohort study, 45 elderly patients aged 65–84 years were analyzed. Group 1 included 11 patients with atraumatic vertebral fractures, Group 2 included 11 patients with non-vertebral fractures and Group 3 included 23 patients without fractures. T-scores and bone mineral density (BMD) values of spinal (lumbar 1-4) and femoral (neck) regions measured by both DXA and QCT were evaluated.

Results: Spinal and femoral T-scores and BMD values measured by DXA and QCT were similar between the groups ($P>0.05$ for all). In Group 1, lumbar BMD value, lumbar and femoral neck T-scores measured by QCT were significantly lower than DXA ($P<0.001$, $P=0.004$ and $P=0.037$, respectively). In Group 2, lumbar BMD value and T-score measured by QCT were significantly lower than DXA ($P<0.001$ and $P<0.001$). In Group 3, lumbar T-score, lumbar and femoral neck BMD values measured by QCT were significantly lower than DXA ($P<0.001$, $P<0.001$ and $P=0.004$, respectively).

Conclusion: QCT is an effective method that can be used in elderly patients with fractures and arthrosis where DXA may yield false-positive results.

Keywords: Geriatrics, Ostoeporosis, Vertebral fracture, Bone density, DXA, QCT

Öz

Amaç: Günümüzde Dual-enerji X-ışını absorbsiyometrisi (DXA) ve kantitatif bilgisayarlı tomografi (KBT) kemik kütle ve yapısını değerlendirmek, kırık riskini belirlemek için kullanılan yöntemlerdir. Bu çalışmada vertebral ve vertebral bölge dışında kırığı olan yaşlı hastalarda, DXA ve KBT ile ölçülen spinal ve femoral bölge dansitometri sonuçlarını karşılaştırarak, osteoporoz ve kırık riskini belirlemede en etkin yöntemi araştırmayı amaçladık.

Yöntemler: Bu retrospektif kohort çalışmasında 65- 84 yaş aralığında 45 yaşlı hasta analiz edildi. Grup 1'e atravmatik vertebral kırığı olan 11 hasta, Grup 2' ye spinal bölgenin dışında kırığı olan 11 hasta, Grup 3'e ise kırığı olmayan 23 hasta dahil edildi. Spinal (lumbar 1-4) ve femoral (boyun) bölgelerden ölçülen, DXA ve KBT ile yapılan kemik mineral yoğunluğu (BMD) ölçümleri ve T skorları değerlendirildi.

Bulgular: Gruplar arası değerlendirmede, DXA ve KBT ile ölçülen, lumbar ve femoral boyun BMD değerlerinde ve T skorlarında üç grup arasında istatistiksel olarak anlamlı bir farklılık bulunmadı (tümü $P>0,05$). Grup 1'de KBT ile ölçülen lumbar BMD değeri, lumbar ve femoral boyun T skor değerleri, DXA ölçümlerinden istatistiksel olarak anlamlı düşük bulundu (sırasıyla, $P<0,001$, $P=0,004$ ve $P=0,037$). Grup 2'de KBT ile ölçülen lumbar bölge BMD ve lumbar bölge T skor değerleri, DXA ölçümlerinden istatistiksel olarak anlamlı derecede düşük bulundu ($P<0,001$ ve $P<0,001$). Grup 3'de KBT lumbar bölge T skoru, lumbar ve femoral boyun BMD değerleri, DXA ölçümlerinden istatistiksel olarak anlamlı derecede düşük dulundu (sırasıyla, $P<0,001$, $P<0,001$ ve $P=0,004$).

Sonuç: KBT, ileri yaş olgularda kırık ve artroz gibi DXA yönteminin yanlış pozitiflik verebileceği durumlarda kullanılabilecek etkin bir kemik mineral yoğunluğu ölçüm metodudur.

Anahtar kelimeler: Yaşlı, Osteoporoz, Spinal kırık, Kemik yoğunluğu, DXA, KBT

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Introduction

Osteoporosis is a systemic metabolic bone disease with an increasing prevalence among the geriatric population and causes decreased bone mineral density, deterioration of the microarchitecture, and increased risk of bone fractures [1]. Prevalence of osteoporosis increases with age and it is reported to be 15% in patients aged between 50–59 years and 70%–80% in patients aged ≥80 years [1-3]. The prevalence of osteoporotic fractures, which is the main complication of osteoporosis, also increases with age. Osteoporotic fractures, or fragility fractures, are classified into vertebral and non-vertebral fractures [2,3]. Fragility fractures are most commonly observed in the vertebra, whereas non-vertebral fracture locations include the forearms, hips, rarely the ribs, pelvis, and clavicle [3,4]. Vertebral fractures constitute 27% of all osteoporotic fractures among women and men. This rate is higher among the geriatric population and the prevalence increases to 50% in patients aged ≥80 years, which is very close to the prevalence of coronary artery disease in developed countries [5-8].

Although vertebral and non-vertebral osteoporotic fractures are preventable among the geriatric population, they constitute a public health concern that causes increased morbidity, mortality, and health expenditure. The presence of a single vertebral fracture increases the risk of a future vertebral fracture by 5-fold and other fractures by 2/3-fold [9]. History of vertebral fracture in patients older than 65 years increases the risk of a new vertebral fracture by 7 to 10-fold within 5 years [9,10]. Moreover, it increases the risk of a non-vertebral fracture by 2.8 to 4.5-fold [3]. Therefore, early diagnosis and treatment of osteoporosis are important for the geriatric population. Bone mineral density measurement in the diagnosis of osteoporosis is an important predictor of fracture risk. Dual-energy X-ray absorptiometry (DXA) is the standard modality of bone mineral density measurement. However, with the recent advancements in technology, quantitative computed tomography (QCT) is recommended as an alternative or complementary diagnostic method due to its ability to separately evaluate three dimensional volumetric trabecular and cortical bone mineral densities and to show correct volumetric bone mineral density without being influenced by factors that affect bone size and shape such as degeneration and hypertrophic changes [11-13].

There are a few studies comparing QCT and DXA modalities in patients with vertebral fractures in the geriatric population; however, there is only one study analyzing the relationship of these modalities with non-vertebral fractures conducted in older males [13,14]. In this study, in male and female elderly patients with vertebral and nonvertebral fractures, spinal and femoral bone mineral density results measured by DXA and QCT were compared to identify the most effective modality in determining the risk of osteoporosis and fractures.

Materials and methods

A total of 45 geriatric patients (age >65 years) who were referred to the Radiology Clinic for osteoporosis screening from the Physical Therapy and Rehabilitation outpatient clinic between December 2018 and June 2019 were included in this retrospective study. Informed consent was waived because of the retrospective nature of the study. This study was approved by the Ethics Committee of the Fatih Sultan Mehmet Training and Research Hospital (17073117-050.06 FSM EAH-KAEK 2020/12-26). Patients <65 years, those with metabolic or metastatic bone disease, those with a history of radiation therapy, and cortisone use were excluded. We included all cases that have performed both QCT and DXA and match our study criteria since the beginning of the QCT service in our hospital, until the date of scientific committee approval. Patients who had vertebral fractures occurring without trauma or with mild trauma and whose fractures were detected using direct radiography or advanced imaging methods were included in group 1 (n = 11). The vertebral compression fracture was in the lumbar region in 5 cases, the dorsal region in 5 cases, and both dorsal and lumbar regions in 1 case. Patients who had non-vertebral or peripheral fractures occurring without trauma or with mild trauma and whose fractures were detected with the medical history taken from the patient or with current imaging methods were included in group 2 (n = 11). Patients without fracture history, spinal pathology, and without a pathology that can cause secondary osteoporosis such as rheumatic disease and medication use were included in group 3 (n = 23).

Bone mineral density value (BMD) measurement with DXA was performed with the Lunar DPXL (GE-Lunar Prodigy, Madison, WI, USA, 2013) device from the lumbar (L1-4) spine and left femoral neck regions with the use of projections in anteroposterior (AP) direction. The position of the patients, measurement technique and analysis were adjusted according to the recommendations of the manufacturer. Daily calibration with a phantom was performed for device standardization. The precision error of the phantom was 0.3% and in vivo precision error was <1% in all measurement regions. Bone density measurement with QCT was performed with the 64-detector and 128-slice CT device (Optima CT660, GE Healthcare, Tokyo, Japan, 2014) from the L1-4 lumbar region and proximal femur region (kVp = 80/120/140, mAs = 160, slice thickness = 2–3 mm). The femoral neck and lumbar analyses were performed using QCT PRO with CliniQCT bone mineral density analysis software (Mindways, Austin, TX, USA). DoseWatch monitor of the CT device used in our hospital enabled the examination of the patients with the use of the lowest dose possible.

Statistical analysis

For evaluating the results, IBM SPSS Statistics 22 (IBM SPSS, Turkey) software was used for statistical analyses. In the evaluation of study data, compliance of parameters with normal distribution was evaluated using Shapiro–Wilk test. For evaluating study data, besides the descriptive statistical methods (Mean, Standard deviation, and frequency), one-way ANOVA was used in the intergroup comparison of the parameters showing normal distribution for comparing quantitative data and Tukey HDS test was used in identifying the group causing the difference. Paired sample t-test was used in the comparison of the DXA and QTC methods in terms of quantitative data showing normal distribution. McNemar's test was used in the evaluation of qualitative data. A *P*-value of <0.05 was considered statistically significant.

Results

Ages of the 45 patients included in the study varied between 65 and 84 years and the mean age was 72.84 (5.49) years. Demographics of the patients are presented in Table 1 and no statistically significant difference was observed except for BMI.

According to the intergroup comparison, there was no statistically significant difference between the three groups in terms of lumbar BMD, neck BMD, lumbar T, and neck T values in the DXA and QCT measurements (P>0.05) (Table 2). According to the intragroup comparison, QCT lumbar BMD (P<0.001.), QCT lumbar T (P=0.004), and QCT neck T (P=0.037) values were lower than DXA lumbar BMD, lumbar T, neck T values in group 1 (P<0.05). There was no statistically significant difference between DXA and QCT methods in terms of neck BMD values (P>0.05). In group 2, QCT lumbar BMD (P<0.001) and lumbar T (P<0.001) values were lower than DXA lumbar BMD and lumbar T values (P<0.05). There was no significant difference between DXA and QCT methods in terms of neck BMD and neck T values (P>0.05). In group 3, QCT lumbar BMD (P<0.001.), lumbar T (P<0.001), and neck BMD (P=0.004) values were lower than DXA lumbar BMD, lumbar T, and neck BMD values (P<0.05). There was no statistically significant difference between DXA and QCT methods in terms of neck T values (P>0.05) (Table 3).

Table 1: Demographic characteristics

		Group 1 Mean (SD) n=11	Group 2 Mean (SD) n=11	Group 3 Mean (SD) n=23	*P*-value
Age (years)		73.36 (6.52)	72.18 (6.27)	72.9 (4.76)	0.882
Height (cm)		157.09 (8.98)	154.64 (6.59)	158.3 (10.33)	0.561
BMI (kg/m²)		27.59 (3.82)	37.99 (7.41)	29.92 (3.83)	<0.001
Gender	Male	3 (27.3 %)	1 (9.1 %)	3 (13 %)	0.556
	Female	8 (72.7 %)	10 (90.9 %)	20 (87 %)	

SD: standard deviation

Table 2: Comparison of BMD values and T scores measured by QCT and DXA between the groups

	Group 1 Mean (SD) n=11	Group 2 Mean (SD) n=11	Group 3 Mean (SD) n=23	*P*-value
DXA lumbar BMD (g/cm²)	1.01 (0.14)	1.2 (0.29)	1.2 (0.23)	0.074
DXA femoral neck BMD (g/cm²)	0.71 (0.23)	0.82 (0.38)	0.81 (0.18)	0.490
DXA lumbar T score	0.98 (1.13)	-0.31 (1.92)	0.29 (1.83)	0.135
DXA femoral neck T score	-1.45 (0.92)	-1.25 (1.05)	-1.04 (0.77)	0.440
QCT lumbar BMD (g/cm³)	0.06 (0.03)	0.08 (0.02)	0.08 (0.03)	0.342
QCT femoral neck BMD (g/cm³)	0.57 (0.07)	0.65 (0.15)	0.63 (0.2)	0.473
QCT lumbar T score	-3.56 (2.32)	3.43 (0.83)	-3.53 (1.01)	0.974
QCT femoral neck T score	-2.07 (0.58)	-1.34 (1.36)	-1.48 (1.79)	0.465

QCT: Quantitative Computed Tomography DXA: Dual X-ray Absorptiometry, BMD: Bone Mineral Density

Table 3: Comparison of BMD values and T scores measured by QCT and DXA within the groups

		DXA (gm/cm²)	QCT (gm/cm³)	*P*-value
Group 1	Lumbar BMD	1.01 (0.14)	0.06 (0.03)	<0.001
Mean (SD)	Femoral neck BMD	0.71 (0.23)	0.57 (0.07)	0.088
n=11	Lumbar T score	-0.98 (1.13)	-3.56 (2.32)	0.004
	Femoral neck T score	-1.45 (0.92)	-2.07 (0.58)	0.037
Group 2	Lumbar BMD	1.2 (0.29)	0.08 (0.02)	<0.001
Mean (SD)	Femoral neck BMD	0.82 (0.38)	0.65 (0.15)	0.079
n=11	Lumbar T score	-0.31 (1.92)	-3.43 (0.83)	<0.001
	Femoral neck T score	-1.25 (1.05)	-1.34 (1.36)	0.795
Group 3	Lumbar BMD	1.2 (0.23)	0.08 (0.03)	<0.001
Mean (SD)	Femoral neck BMD	0.81 (0.18)	0.63 (0.2)	0.004
n=23	Lumbar T score	0.29 (1.83)	-3.53 (1.01)	<0.001
	Femoral neck T score	-1.04 (0.77)	-1.48 (1.79)	0.229

QCT: Quantitative Computed Tomography DXA: Dual X-ray Absorptiometry, BMD: Bone Mineral Density

Discussion

Although DXA is a frequently used method for measuring bone mass, diagnosing osteoporosis, and determining the risk of vertebral and non-vertebral fractures, many studies have shown that DXA has limitations in predicting and determining the risk of vertebral and non-vertebral fractures. The most important limitation is that DXA is affected by the bone size as well as osteophytes and hypertrophic changes of the vertebra that influence bone size. On the other hand, QCT performs three-dimensional measurements. It evaluates the density and geometry of the bone separately while determining the risk of fracture. Another important difference between the two measurement modalities is that QCT separately evaluates the cortical and trabecular bones [13-16] (Figure 1).

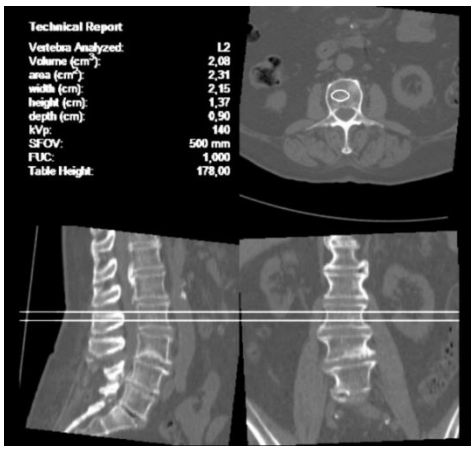

Figure 1: Three-dimensional QCT measurement technique of trabecular bone density of the L2 vertebra in a geriatric patient with lumbar spondylosis findings

Cortical and trabecular bones show different amounts of decreased density in different musculoskeletal regions, in relation to age and menopause [13,17-20]. It was shown that many types of fractures were associated with QCT volumetric BMD and DXA two-dimensional areal BMD measurements. In the volumetric BMD measurements, there was a stronger relationship with the trabecular bone compared to the cortical bone. However, this relationship varies according to the fracture type [14]. Considering all age groups, there are many studies emphasizing that QCT lumbar and total hip measurements are more effective than DXA in showing vertebral fractures [15,16,21]. The relationship with hip fractures and other non-vertebral fractures was evaluated in a limited number of studies [14,21].

In a study comparing DXA and QCT among patients with a vertebral fracture in the geriatric population, Lang et al. found that lumbar and femoral measurement values were significant in evaluating the risk of vertebral fracture in both measurement methods, that there was no difference between the two measurement methods and that the most relevant measurement value was lumbar spinal integral BMD in both measurement methods. However, they did not evaluate the relationship with non-vertebral fractures among the geriatric population [13]. Chalhoub et al. [14] performed a 9.7-year follow-up in a geriatric male population using both methods and underlined that lumbar and femoral BMD measurements could detect the risk of vertebral and non-vertebral fractures. However, they also stated that while QCT exhibited significant differences in detecting spinal and hip fractures, there was no difference between DXA and QCT in other peripheral fractures. In our study, in compliance with these two studies conducted with the geriatric population, there was no significant difference according to the intergroup comparison, whereas intragroup comparisons showed that QCT lumbar spinal and femoral measurement values were lower than DXA measurements in all

three groups. However, in our study, lumbar QCT measurement values were also found to be significantly lower than DXA measurements in the intragroup comparison of the patients with non-vertebral fractures. Chalhoub et al. found QCT is effective only in showing hip fracture as a peripheral fracture. Differently, we found it to be more sensitive in the patient group with hip and different peripheral fracture types. On the other hand, we did not classify peripheral fractures among themselves. As our study was conducted with the geriatric population, which exhibits senile osteoporosis that affects both the cortical and trabecular bones, we believe that QCT measurement values can be guiding in predicting both vertebral and non-vertebral fractures. However, due to the lack of difference between the groups, we believe that instead of the recently speculated opinion of replacing DXA with QCT in the geriatric population, QCT can be additionally used, when necessary.

International Society for Clinical Densitometry Official Positions emphasized that QCT was more sensitive than DXA and that it showed the characteristics and structural changes of the bone via a complex imaging technique [22]. However, high radiation dose and high costs are the disadvantages of QCT [23]. There are studies in the literature reporting that DXA and QCT lumbar and femoral measurements were correlated in premenopausal women without fractures [23,24]. Amstrup et al. [25] emphasized that there was a correlation between DXA and QCT in femoral and lumbar measurements in their correlation study conducted with postmenopausal women. They suggested that this correlation was weak in lumbar measurements and increased up to moderate-strong in the hip region. QCT measurements were also lower than DXA measurements in our geriatric patient group without fractures. We believe that degenerative changes which are prevalent among the geriatric population can cause a false increase in the DXA measurements of the lumbar region. In the group with vertebral fractures, the fact that compression fractures in the lumbar region could not be excluded in the DXA method, which can only be measured on AP images, may have caused a false elevation in density values. However, in QCT, after the lumbar vertebrae are scanned cross-sectionally, the vertebra with compression fracture can be excluded and the measurement can be taken from the appropriate location. At the same time, aortic calcifications, which are likely to be seen in the geriatric age group, can be included in the measurement field in DXA and causes an increase in density measurements. This obscures osteopenia /osteoporosis and leads to delay in diagnosis.

Limitations

This study had some limitations. One of the limitations was the low number of patients. Another limitation was that the patient population in our study was heterogeneous and normal, osteopenic and osteoporotic patient groups were not separated. There is a need for further studies conducted with a higher number of patients and homogenous patient groups in order to clarify the indications of both bone density measurement methods.

Conclusion

We believe that QCT can be a more sensitive method as it provided lower values in all three groups compared to DXA, but due to the lack of difference between groups in terms of fracture risk assessment, it may be beneficial to use QCT when indicated, rather than the view that QCT should replace DXA in the geriatric population. It seems more reasonable to prefer QCT in patient groups where DXA is not sufficient, such as marked degenerative changes or situations that require early diagnosis of osteoporosis.

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Psoriatic arthritis is associated with myocardial repolarization dysregulation as assessed by the QTc interval and the Tp-e/QTc ratio

Psöriatik artrit, QTc aralığı ve Tp-e/QTc oranı ile değerlendirilen miyokardiyal repolarizasyon düzensizliği ile ilişkilidir

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Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Dışkapı Training and Research Hospital (the approval number of 81/06 at 3/2/2020). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
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Abstract

Aim: An increased risk of arrhythmia has been shown in patients with psoriatic arthritis (PsA). Tp-e interval and Tp-e/QT ratio are considered useful markers for the assessment of myocardial repolarization heterogeneity. In present study we aim to investigate the characteristics of ventricular repolarization on the basis of QTc interval and Tp-e/QTc ratio in patients PsA.

Methods: This cross-sectional observational study included patients with psoriatic arthritis who were over 18 years of age. A control group was created with healthy volunteers. The diagnosis of psoriatic arthritis were done according to the CASPAR criteria. QT interval, corrected QT (QTc), Tp-e interval, Tp-e/QT ratio and Tp-e/QTc ratio were measured from the 12-lead electrocardiograms (ECG) of the PsA patients and control group.

Results: The study population consisted of 82 patients with PsA and 82 healthy volunteers. According to electrocardiographic parameters the heart rate was similar in both groups, but QT, QTc, Tp-e intervals; Tp-e /QT and Tp-e/ QTc ratios were significantly higher in the PsA group. The median Tp-e/QTc ratio of the patients with PsA was significantly higher than the median Tp-e/QTc ratio of the control group (0.21 (0.20-0.25) vs. 0.18 (0.17-0.19, P<0.001). The correlation analysis showed a weak correlation between Tp-e/QTc ratio and CRP value (r=0.197, P=0.012).

Conclusions: This is the first study to demonstrate the prolongation of the Tp-e/QTc ratio in patients with PsA. Prospective clinical studies to observe clinical importance of this finding particularly with regard to the arrhythmias and sudden death may be more valuable.
Keywords: Psoriatic arthritis, Electrocardiography, Tp-e/QTc ratio, Myocardial repolarization

Öz

Amaç: Psoriatik artritli (PsA) hastalarda aritmi riski artışı olduğu gösterilmiştir. Tp-e aralığı ve Tp-e/QT oranı, miyokardiyal repolarizasyon heterojenitesinin değerlendirilmesinde yararlı belirteçler olarak kabul edilmektedir. Bu çalışmada PsA hastalarında QTc aralığı ve Tp-e/QTc oranı temelinde ventriküler repolarizasyonun özelliklerini incelemeyi amaçladık.

Yöntemler: Bu kesitsel gözlemsel çalışmaya 18 yaşın üzerinde psoriatik artritli hastalar dahil edildi. Sağlıklı gönüllülerden bir kontrol grubu oluşturuldu. Psoriatik artrit tanısı CASPAR kriterlerine göre yapıldı. PsA hastalarının ve kontrol grubunun 12 kanallı elektrokardiyogramlarından (EKG) QT aralığı, düzeltilmiş QT (QTc), Tp-e aralığı, Tp-e/QT oranı ve Tp-e/QTc oranı ölçüldü.

Bulgular: Çalışma popülasyonu 82 PsA hastası ve 82 sağlıklı gönüllüden oluşuyordu. Elektrokardiyografik parametrelere göre kalp hızı her iki grupta da benzerdi, ancak QT, QTc, Tp-e aralıkları; Tp-e/QT ve Tp-e/QTc oranları PsA grubunda anlamlı olarak yüksekti. PsA'lı hastaların medyan Tp-e/QTc oranı, kontrol grubunun medyan Tp-e/QTc oranından (0,21 (0,20-0,25) ve 0,18 (0,17-0,19, P<0,001) anlamlı olarak daha yüksekti. Korelasyon analizi Tp-e/QTc oranı ile CRP değeri arasında zayıf bir korelasyon gösterdi (r=0,197, P=0,012).

Sonuçlar: Bu çalışma PsA hastalarında Tp-e/QTc oranının uzadığını gösteren ilk çalışmadır. Bu bulgunun özellikle aritmiler ve ani ölüm açısından klinik önemini gözlemlemeye yönelik ileriye dönük klinik çalışmalar daha değerli olabilir.
Anahtar kelimeler: Psoriatik artrit, Elektrokardiyografi, Tp-e/QTc oranı, Miyokardiyal repolarizasyon

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Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory joint disease and included as one of the spondyloarthropathies (SpA) [1], with a prevalence of PsA in the general population of about 0.1–0.25 % [2,3]. It is known that concomitant cardiovascular risk factors are higher in psoriatic arthritis patients than in the normal population [4,5]. Cardiovascular events have also been shown to be more common in these patients than in the normal population [6].

Cardiovascular disease is the most common cause of death in psoriatic arthritis. It is thought that endothelial dysfunction and arterial stiffness may have an effect on cardiovascular morbidity and mortality in psoriatic arthritis as in many other inflammatory diseases [6].

Some previous studies have reported an increased risk of cardiac arrhythmia in psoriasis [7]. Heart rate variability, which is an indicator of cardiac autonomic regulation, has been shown to decrease in psoriatic arthritis [8]. In another study, it was shown that the Tp-e interval and Tp-e/QT ratio, which are considered the predictors of ventricular arrhythmia, were prolonged in patients with psoriasis vulgaris [9]. In our study, we planned to investigate the characteristics of ventricular repolarization on the basis of QTc interval and Tp-e/QTc ratio in patients with psoriatic arthritis, which can be seen in 6-39% of psoriasis patients [2,3].

Materials and methods

This cross-sectional observational study included patients with psoriatic arthritis who were over 18 years of age who presented to the rheumatology outpatient clinic between February 2020 and June 2020 and were diagnosed with psoriatic arthritis according to the CASPAR criteria [10] and have been treated at least 6 months.

Patients with a history of coronary artery disease, moderate to severe valvular heart disease, prior pacemaker insertion, history of dysrhythmia, cardiomyopathy, acute and chronic renal failure, abnormal thyroid function test, abnormal electrolyte values, and those who were on antiarrhythmic drug treatment and using other drugs that can affect Tp-e and QTc intervals such as antiarrhythmic agents, antipsychotic agents, tricyclic antidepressants, and b-blockers were excluded from the study. The study protocol was approved by the Ethics Committee of Dışkapı Training and Research Hospital with the approval number of 81/06 at 3/2/2020, and informed consent was obtained from each patient.

Demographic information of the patients, including age, gender and body mass index (BMI), history of hypertension (HT), hyperlipidemia, and smoking status were recorded. The laboratory tests included complete blood count, erythrocyte sedimentation rate (ESH), C- reactive protein (CRP), fasting glucose level, lipid profile, liver, and kidney and function tests.

Assessment of ECG

The 12-lead ECG recordings were taken at the supine position with a paper speed of 50 mm/sec and voltage of 10 mm/mV using standard ECG system (CardiofaxV model 9320, Nihon Kohden, Tokyo, Japan). QT interval, and Tp-e interval were measured manually. Tp-e/QT ratio and Tp-e/QTc ratio were calculated from these measurements. The onset of P wave was defined as the first visible upward departure from the baseline, and the end of P wave was defined as returning to baseline. QT interval was defined as the time from the onset of the QRS to the point at which T wave returns to baseline. QTc interval was calculated using the Bazett's formula. We used the tangent method to measure Tp-e in leads V2 and V5. The 'tangent' method of measuring Tp-e defines T-peak as the maximum positive or negative deflection of T wave from the isoelectric line. The T-end is defined as the intersection of the isoelectric line with the tangent to the down slope of the T wave. Tp-e/QTc ratio was also calculated because of the uncertainty in the literature regarding whether Tp-e is rate- dependent. All measurements were performed by two independent investigators who were blinded to the clinical status of the subjects. Tp-e measurement was not performed in cases of excessive artifact or T wave flatness.

Statistical analysis

Statistical analysis was performed using SPSS Version 23 (IBM Corp; Armonk, NY, USA) statistical software. Categorical data were presented as numbers and percentages. Continuous variables were presented as mean (standard deviation) when normally distributed, and as median and interquartile ranges otherwise. The Kolmogorov-Smirnov test was performed in order to test the normality of the numerical variables. For variables that were not normally distributed, non-parametric statistical methods were used and Mann-Whitney *U* test was performed in order to compare two independent groups. Student T test was performed in order to compare two independent groups for normally distributed variables. Categorical variables were compared with the x^2 test. Correlation analyses were used to identify the related parameters with the Tp-e/QTc ratio. Pearson's correlation coefficients were used to assess the strength of the relationship between continuous variables and Spearman's correlation analysis for non-continuous and categorical variables. A *P*-value <0.05 was considered statistically significant.

Results

Our study included 82 PsA patients and 82 age and gender-matched controls. The demographic, laboratory and data of patients with and without PsA are presented in Table 1. Patient groups with and without PsA were similar in terms of basal characteristics. Median age of the PsA group was 53.5 (45.7-60.2) years and the median age of the control group was 50 (48-55) years (*P*=0.064).

Patient groups with and without PsA were similar in terms of gender distribution, comorbidities, hypertension hyperlipidemia and smoking status. According to electrocardiographic parameters the heart rate was similar in both groups, but QT, QTc, Tp-e intervals, Tp-e /QT and Tp-e/ QTc ratios were significantly higher in the psoriatic arthritis group. The median Tp-e/QTc ratio of the patients with PsA was 0.21 (0.20-0.25). The median Tp-e/QTc ratio of the control group was 0.18 (0.17-0.19) (*P*<0.001). The electrocardiographic parameters of both the groups are shown in Table 2. Table 3 presents the correlation analyses between the Tp-e/QT ratio and the study

parameters. The single parameter that is associated with the Tp-e/QTc ratio was CRP value (r=0.197, *P*=0.012).

Table 1: Basal characteristics of the study participants

	Psoriatic arthritis (n=82)	Control (n=82)	*P*-value
Age (years)	53.5(45.7-60.2)	50(48-55)	0.064
Female Gender, n (%)	47 (57.3)	49 (59.8)	0.874
Diabetes mellitus, n (%)	6 (7.3)	8 (9.8)	0.781
Hypertension, n (%)	25 (30.5)	31 (37.8)	0.410
Hyperlipidemia, n (%)	21 (25.6)	31 (37.8)	0.131
Smoking, n (%)	13 (15.9)	16 (19.5)	0.683
BMI (kg/m^2)	23.3 (1.8)	23.1 (1.7)	0.484
Creatinine (mg/dL)	0.85 (0.3)	0.81 (0.1)	0.303
Potassium (mEq/L)	4.3(4.0-4.5)	4.4(4.1-4.5)	0.129
Fasting glucose (mg/dL)	90 (87-98)	87(86-94)	0.051
AST U/L	20 (16.5-25)	19 (16-23)	0.186
ALT U/L	20 (14.5-25)	20 (12-27)	0.941
TC (mg/dL)	194 (168-218)	181 (169-205)	0.233
Triglyceride (mg/dL)	116 (91-171)	117 (89-181)	0.897
HDL (mg/dL)	51 (46-57)	48 (41-52)	0.547
LDL (mg/dL)	123(108-143)	115 (102-130)	0.285
Hemoglobin (mg/dL)	13.2(12.3-14.2)	13.5 (13.2-13.8)	0.303
WBC	6.7 (5.7-8.1)	6.5 (5.4-8.8)	0.649
ESR (mm/sec)	10 (4.7-17.2)	7.6 (7-8.1)	0.045
CRP (mg/L)	3.8 (1.7-8.9)	3(2-4)	0.028

BMI: body mass index, TC: total cholesterol, WBC: White blood cell count, ESR: erythrocyte sedimentation rate, CRP: C reactive protein

Table 2: Electrocardiographic findings of the study participants

	Psoriatic arthritis (n=82)	Control (n=82)	*P*-value
Heart rate	79.5 (11)	78 (11)	0.720
QT (ms)	390 (378-400)	380 (370-390)	0.007
QTc (ms)	406 (390-428)	399 (380-408)	0.001
Tpe (ms)	90 (80-100)	72 (68-75)	<0.001
Tp-e/QT	0.22 (0.21-0.27)	0.19 (0.17-0.20)	<0.001
Tp-e/ QTc	0.21 (0.20-0.25)	0.18 (0.17-0.19)	<0.001

Table 3: The association between the Tp-e/QTc ratio and variables

Variables	Bivariate correlation	
	r	*P*-value
Age	0.061	0.440
Female gender	-0.018	0.820
Diabetes mellitus	-0.072	0.358
Hypertension	-0.101	0.197
Hyperlipidemia	-0.017	0.827
Smoking	0.088	0.264
BMI	0.039	0.619
WBC	0.023	0.775
ESR	0.100	0.204
CRP	0.197	0.012

BMI: body mass index, WBC: White blood cell count, CRP: C reactive protein, ESR: erythrocyte sedimentation rate

Discussion

The prevalence of cardiovascular diseases is increased in psoriatic arthritis patients and the leading cause of mortality is cardiovascular diseases [6,11-13]. There are studies about the increased risk of arrhythmia in these patients [14]. The Tp-e/QTc ratio is an electrocardiographic parameter and useful in the prediction of ventricular arrhythmias [15-17]. The association between the presence of PsA and Tp-e/QTc prolongation has not been studied before. In the present study, we showed that the Tp-e/QTc ratio is prolonged in psoriatic arthritis patients.

The T-peak to T-end interval (Tp-e) on the 12-lead electrocardiogram (ECG) is in correlation with dispersion of ventricular repolarization and considered as a predictor of ventricular tachyarrhythmia and death [18-20]. The heterogeneity of ventricular repolarization dispersion causes heterogeneity in myocardial refractoriness. This variability provides a predisposition to the ventricular arrhythmias [21]. Tp–e interval is affected by heart rate variability, Tp–e/QTc index is thought to be more meaningful to eliminate this effect [22].

In the present study both QTc and Tp-e/QTc were prolonged in PsA patients. These findings show us that repolarization is delayed and at the same time the distribution of repolarization is impaired. In a previous study it was shown that patients with psoriasis were at higher risk of developing arrhythmia, particularly for those with psoriatic arthritis, independent of traditional cardiovascular risk factors [14]. The underlying mechanism beneath the increased arrhythmic risk in PsA is not known.

Many chronic inflammatory diseases are associated with an increased incidence of atrial and ventricular arrhythmias [23,24]. Many inflammatory markers, such as tumor necrosis factor-alfa, IL-2, IL-6 were associated with cardiac arrhythmias [25].

In previous studies, elevated CRP values were associated with QTc prolongation in healthy individuals [26,27] and in patients with chronic inflammatory arthritis [28]. In our present study, CRP value was associated with Tp-e/ QTc prolongation.

The prolongation of the Tp-e/QTc ratio has been shown in many chronic inflammatory diseases in various studies [29-31]. Our study is the first that shows the prolonged Tp-e/QTc ratio in psoriatic arthritis patients. In psoriatic arthritis, many factors besides inflammation are thought to play a role in repolarization heterogeneity and increased arrhythmia risk. In some studies, patients with psoriasis have been shown to have endothelial dysfunction and coronary microvascular dysfunction [32,33]. It has also been shown that psoriasis is associated with subclinical atherosclerosis [34]. Besides the evidence showing subclinial atherosclerosis, increased comorbid cardiovascular risk factors cause the increase in cardiovascular morbidity and mortality in these patients [34-36]. In psoriatic arthritis, unlike psoriasis vulgaris, the presence of joint involvement in addition to skin findings suggests that the burden of inflammation is heavier than patients with only skin involvement and that cardiovascular risk may be higher [37]. Future studies comparing psoriasis and psoriatic arthritis patients in terms of cardiovascular risk and outcome will illuminate this issue. There are studies showing an increase in arrhythmic events in psoriasis, especially in psoriatic arthritis [14]. It is thought that severe inflammation causes atrial fibrosis, increasing atrial arrhythmia risk and, because of the damage done by vascular inflammation to the artery wall, arrhythmia risk increases due to ischemia and major cardiovascular events [38,39]. In addition, inflammation is thought to increase the risk of arrhythmia by affecting cardiomyocyte electrophysiology on ion channels dysregulation [23].

The detection of prolonged Tp-e and Tp-e/QTc ratios in PsA patients in our study suggests that there is myocardial repolarization heterogeneity and this may play a role in arrhythmic events. However, in our study, there is no clinical data about arrhythmic outcome. In the future, studies supported by ECG data such as Tp-e and Tp-e/QTc ratio, which also include data on arrhythmic outcome, will help to enlighten the pathophysiology of the increased arrhythmia risk in PsA.

Limitations

This study has some limitations. Most importantly, since this study was designed as a single-center and an observational study, we could not achieve any significant evidence about the clinical importance of the prolongation of Tp-e and Tp-e/QTc in PsA patients. Future studies comparing psoriasis patients with and without arthritis may be useful in evaluating the effect of the severity of inflammation on ECG findings.

Conclusion

Our study is the first to demonstrate the prolongation of the Tp-e interval and Tp-e/QTc ratio in patients with psoriatic arthritis. Prospective clinical studies that monitor PsA patients with ECG findings and observe their clinical outcomes, particularly with regard to the arrhythmias and sudden death in follow-up, may be more valuable.

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Evaluation of primary lateral neck mass in adults: Cross sectional study

Erişkinlerde primer lateral boyun kitle değerlendirilmesi: Kesitsel çalışma

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Abstract

Aim: Primary Lateral neck mass (PLNM) is a disease that expresses a pathology in neck, excluding thyroid and skin tumors. The spectrum ranges from "lumps, mass or tumors," congenital tumors, inflammatory diseases, and benign neoplasm to malignant neoplasm. The current Skandalakis algorithm excludes thyroid pathology. Correct anamnesis and physical examination are especially important for data collection. We herein analyzed the methods of study in PLNM.

Methods: This cross-sectional study was performed with review of medical records from January 2010 to July 2019. All patients with diagnoses of PLMN and older than 15 years of age were analyzed. We excluded patients with "classic" and unknown lateral neck masses. Standardized protocols for data collection were implemented to minimize or avoid bias. The statistical analysis was carried out with STATA v 14.0.

Results: A total of 78 patients were studied. Age and time of evolution were the most crucial factors in presumptive diagnoses. The most frequent location was the anterior triangle in the neck (77%). Murmurs and thrills were clinically defined as vascular pathologies. Mobility on all axes without fixation to deep planes were clinically defined as Lipoma. The pathological examinations were more frequently reported as lymphomas (32), which were followed by Branchial Cleft Cysts. Ultrasound was a complementary study useful in congenital malformations to determine cystic characteristics. The presence of "B symptoms" and FNA (fine needle aspiration) are useful in primary Lymphoproliferative adenopathy. MRI (Magnetic resonance image) and Angio-MRI are useful in tumors of nervous origin (schwannomas, neurofibromas, and paragangliomas tumors). Malignant soft tissue tumors (sarcomas) need complementary studies and imaging for surgical planning.

Conclusion: Differential diagnoses of the primary lateral neck masses challenge surgeons. Anamnesis and physical examination are the most crucial factors for the presumptive diagnoses. Complementary studies and imaging should be requested with selective criteria.

Keywords: Primary lateral neck mass, Lateral neck mass, Head and neck tumors

Öz

Amaç: Primer Lateral boyun kitlesi (PLNM), tiroid ve deri tümörleri dışında boyundaki patolojileri ifade eden bir hastalıktır. Spektrum "topaklar, kitle veya tümörler", konjenital tümörler, enflamatuar hastalıklar ve iyi huylu neoplazmadan kötü huylu neoplazmaya kadar değişir. Mevcut Skandalakis algoritması tiroid patolojisini dışlamaktadır. Veri toplama için doğru anamnez ve fiziksel muayene özellikle önemlidir. Burada PLNM'de çalışma yöntemlerini analiz ettik.

Yöntemler: Bu kesitsel çalışma, Ocak 2010'dan Temmuz 2019'a kadar tıbbi kayıtların gözden geçirilmesi ile gerçekleştirildi. PLMN tanısı olan ve 15 yaşından büyük tüm hastalar analiz edildi. "Klasik" ve bilinmeyen lateral boyun kitlesi olan hastaları dışladık. Önyargıyı en aza indirmek veya önlemek için veri toplama için standartlaştırılmış protokoller uygulandı. İstatistiksel analiz STATA v 14.0 ile gerçekleştirildi.

Bulgular: Toplam 78 hasta incelendi. Yaş ve süregelme zamanı, varsayımsal tanılarda en önemli faktörlerdi. En sık yerleşim yeri boyundaki ön üçgendi (% 77). Üfürüm ve thrill, klinik olarak vasküler patolojiler olarak tanımlandı. Derin planlara fiksasyon olmaksızın tüm eksenlerde hareketlilik klinik olarak Lipoma olarak tanımlandı. Patolojik incelemeler daha sık lenfoma (32) olarak bildirilmiş, bunu Branşiyal Yarık Kistleri izlemiştir. Ultrason, kistik özelliklerin belirlenmesinde konjenital malformasyonlarda yararlı tamamlayıcı bir çalışmaydı. "B semptomları" ve FNA'nın (ince iğne aspirasyonu) varlığı, birincil Lenfoproliferatif adenopatide faydalıdır. MRI (Manyetik rezonans görüntüsü) ve Anjiyo-MRI, sinir kaynaklı tümörlerde (schwannomlar, nörofibromlar ve paraganglioma tümörleri) faydalıdır. Kötü huylu yumuşak doku tümörleri (sarkomlar), cerrahi planlama için tamamlayıcı çalışmalara ve görüntülemeye ihtiyaç duyar.

Sonuç: Primer lateral boyun kitlelerinin ayırıcı tanısı cerrahları zorlamaktadır. Anamnez ve fizik muayene, olası tanılar için en önemli faktörlerdir. Seçici kriterler ile tamamlayıcı çalışmalar ve görüntüleme talep edilmelidir.

Anahtar kelimeler: Primer lateral boyun kitlesi, Lateral boyun kitlesi, Baş ve boyun tümörleri

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Introduction

One of the most important considerations in an adult with a lump in the neck, is that the mass may represent a metastatic tumor from a primary cancer, often but not always in the upper respiratory or alimentary tract. Primary lateral neck mass (PLNM) is a disease that expresses a pathology in the neck, excluding thyroid and skin tumors. The Spectrum ranges from "lumps, mass or tumors," congenital tumors, inflammatory diseases, benign neoplasm, to malignant neoplasm. The current Skandalakis algorithm excludes thyroid pathology [1]. Correct anamnesis and physical examination are especially important for the data collection. The anatomical location of the mass, and overall time course are crucial factors to help differentiate neoplastic disease from other possibilities. In addition, the patient's age plays a key role.

The neck is divided into cervical triangles, all of which have a common boundary, the sternocleidomastoid muscle. The posterior cervical triangle is bound anteriorly by the posterior aspect of the sternocleidomastoid muscle, posteriorly by the anterior border of the trapezius muscle, and inferiorly by the clavicle. The boundaries of the anterior cervical triangle are the median line of the neck, the inferior border of the mandible superiorly, and the anterior border of the sternocleidomastoid muscle posteriorly. The location of the neck mass in a particular lymphatic zone also provides the clinician a key to the site of origin of a primary tumor or inflammatory process.

In these groups of patients, the diagnosis should made quickly so that correct management of the disease can be instituted. Imaging is often an essential component in evaluating PLNM and can be helpful in characterizing congenital, inflammatory, vascular, and neoplastic lesions [2]. In some cases, characteristic imaging appearances can be diagnostic, so correct evaluation provides framework for timely diagnosis [3]

Ultrasound of the neck is usually performed with the patient in the supine position, with the neck extended. A high-frequency linear transducer provides good resolution of superficial structures and is therefore useful for evaluation of most palpable masses in the neck. Doppler imaging provides visualization of arterial and venous flow and can be used to evaluate the presence and distribution of flow within a mass. The examination should also include assessment of the sub mandibular, parotid, and thyroid glands, when indicated. Identifying a normal thyroid gland is important in the preoperative workup of some congenital neck masses such as thyroglossal duct cyst or ectopic thyroid [4].

One of the primary advantages of an ultrasound is its ability to distinguish between solid and cystic masses. Simple cystic masses are anechoic and demonstrate posterior acoustic enhancement. This phenomenon is sometimes referred to as increased through transmission, making the tissues behind the cyst appear brighter than the adjacent soft tissues due to the increased velocity of sound waves through fluid in the cyst relative to soft tissues. Doppler imaging can also elucidate how flow is distributed within a mass (centrally, peripherally, or evenly throughout), and whether the flow is normal, increased, or decreased, all which may have diagnostic significance.

In most situations, computed tomography (CT) of the neck with contrast is the best initial imaging study for evaluation of a neck mass in an adult. CT with contrast provides adequate information regarding the size, extent, location, and characteristics of the mass. Cystic and solid lesions can be distinguished, and the relationship of the mass to other vital structures such as the airway, cranial nerves, and major blood vessels can be assessed. The scan will also reveal possible primary sites in the case of neoplastic disease. To encompass the entire upper aerodigestive tract, the ordering physician should request that the CT scan of the neck extend from the base of the skull to the thoracic inlet [5].

Magnetic resonance image (MRI) is an excellent imaging modality for soft tissue lesions, but is not required in most situations. MRI is more expensive and time-consuming. However, it may be useful in certain clinical scenarios, for example, in a patient with paraganglioma. Angio MRI is the gold standard for diagnosis. A typical neck MRI protocol includes multiplanar T1, fat-suppressed T2 or short tau inversion recovery (STIR) sequences, diffusion-weighted images (DWI), and post contrast, fat-suppressed T1 weighted sequences. Compared with CT, MRI protocols are more complex, and may require tailoring to specific pathologies. T1 weighted images are helpful for delineation of anatomy. Fat appears bright on T1 and T2 weighted images, and fat suppression is helpful for elucidating underlying lesions on T2 weighted and post contrast sequences. Various fat-suppression sequences are available, which vary by technique and manufacturer, including STIR [6].

Fine needle aspiration cytology offers an accurate, sensitive, inexpensive, and rapid method for evaluation of a cervical adenopathy or mass. Slide preparation is critical for accurate diagnosis, and immediate inspection in a specialized cytopathology clinic allows additional material to be acquired if the aspirate is acellular or if further material is required for immunocytochemistry or culture. For patients with poorly defined or deep-seated lesions, image or ultrasound guidance can be used. Inevitably, there will be cases in which the validity of fine needle biopsy is called into question. In these circumstances an open biopsy may be the only way to determine the diagnosis. The objective of the study is to analyze the approach in diagnosing PLNM.

Materials and methods

This cross-sectional study was performed with a review of medical records from January 2010 to July 2019. All patients with diagnoses of PLMN and older than 15 years of age were analyzed. We excluded patients with "classic" and unknown lateral neck masses. Standardized protocols for data collection were implemented to minimize or avoid bias. Preformed strategies on recollection of information were defined before the study started. All procedures performed in this study involving human participants were in accordance with the ethical national and international standards.

We aimed to determine the utility of anamnesis (age, time of evolution and medical history), physical examination (anatomical location and characteristics of the tumor) and complementary studies requested.

Statistical analysis

Statistical analysis was carried out with STATA v 14.0, which allowed for the application of the corresponding statistical epidemiologic techniques by analyzing descriptive statistical variables.

Results

A total of 78 patients (42 women and 36 men) with a mean age of 27 (10) years (15-63 years) were included. Age and time of evolution were the most crucial factors on presumptive diagnoses. The Skandalakis algorithm was used. Congenital tumors, inflammatory diseases, benign neoplasm were more frequent in young patients. Malignant tumors were diagnosed in adults older than 45 years of age. Lymphoproliferative diseases were frequent in young, adult, and old patients. When the time of evolution was less than 30 days, the diseases were most clinically defined as inflammatory diseases or benign tumors. Hard, painful, and fast-growing neck tumors were defined as malignant. The most frequent anatomical location was the anterior triangle in the neck (77%). Murmurs and thrills indicated vascular pathology. The mobility on all axes without fixation to deep planes indicated lipoma. The pathological examinations more frequently reported as lymphomas (32), followed by Branchial Cleft Cysts (19), Lipomas (7), Lymphangioma (6), Paragangliomas Tumors (5), Schwannomas (3), Neurofibromas (2), Undifferentiated Sarcoma (2), Liposarcoma (1), and arteriovenous malformation (1) (Table 1). Ultrasound and doppler were complementary studies useful in congenital malformations to determine cystic characteristics and vascularization. The presence of “B symptoms” and FNA (fine needle aspiration) are useful in primary Lymphoproliferative adenopathy. Unilocular cyst diagnoses indicated Branchial Cleft Cysts, while multilocular cyst with tracts were diagnosed as Lymphangioma. The presence of “B symptoms” and FNA (fine needle aspiration) are useful in primary Lymphoproliferative adenopathy. MRI and Angio-MRI were useful in tumors of nervous origin (schwannomas, neurofibromas, and paragangliomas). Malignant soft tissue tumors (sarcomas) needed complementary studies for surgical planning, like CT or MRI.

Table 1: Distribution of pathological diagnoses of the patients

Pathology	Percent
Lymphomas	41
Branchial Cleft Cysts	24
Lipomas	9
Lymphangioma	8
Paragangliomas Tumors	6
Schwannomas	4
Neurofibromas	3
Undifferentiated Sarcoma	3
Liposarcoma	1
Arteriovenous Malformation	1

All patients with primary Lymphoproliferative adenopathy underwent open biopsy to determinate cytogenetic characteristics for immunocytochemistry studies. All other patients had resection of the tumor with open surgery. Four seromas were presented. Among patients operated due to schwannomas, there were patients with dysphonia and 1 with a swallowing disorder. Four patients died (3 advanced lymphomas, and a patient with sarcoma). The median follow-up was 27 months. There were no recurrences.

Discussion

Primary lateral neck mass (PLNM) includes pathologies in the neck excluding the thyroid, and skin tumors metastases of upper respiratory or alimentary tract. The diagnosis is highly challenging in a variety of these cases. Understanding the basic evaluation of the neck mass is essential in determining when a mass is insignificant or significant, and potentially malignant. Beginning with an understanding of neck anatomy, a thorough history-taking and physical examination can become straightforward and well directed.

Patient’s age, duration and progression of the neck mass, and associated symptoms if any, can often significantly narrow the possible diagnosis. In general, the potential for malign neoplasm increases with increasing patient age [7].

Progressive neck masses present for more than two weeks are more likely to be neoplastic. Definition of the size, location, and physical qualities of the neck mass provide insight into its origin. All patients with a neck mass deserve a thorough exam of the skin. For almost all patients with a progression neck mass, except for suspected vascular tumors, fine needle aspiration is a good next step.

Branchial cleft cysts are most commonly found in late childhood or early adulthood. Similar to thyroglossal duct cysts, they are frequently diagnosed following an upper respiratory tract infection when the mass becomes inflamed. Occasionally the mass resolves, but most often they persist as a soft mass in the neck. The first branchial cleft cyst is found at the mandibular angle inferior to the ear lobule along the inferior border of the mandible and may have a tract that connects to the external auditory canal. The second branchial cleft cyst is the most common type and may have a tract that opens along the anterior border of the sternocleidomastoid muscle. This cyst sometimes has a tract that opens in the oropharynx at the superior portion of the tonsillar fossa. Patient’s age, duration, location, and progression of the neck mass with ultrasound and aspiration of cholesterol fluid is sometimes enough for diagnosis. However, congenital cystic lesions such as branchial cleft cysts are often well depicted on CT examinations. In some cases, however, branchial cleft cysts and associated sinus tracts may be collapsed, rendering them difficult to identify on any imaging modality. Uncomplicated branchial cleft cysts appear as hypoattenuating lesions with a thin wall. In cases of infected branchial cleft cysts, CT demonstrates a hypoattenuating cystic lesion, which may have a thickened wall, and inflammatory changes in the surrounding soft tissues [8] (Figure 1).

MRI may be helpful in evaluating atypical features of branchial cleft cysts, which can result from intracapsular hemorrhage or solidification of cystic fluid, appearing as abnormal signal intensities of the contents. Intracystic hemorrhage can demonstrate hyperintensity on T1 and T2 weighted images, while solidification of cystic fluid displays homogeneous hypo intensity on T2 weighted images without enhancement. Atypical branchial cleft cysts can be difficult to differentiate from cystic malignancies even on MRI, and tissue sampling may be necessary [9]. Definitive treatment is complete surgical excision of the cyst and tract.

Figure 1: 18-year-old patient with left neck mass, mobile, elastic, 5 years of evolution. Ultrasound: cystic lesion, anechogenic image with posterior reinforcement. Diagnosis: Branchial cleft cysts

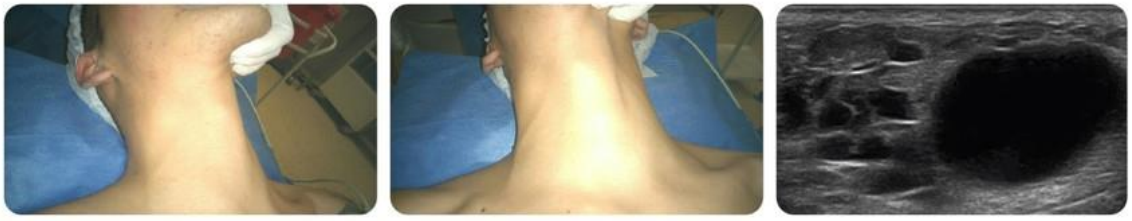

Figure 2: 15 -year-old male patient with right neck mass, elastic, 2 years of evolution. Ultrasound: multi trabecular cyst image in right supraclavicular region

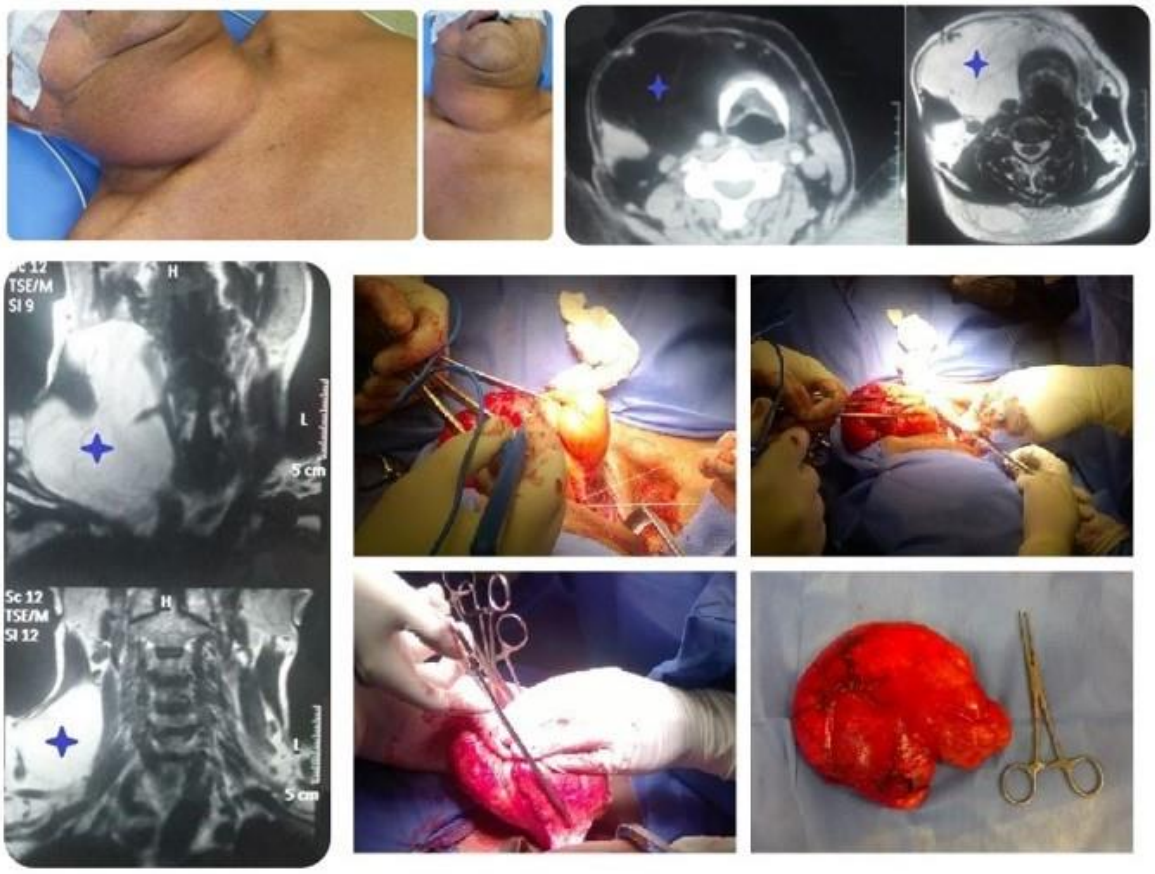

Figure 3: 54-year-old male patient. 6 years of evolution and slow growth. MRI. Lipoma in STIR sequence of fat suppression is confirmed.

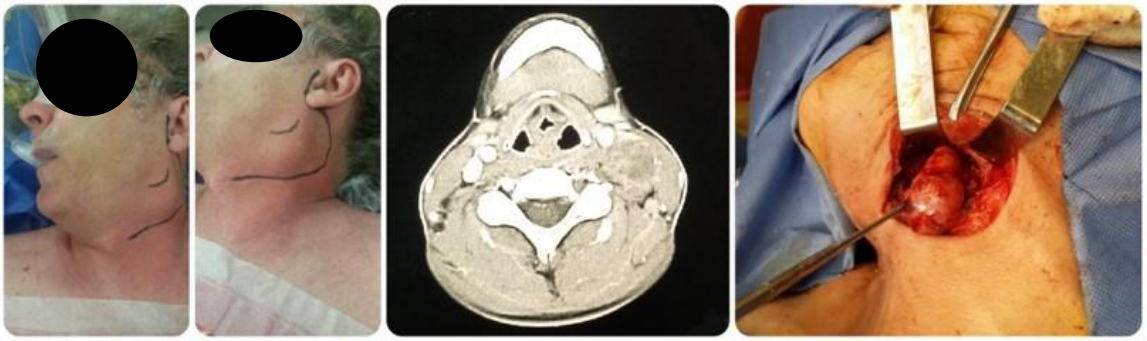

Figure 4: 65-year-old patient with a history of B symptoms and lateral neck tumor. TC: nodal image with central necrosis. FNA: lymphoproliferative syndrome. Biopsy is decided to perform immunohistochemistry.

Lymphangioma, or lymphatic malformation, is a rare, congenital anomaly that usually presents in childhood and occasionally in adults. The majority of cases occur in the head and neck, mostly in the posterior triangle [10]. Diagnosis is by history of a soft, compressible neck mass that usually enlarges proportionally with the growth of the patient. Characteristic findings of trabecular cyst-like structures on imaging studies like ultrasound or CT scan of the neck. Macrocystic lymphatic malformation appears as an unilocular or multilocular cystic lesion, usually with thin septations (Figure 2). Definitive diagnosis of lymphangioma is from operative pathology. Treatment regimens vary depending on macrocystic or microcystic features, but usually involve an attempt at complete surgical excision [11].

Lipomas and especially liposarcomas are extremely rare lesions presenting above the clavicles, as they usually occur in extremities and the trunk. In general, patients present with a slowly enlarging, painless neck mass. A history of trauma to the area affected may also be elicited [12]. Physical examination reveals a subcutaneous, smooth-surfaced soft tissue mass. For most subcutaneous lipomas, no imaging studies are required, but a deep lipoma requires contrast-enhanced CT scan or MRI of the neck to determine the extent of the process before complete surgical excision. STIR sequences with fat suppression on MRI are useful to determinate fat tumors (Figure 3). Although simple lipomas and well-differentiated liposarcomas are both grossly fatty masses, MRI has been described as useful in attempting to distinguish these two lesions. Several imaging features are more closely associated with well-differentiated liposarcomas, including thickened or nodular septa, associated non-adipose masses, prominent foci of high T2 signal, and prominent areas of enhancement. Higher grade liposarcomas generally do not confound the MRI diagnosis of grossly fatty lesions because they typically contain little or no macroscopic fat [13]. A significant number of lipomas will have prominent non-adipose areas and will demonstrate an imaging appearance traditionally ascribed to well-differentiated liposarcoma. Features that suggest malignancy include increased patient age, large lesion size, presence of thick septa, presence of nodular and/or globular or non-adipose mass like areas, and decreased percentage of fat composition [14].

Lymphomas are a heterogeneous group of lymphoproliferative disorders and are classified as Hodgkin or non-Hodgkin lymphoma. Young adults with chronic non-tender nodal enlargements in the anterior or posterior triangle of the neck may have Hodgkin's lymphoma [15]. Seventy percent of Hodgkin's disease is first diagnosed in the neck and only 25% of these will have B symptoms (fever, chills, night sweats or weight loss). The size, consistency, tenderness, and mobility of the mass provide diagnostic clues. Symptoms include odynophagia, globus sensation, otalgia, or hearing loss associated with otitis media and dysphagia. Classic constitutional symptoms include fever, night sweats, and weight loss. Lymphomas present most frequently with lymphadenopathy and frequently involve the head and neck region. In the head and neck region this disease most often presents as a painless nodal mass, which may become painful with rapid growth. Hodgkin disease rarely presents in extra nodal sites in the head and neck area, whereas non-Hodgkin lymphoma often presents with extra nodal manifestation in the Waldeyer ring, mainly the palatine tonsil and nasopharynx. FNA are useful in primary lymphoproliferative adenopathy (Figure 4). CT imaging studies of the head and neck, chest, abdomen, and pelvis assist in staging, in addition to planning the most appropriate site for biopsy to confirm the diagnosis [16]. Open biopsy is frequently necessary to ensure an adequate specimen for appropriate cytogenetic studies. Vascular anomalies are disorders of the endothelium and surrounding cells that can affect the vasculature and involve any anatomical structure. Arteriovenous malformations (AVMs) are defects in the vascular system, consisting of tangles of abnormal blood vessels (nidus) in which the feeding arteries are directly connected to a venous drainage network without interposition of a capillary bed. The most common site of extracranial AVM is the head and neck [17]. AVM is present at birth but may not become evident until childhood. AVM has a pink-red cutaneous stain with a palpable thrill or bruit, and it is important to distinguish AVM from a capillary malformation or hemangioma (Figure 5). Common complications are pain, ulceration, bleeding, and congestive heart failure. AVM can cause disfigurement, compression, or destruction of adjacent tissues AVMs are usually diagnosed through a combination of MRI and angiography [18]. These tests may need to be repeated to analyze a change in the size of the AVM, recent bleeding, or the appearance of new lesions. AVM is not a static malformation, it progresses over time, and recurs. Genetic abnormalities cause certain types of familial AVMs. The goal of treatment is usually to control AVM. For superficial AVMs, patients should prevent desiccation and subsequent ulceration, and compression garments for extremity lesions may reduce pain and swelling. Intervention including embolization, resection, or a combination is focused on reducing symptoms, preserving vital functions, and improving deformities [19].

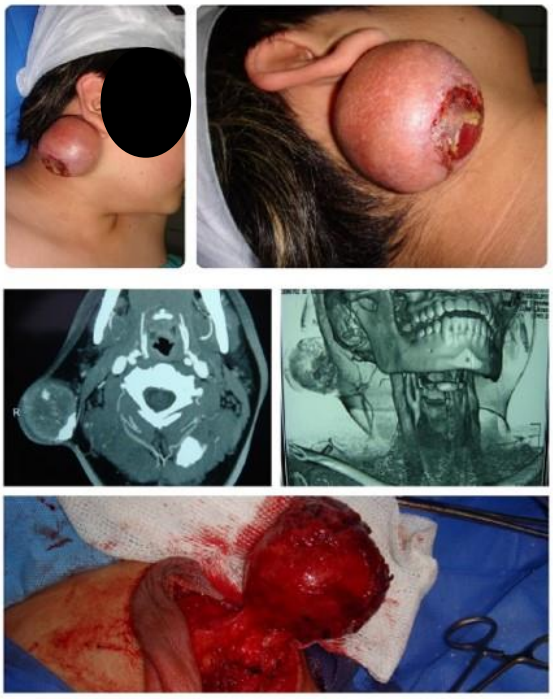

Figure 5: 15-year-old patient with AVM showed as a lateral neck tumor. Angio CT confirmed diagnosis.

Adults older than 40 years have a high likelihood of harboring a malignant neoplasm. Some other more common

benign and malignant neck neoplastic lesions are discussed here, including, primary vascular neoplasms, neurogenic neoplasms, and lymphoma benign neoplasms presenting in the neck involve tumors arising from elements of the parapharyngeal space (PPS). These neoplasms include salivary gland tumors, neurogenic tumors, and paragangliomas (carotid body tumors, glomus jugulare, glomus vagale). The patient may complain of dysphagia, dyspnea, symptoms of obstructive sleep apnea, symptoms of eustachian tube dysfunction, or other symptoms related to cranial neuropathies. These symptoms usually present with significant tumor size. In addition, symptoms of flushing, hypertension, and palpitations may occur in association with functional paragangliomas [20]. The most common finding on physical examination is that of a painless neck mass or painless oropharyngeal mass. The neck mass may have a palpable thrill or audible bruit. Paragangliomas derived from the carotid body are mobile in an anteroposterior direction but not in a vertical direction. Patients with these symptoms and clinical findings warrant a contrast-enhanced CT scan of the neck, preferably from the skull base through the clavicles, before referral to an otolaryngologist. In addition, patients with symptoms of a secreting paraganglioma should undergo a 24-hour urine collection for catecholamines and their metabolites.

Radiographic distinction between paragangliomas and nerve sheath tumors (schwannoma and neurofibroma) is generally easy because paragangliomas are very vascular tumors. They arise from the neural crest and are most commonly located within the bifurcation of the common carotid artery (carotid body tumors), in the perineurium of the vagus nerve (glomus vagale), at the jugular bulb (glomus jugulare), or in the middle ear cavity (glomus tympanicum). Of these four common sites, only glomus vagale and glomus jugulare are in direct relationship to the PPS. They enhance intensely on CT and MRI and have flow voids are diagnostic of paragangliomas but may not be readily apparent on MRI if the tumor is 2 cm in diameter or smaller. Contrast-enhanced CT scan can help make the diagnosis because paragangliomas enhance intensely compared to nerve sheath tumors, which may or may not enhance. The classic carotid body tumor is located within the carotid bifurcation in the infrahyoid neck and is not in immediate proximity to the PPS. It tends to splay the internal and external carotid arteries and this finding helps differentiate a carotid body tumor from a glomus vagale that tends to displace the carotid artery anteriorly [21] (Figure 6). Another distinction between other paragangliomas and carotid body tumors is that unlike carotid body tumors, other paragangliomas often have demonstrable feeder vessels that most commonly arise from the ascending pharyngeal artery. Conventional angiography can demonstrate vascular anatomy and is useful if embolization is part of the treatment plan, such as for paragangliomas at the skull base. Radiologic differential diagnosis of schwannoma versus neurofibroma may not be easy. Heterogeneity within the lesion is more commonly seen in schwannomas because of cystic change or hemorrhage. Schwannomas arise from the Schwann cells of the peripheral nerve sheath and in the Carotid Space (CS), the vagus nerve and the sympathetic chain are the common nerves of origin. These well encapsulated tumors appear as a round or ovoid mass that is isointense to muscle on T1-weighted images, hyperintense on T2-weighted images, and enhance following contrast administration. These imaging characteristics are by no means unique to schwannomas, and paragangliomas can appear similar. However, schwannomas do not have flow voids even when they are large.

Additionally, schwannomas at the skull base cause regressive remodeling of bone, whereas permeative changes are seen with paraganglioma. Neurofibroma, on the other hand, is a benign heterogeneous peripheral nerve sheath tumor arising from the connective tissue of peripheral nerve sheath, three types of neurofibromas are described: Localized, plexiform, and diffuse. On MRI, localized neurofibroma usually shows nonspecific signal intensity and variable contrast enhancement. Plexiform neurofibroma represents diffuse involvement of a long nerve segment and its branches, and its gross appearance has been described as a “bag of worms.” The classic target sign appearance, which is a less common imaging feature, but almost always is pathognomonic, is seen on T2-weighted images with high-signal-intensity myxoid material peripherally and a relatively low-signal-intensity fibrous component centrally. The reverse target sign may be present on T1-weighted images after IV administration of gadolinium-based contrast material, characterized by enhancement of the central fibrous component and a relative lack of enhancement of the surrounding myxoid component (Figure 7). Diffuse neurofibroma is a less common subtype of neurofibroma that has received little attention in the imaging literature [22].

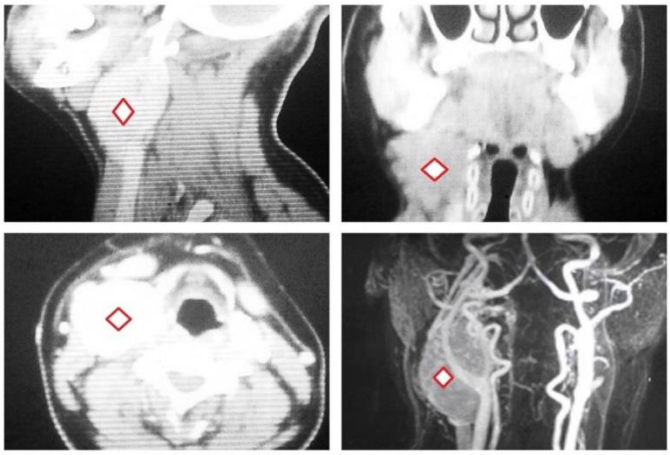

Figure 6: The classic carotid body tumor is located within the carotid bifurcation in the infrahyoid neck and is not in immediate proximity to the PPS. They enhance intensely on CT and have flow voids. Flow voids are diagnostic of paragangliomas.

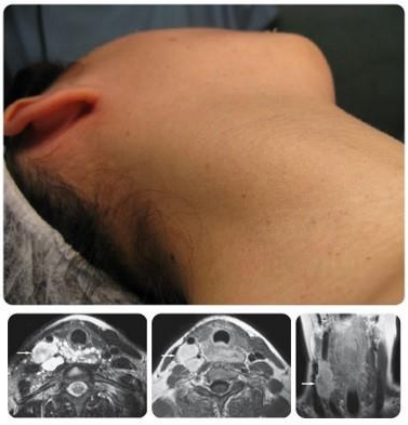

Figure 7: MRI: T2-weighted images with high-signal-intensity myxoid material peripherally and a relatively low-signal-intensity fibrous component centrally. The reverse target sign may be present on T1-weighted images after IV administration of gadolinium-based contrast material, characterized by enhancement of the central fibrous component and a relative lack of enhancement of the surrounding myxoid component. Right Vagus Plexiform neurofibroma.

Sarcomas are malignant neoplasms originating from mesodermal tissues that constitute connective tissues of the body. They are rare group of malignancies that constitute less than 1% of body's tumors, including those of the head and neck region. In head and neck region, based on histological subtyping, 50% of sarcomas are constituted by osteosarcoma, rhabdomyosarcoma, malignant fibrous histiocytoma, fibrosarcoma and angiosarcoma. The most common symptom of head neck soft tissue sarcoma is a painless mass (in 80% of cases). Pain could be present occasionally and it is the most common presenting symptom in bone sarcomas. Visual anomalies, epistaxis, chronic sinusitis, otalgia, sensory and/or motor anomalies are the other presenting features [23]. The detailed history and physical examination play a major role in the diagnosis of the head and neck sarcomas. It is recommended to stage these lesions prior to any biopsy. Imaging plays a major role in defining the extent of the tumor to nearby vital structures for treatment planning and deciding surgical approach decision. The imaging modalities best indicated for head and neck sarcoma are similar to those elsewhere in the body. MRI is generally better to computed tomography scans in soft tissue sarcomas. CT scan is preferred to assess bone involvement. CT scan reconstruction is to be considered in the treatment planning [24]. Due to the complex anatomy in the head and neck region, combined MRI and CT scan are recommended (Figure 8). The classical treatment modalities employed in head and neck sarcoma include surgery, radiotherapy and/or chemotherapy. Treatment of sarcomas is dictated by tumor type, stage, location, size, and patient age. Due to the anatomical complexity and surrounding vital structures in the head and neck region, wide excision with adequate margin is not possible in all cases [25].

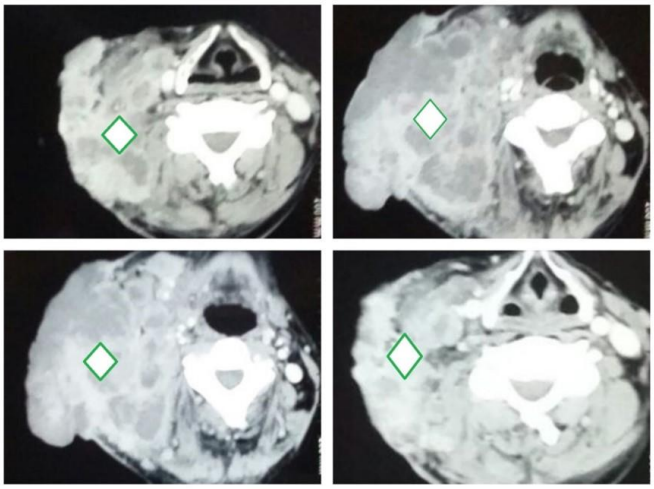

Figure 8: 48-year-old patient with a history of HIV. FNA: Sarcomatoid type lesion. CT: heterogeneous lesion, very bulky, no contrast-enhanced, and with hypodense center compatible with central necrosis

Limitations

The limitations of this study are inferior level of evidence compared with prospective studies, temporal relationships are often difficult to assess and cannot determine causation, only association. The strength of the study is providing novel information to the research community about PLNM.

Conclusion

The differential diagnosis of the primary lateral neck masses requires an effort to the surgeons. Anamnesis and physical examination are the most important for the presumption diagnoses. It is important the frequency of different pathologies, so it has not lost validity Skandalakis algorithm. Complementary studies images should be requested with selective criteria.

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Airway management of a huge thyroid mass: A case report

Dev tiroidal kitlede havayolu yönetimi: Olgu sunumu

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Abstract

In large thyroidal masses with excessive tracheal shift, the laryngeal opening is usually in the normal position and intubation may not be difficult. However, in some cases, such as retrosternal big thyroid glands, airway management can get challenging. Failure to successfully manage difficult airways is responsible for 30% of deaths attributed to anesthesia, with approximately 600 deaths annually. Successful awake intubation can be performed in 88-100% by considering the appropriate position and experience of anesthesiologist with a fiberoptic bronchoscope. However, the path to be followed should be determined according to each patient.

Keywords: Difficult airway, Fiberoptic, Huge goiter, Intubation

Öz

Özellikle retrosternal guatra bağlı olarak, trakea üzerine bası yapan büyük tiroidal kitleler nedeniyle havayolu kontrolü zor olabilir. Aşırı trakea kayması olan büyük tiroidal kitlelerde bile laringeal açıklık genellikle normal pozisyonda olup, entübasyon zor olmayabilir. Zor havayolu yönetimini başarı ile yönetememek, yıllık yaklaşık 600 ölümle birlikte anesteziye atfedilen ölümlerin % 30'undan sorumludur. Fiberoptik bronkoskop ile uygun pozisyon ve anestezi uzmanının tecrübesine de bakılarak %88-100'ünde başarılı uyanık entübasyon yapılabilir. Ancak izlenecek yol, her hasta için hastaya göre belirlenmelidir.

Anahtar kelimeler: Zor havayolu, Fiberoptik, Dev guatr, Entübasyon

Introduction

Thyroidectomy is the most common endocrine surgery. Due to compression on the trachea, airway management can be difficult [1]. Preoperative evaluation and management are critical when planning elective thyroidectomy, in which a change in anatomical sites is expected due to a large or substernal goiter. Altered anatomy, laryngeal edema and an inexperienced team may all cause difficulty in intubation. Intubation is rarely difficult if the larynx can be easily seen in preoperative examination. Even in large thyroidal masses with excessive tracheal shift, the laryngeal opening is usually in the normal position and intubation may not be easy. These patients should usually be intubated with a small-sized endotracheal tube to prevent intraoperative surgical trauma. Intubation should be performed by an experienced anesthesiologist who knows different techniques [2]. A large goiter, tracheal compression symptoms and the possibility of malignancy have been found to increase the incidence of difficult intubation in different studies [3].

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Informed Consent: The authors stated that the written consent was obtained from the patient presented with images in the study.
Hasta Onamı: Yazarlar çalışmada görüntüleri ile sunulan hastadan yazılı onam alındığını ifade etmiştir.

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Case presentation

A 77-year-old female patient, who gave her consent for the case report and was evaluated in our outpatient clinic, weighed 77 kg, was 163 centimeters (cm) tall, and had uncontrolled growth of goiter in her history (15 years). She also had hypertension (15 years), and cerebrovascular disease (3 years - at the end of the right upper and lower limb weakness - 3 / 5). The patient, who was ASA II according to American Society of Anesthesiologists guidelines, was planned to undergo right thyroid lobectomy. The patient's large thyroidal mass had been present for about 15 years but had been causing dyspnea for the last 15 days. She was a non-smoker and had no alcohol use in her history. Atrial fibrillation (AF) was detected on electrocardiogram (ECG). Preoperative anticoagulant discontinuation and low molecular weight heparin were recommended until the operation. She had no previous anesthesia experience. In the preoperative evaluation, she had an exceptionally large thyroidal mass and the trachea was absent in the midline (Figure 1). Her Mallampati score equated class III and she had a sternomental distance of approximately 15 cm, while the thyromental distance could not be evaluated due to the neck mass. For this reason, “Difficult Intubation” was noted in the patient's preoperative anesthesia file. Although the patient had labored breathing due to the mass, her breathing was adequate, and she was not hypoxic. After determining the date of operation, preparations, and consultation procedures for tracheostomy or cricotomy were performed.

In addition, her physical examination was unremarkable except for loss of strength in the right upper and lower extremities. In laboratory examination, whole blood, liver-kidney function tests, respiratory tests and thyroid hormone levels were in within normal range. Awake intubation was not considered since the size of the mass and the superior laryngeal nerve could not be blocked. Based on the experience of the team for difficult airway and intubation in the operation room, a standard Macintosh laryngoscope set, a variety of face masks - airways, a fiberoptic bronchoscope, and tracheal tube introducer – a bougie and supraglottic airway devices were prepared. In the operation room, ECG, peripheral oxygen saturation and non-invasive blood pressure monitoring were performed. Premedication was administered as 2 mg intravenous (iv) midazolam. Before induction, 100% oxygen was given for 3 minutes, after which 160 mg propofol and 100 micrograms of fentanyl were given. Before the neuromuscular blocker was administered, the patient was ventilated with a face mask. Then, 50 mg of IV rocuronium was administered (Sugammadex was also made available). After waiting long enough for neuromuscular blockade, Cormack-Lehane score was evaluated as IV on direct laryngoscopic examination. Intubation was performed with a fiberoptic bronchoscope by an experienced anesthesiologist due to lack of glottis in view, when the epiglottis was passed, the glottis was deviated to the left, and the spiral endotracheal tube was directed to the trachea via the fiberoptic endotracheal tube. Intubation was confirmed with end-tidal CO_2 and auscultation (Figure 2). Anesthesia was maintained by 50% O_2 + 50% N_2O + propofol and remifentanil infusion.

After the operation, which lasted approximately 120 minutes, the right thyroidal mass (130x100x65mm) (Figure 3) was removed by lobectomy, a drain was placed, and the operation was terminated. The patient was extubated with 2 milligrams of neostigmine and 0.5 milligrams of atropine (IV).

The patient was observed for 1 hour in the postoperative care unit and discharged with medical treatment of the surgical team.

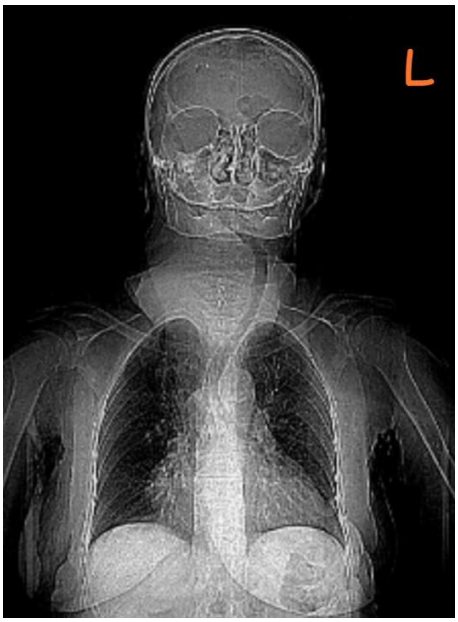

Figure 1: Radiological image of a patient with thyroid mass causing tracheal compression

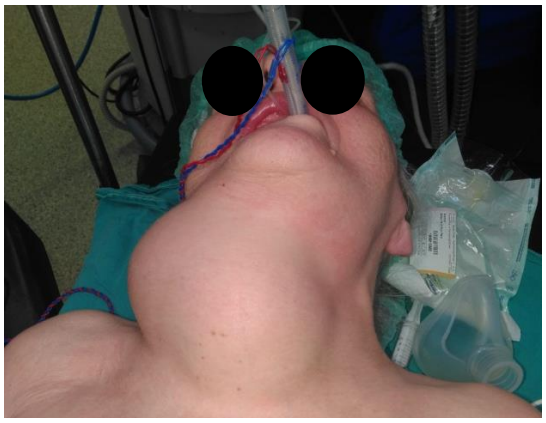

Figure 2: Our case was intubated with an endotracheal tube for neuromonitorization

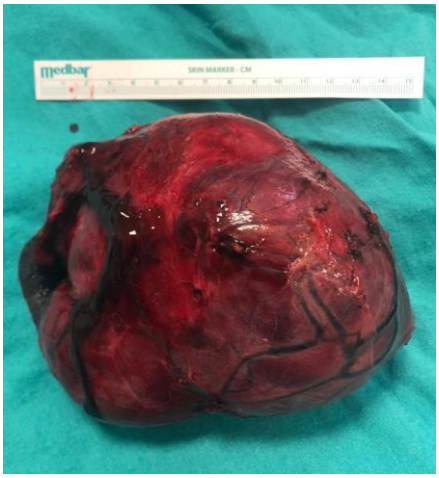

Figure 3: Mass removed after right thyroid lobectomy

Discussion

Thyroid tissue growths or malignancies may lead to changes in the airways, leading to difficulties in intubation [4]. Airway control may be difficult in such surgical procedures, due to large thyroidal masses compressing the trachea [1]. The size of the thyroidal mass is an objective parameter for difficult intubation and poses a serious risk for difficult airway management and intubation [5]. The thyroidal mass in our case was exceptionally large and had deviated the airway due to compression of the trachea. This was considered difficult airway management and difficult intubation for us.

Difficult ventilation and intubation increase the morbidity and mortality, depending on the degree of problems encountered in providing airway patency. It may cause hypoxia, myocardial injury, airway trauma and even death [6]. Failure to successfully manage a difficult airway is responsible for 30% of deaths attributed to anesthesia, with approximately 600 deaths annually [7,8].

In different studies, the researchers found the incidence of difficult intubation in thyroid surgery as 4 - 6.8 - 11.1% [3,9]. An enlarged thyroid, tracheal compression symptoms and malignancy have been found to increase the incidence of difficult intubation [3]. During preoperative evaluation, routine Mallampati score, mouth opening, thyromental and sternomental distance, head and neck movements and body mass index are important for the determination of a difficult airway [10]. Intubation can sometimes be difficult due to altered anatomy, laryngeal edema and an inexperienced anesthesia team. Even in large substernal goiters with massive tracheal deviation, laryngeal patency is usually normal and intubation is not difficult [2]. In our case, Mallampati score, thyromental distance, mouth opening to the sternomental distance, and head and neck movements were noted when evaluating preoperatively. Although the patient had severe tracheal deviation on the chest radiograph, it was evaluated that the laryngeal patency was enough. Preoxygenation studies performed with 100% oxygen preoperatively showed that it increased functional residual capacity, provided sufficient time for difficult airway control and increased tolerance to hypoxia [1,11]. Preoxygenation before general anesthesia is recommended to all patients. With proper preoxygenation, the duration of apnea can extend from 1-2 minutes to 8 minutes without desaturation [8,12]. For this reason, the patient underwent preoxygenation on the operating table after 3 minutes of administering 100% oxygen with a face mask under monitorization and in the appropriate head and neck position.

Fiberoptic use is recommended by a senior and experienced anesthesiologist [2]. Successful awake intubation can be performed in 88-100% by considering the appropriate position and the experience of the anesthesiologist with a fiberoptic bronchoscope [13]. Upon the first laryngoscopy performed after induction of our case, the Cormack-Lehane score was IV. Repeated intubation may cause edema and bleeding and may make it difficult to use supraglottic airway devices in the larynx. Accordingly, the Difficult Airway Association (DAS) recommends a maximum of three tracheal intubations, the fourth attempt should be performed by an experienced anesthesiologist. The same technique should not be repeated after an unsuccessful intubation attempt, and changes should be made to increase the success of the intubation in each additional trial [8]. Video laryngoscope is the first choice for some anesthesiologists because it provides better glottic vision than direct laryngoscopy [14]. In an emergency, fiberoptic bronchoscope should be used by experienced anesthesiologist. Blind techniques should be avoided. In case of failure of tracheal intubation, the patient can be awakened, tracheal intubation can be tried with fiberoptic and supraglottic airway devices, and surgery can be continued using face mask or supraglottic airway devices. However, if ventilation cannot be achieved, airway can be secured by a surgical procedure (tracheotomy or cricotomy) without losing ventilation capacity [8]. There was no postoperative complication in our patient who was extubated after approximately 120 minutes, and the patient was discharged with medical treatment of the surgical team after 24 hours of hospitalization. Approximately one third of complications in difficult airway management occur during extubation or in the postoperative period [15].

In 2015, the management of difficult airway algorithms were revised. The rules should be adapted to the specific skills and individual evaluations of anesthesiologists, the applicability of the devices we have and the patient characteristics [8].

Conclusion

The preoperative evaluation of the patient who is thought to have a difficult airway is especially important. Furthermore, in accordance with the recommendations of the algorithm published by DAS, preoperative equipment and medical treatments should be available. The path to be followed should be determined according to the patient.

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Autistic child with abdominal pain caused by foreign body ingestion

Yabancı cisim alımından kaynaklanan karın ağrısı olan otistik çocuk

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Abstract
Foreign body ingestion is an important condition with a potentially high mortality rate that is encountered in pediatric emergency departments and outpatient polyclinics. Foreign body ingestion occurs in 80% of children, especially those between 6 months and 3 years of age. However, in patients with mental disorders, in this case, autism, foreign body ingestion may occur at any age. A 16-year-old autistic patient presented with complaints of discomfort and restlessness, with no history of ingestion, however, we discovered through further investigations that the patient had in fact swallowed a foreign object. In this case, we would like to emphasize that autistic patients of any age can ingest foreign bodies, even without any suspicious history.
Keywords: Foreign body, Intestinal perforation, Autism, Abdominal pain

Öz
Yabancı cisim yutulması, pediatrik acil servislerinde ve genel polikliniklerde karşılaştığımız, potansiyel olarak yüksek ölüm oranına sahip olabilecek önemli bir durumdur. Yabancı cisim yutulması çocukların % 80'inde ve özellikle 6 ay ile 3 yaş arasındaki çocuklarda görülür. Ancak ruhsal bozukluğu olan hastalarda, özellikle bu olguda olduğu gibi otizimli çocuklarda, yabancı cisim yutulması her yaşta ortaya çıkabilir. 16 yanındaki otistik bir hastada, rahatsızlık ve huzursuzluk şikayeti ile getirildi, öyküsünü sorguladığımızda bize yararlı bir bilgi yoktu, daha ileri incelemelerde hastanın aslında yabancı bir nesneyi yuttuğunu fark ettik. Bu durum nedeni ile her yaştaki otistik hastaların öykü alma sırasında herhangi bir şüphe duymadan yabancı cisim yutabileceğini vurgulamak istiyoruz.
Anahtar kelimeler: Yabancı cisim, İntestinal perforasyon, Otizim, Karın ağrısı

Introduction

Foreign body ingestion is an important condition with a high mortality rate that we encounter in pediatric emergency departments and general polyclinics [1]. Foreign body ingestion occurs in 80% of children, especially in those between 6 months and 3 years of age. The incidence reported in the American Association of Poison Control Centers' National Poison Data System in 2016 is 1,810,030 patients per year [2]. However, in patients with mental disorders, in this case, autism, foreign body ingestion may occur at any age. A 16-year-old autistic patient presented with complaints of discomfort and restlessness, with no suspicious history, and we discovered through further investigations that the patient had in fact swallowed a foreign object. Based on this case, we would like to emphasize that autistic patients of any age can ingest foreign bodies even without any suspicions revealed during history taking.

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Case presentation

A 16-year-old male patient was referred to the pediatric emergency service with complaints of discomfort and restlessness. He was not mentally healthy enough to explain his complaints or history. The family stated that he has been in discomfort for the last 10 days and had clear abdominal pain for the last 2 days. There was nothing suspicious in his history. Physical examination revealed abdominal tenderness, defense, and rebound. There were no findings in laboratory tests. The patient was sent for a Direct Abdominal X-Ray (Figure 1), which revealed a spoon in the duodenal region.

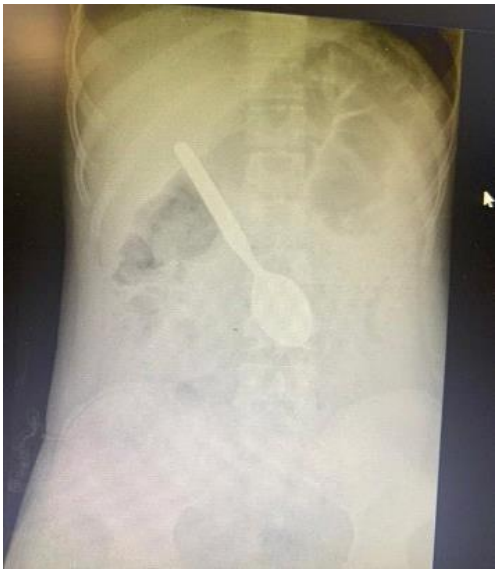

Figure 1: Patients first X-ray taken with the spoon visible

In the esophagogastroduedonoscopy, the spoon was observed in the 2nd part of the duodenum and removed. There was free air under the diaphragm in the direct graph obtained for control purposes (Figure 2). The patient was then transported to the operation room. Operative findings included perforation in the intestinal mucosa contacting the spoon (Figure 3). Primary repair was performed. The patient recovered uneventfully following the operation. His control examination was normal, and he had no complaints.

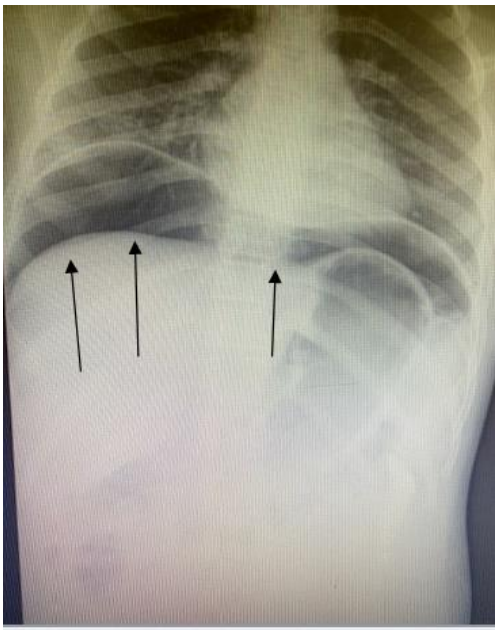

Figure 2: Post esophagogastrodudonoscopy X-ray shows free air under the diaphragm

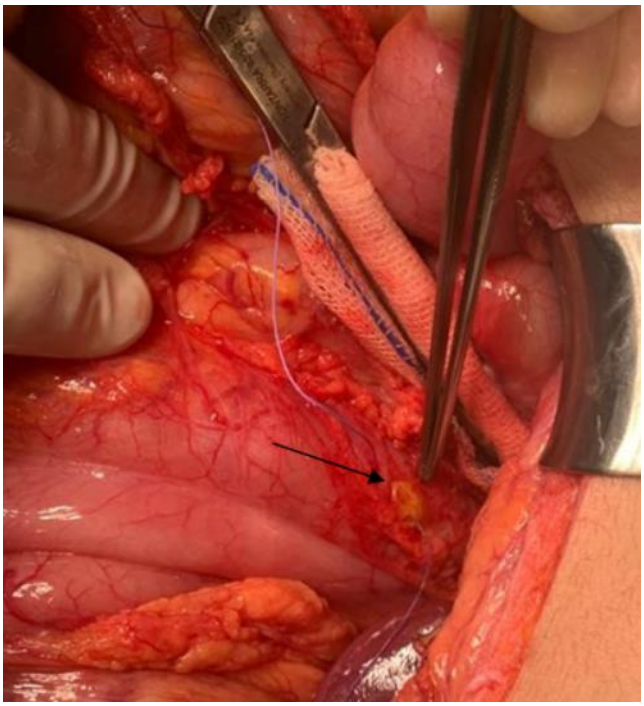

Figure 3: During the operation, the perforation was found in the 2nd part of the duodenum.

Discussion

Foreign body ingestion, a clinical condition we frequently encounter in pediatric outpatient clinics and emergency departments, may have a high mortality. In 80% of the cases, the foreign bodies leave the body naturally by passing through the pylorus and ileocecal valve, while in 20%, endoscopic intervention is required. Surgical intervention is required in approximately 1% of cases due to complications such as obstruction, fistula and perforation [3,4]. Detailed history taking may not be possible in various patient groups, and such was the case in our patient with autism. In some cases, family members may not be aware of the event. A retrospective study reported that 40% of foreign body ingestion cases occurred without witnesses [5]. In cases where the patient cannot describe the situation, unexplained abdominal pain is an important symptom and one should always consider foreign bodies ingestion. The size and localization of the ingested body increases the risk of perforation. The period between ingestion and diagnosis varies, depending on the small age group and the absence of witnesses, which affects the development of perforation and fistula [3,4]. In our patient, we removed the foreign body, which was localized in the 2nd part of the duodenum, with an esophagogastroduedonoscope. Due to duodenal folds and peristalsis, the mucosal appearance may not be thoroughly evaluated macroscopically, and mucosal damage caused by foreign body may be overlooked. As in our patient, the perforated area could not be evaluated and was only noticed on the abdominal direct radiograph obtained postoperatively, which showed intraabdominal free air. With this case, we wanted to emphasize the need for radiological examination after removal of the foreign body. It is of foremost importance not to overlook the possible perforations.

Conclusion

Foreign body ingestion can be seen in all pediatric age groups. Especially in patients brought to the emergency department with complaints of abdominal pain and discomfort

who cannot express themselves, foreign body ingestion should be investigated. We wanted to emphasize that after foreign bodies that are difficult to remove endoscopically, radiological examination is necessary to rule out perforation.

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Spontaneous retroperitoneal hematoma mimicking retroperitoneal malignancy in a pregnant woman

Gebe bir hastada retroperitoneal maligniteyi taklit eden spontan retroperitoneal hematom

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Abstract
Spontaneous retroperitoneal hematomas can cause maternal and fetal complications during pregnancy. A female patient with 10 weeks' gestation was referred to our clinic with back pain by her gynecologist for retroperitoneal mass excision and termination of pregnancy, due to the retroperitoneal malignancy seen on ultrasonography. MRI revealed a 90x110 mm retroperitoneal hematoma adjacent to the posterior of the left kidney. The patient was followed conservatively for 7 days and discharged without any fatal or maternal complications. We recommend that advanced imaging methods should be preferred in selected cases.
Keywords: Spontaneous retroperitoneal hematoma, Retroperitoneal hematoma, Pregnancy, Pregnant women

Öz
Spontan retroperitoneal hematomlar hamilelik sırasında maternal ve fetal komplikasyonlara neden olabilir. 10 haftalık gebeliği olan bir kadın hasta sırt ağrısı ile kliniğimize başvurdu. Hasta jinekoloğu tarafından, ultrasonografide görülen retroperitoneal malignite nedeniyle retroperitoneal kitle eksizyonu ve gebeliğin sonlandırılması için yönlendirilmişti. MRG'de sol böbreğin arka tarafına bitişik 90x110 mm retroperitoneal hematom saptandı. Hasta 7 gün boyunca konservatif olarak takip edildi ve ölümcül veya maternal komplikasyon gelişmeksizin taburcu edildi. Seçilmiş vakalarda gelişmiş görüntüleme yöntemlerinin tercih edilmesini öneririz.
Anahtar kelimeler: Spontan retroperitoneal hematom, Retroperitoneal hematom, Gebe, Gebelik

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Introduction

The retroperitoneum is a large area bounded by the posterior parietal peritoneum, the transversalis fascia, posterior and superior diaphragm. It includes gastrointestinal, musculoskeletal, vascular, visceral, and neural structures, including the distal esophagus, the second, third and fourth parts of the duodenum, posterior parts of the ascending and descending colon, the pancreas, rectum, kidneys, bladder, abdominal aorta, vena cava inferior, psoas major, quadratus lumborum and iliacus muscles [1]. Bleeding in any these organs may cause a retroperitoneal hematoma. Computed Tomography (CT) scan of the abdomen is the main diagnostic method. However, in some cases, such as our pregnant patient, CT cannot be preferred [1,2]. Early diagnosis and watchful conservative treatment can improve the outcome in retroperitoneal hematoma.

In this case report, we aimed to discuss the case of a spontaneous retroperitoneal hematoma mimicking retroperitoneal malignancy in a 10-weeks pregnant woman.

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Case presentation

A 41-year-old, gravida 2, para 1, female patient was referred to our clinic at 10 weeks' gestation with back pain by her gynecologist for retroperitoneal mass excision and termination of pregnancy due to a retroperitoneal malignancy seen on ultrasonography.

On the patient's admission, she had left side pain. Vital parameters were as follows: Arterial blood pressure: 107/70 mm/Hg, heart rate: 95 /min, SpO2: 98% and fever: 36,7 ºC. Her obstetrical history included spontaneous vaginal delivery of a child without any gestational complications. Her medical history was not significant for inherited bleeding disorders, allergy, medication, or any other diseases. Physical examination revealed no tenderness in the abdomen. Left costovertebral angle tenderness was noted.

Her complete blood count revealed hemoglobin value of 8.61 g/dl, hematocrit value of 26.2%, leukocyte value of 27.8 K/uL, and platelet count of 220,000 /nl. Her aPTT (activated partial prothrombin time) level was 24.6 s (normal 25–40 s) and INR was 1.29. Biochemical parameters were within the normal ranges. Pregnancy, compatible with 10 weeks' gestation, and fetal heartbeat were observed in obstetric ultrasonography. Abdominal ultrasonography showed an exogenous solid mass lesion of 85.5x80 mm, extending in the upper zone of the left kidney (Figure 1).

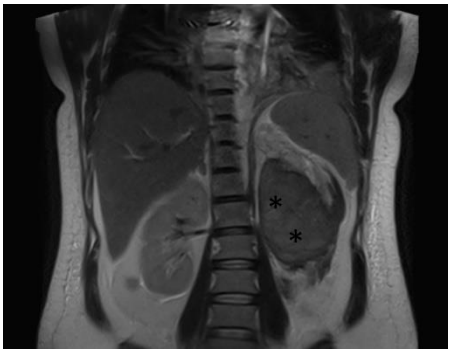

Figure 1: Non-Contrast enhanced abdominal MRI showing a 90x110 mm retroperitoneal hematoma adjacent to the posterior of the left kidney in T2-weighted images (asterisks). An evidence of retroperitoneal hematoma is the displacement of the left kidney.

Patient was hospitalized and magnetic resonance imaging (MRI) was performed after obtaining consent from the patient and relatives. MRI revealed a 90x110 mm retroperitoneal hematoma adjacent to the posterior of the left kidney. Upon a decrease in hemoglobin values during the hospitalization of the patient (Figure 2), 2 units of erythrocyte suspension and 1 unit of fresh frozen plasma were given. The patient was followed conservatively for 7 days and discharged without any fetal or maternal complications.

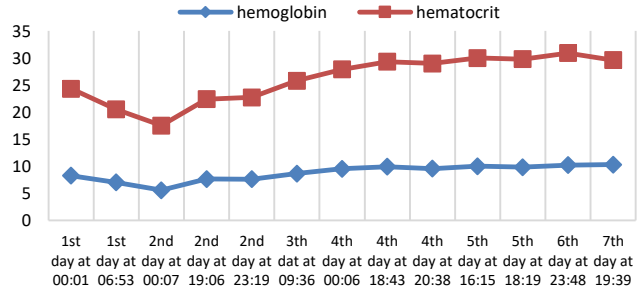

Figure 2: Hemoglobin and Hematocrit Monitoring Chart of Patient

Discussion

Spontaneous retroperitoneal hemorrhage occurs regardless of trauma or iatrogenic causes. SRHs are rare causes of back pain [2] and are most seen in patients receiving anticoagulation therapy and hemodialysis, as well as in those with bleeding abnormalities. They may present as one of the potentially lethal and most serious complications of anticoagulation therapy [3,4], and lead to fetal loss in pregnancy [5]. Although there are various explanations of its pathogenesis in the literature, it is yet to be fully elucidated. Whether it is caused by using low molecular heparin, spontaneous muscle rupture or atherosclerosis of small vessels is still not clear (3). Our case had no history of recent anticoagulant, heparin and antiplatelet use and aPTT and INR values were within normal limits.

Clinical SRH findings, such as back pain, groin pain, abdominopelvic discomfort, abdominal distention, tachycardia, hypotension are nonspecific, and paralysis due to femoral nerve compression depends on the severity of the bleeding [3].

Conventional radiography and ultrasonography are the primarily preferred imaging modalities with low sensitivity and specificity. Plain abdomino-pelvic radiography occasionally reveals loss of psoas shadow. Ultrasonography can show spillage of hemorrhage into the peritoneal cavity, a large hematoma in the retroperitoneum and displacement of retroperitoneal structures. In ultrasonography, the presence of an abdominal aortic aneurysm with peri-aortic hemorrhage could favor a ruptured aortic aneurysm. MRI and CT imaging are superior to ultrasound and should be the preferred imaging modality [6]. However, even when high-resolution MR and CT imaging are used, the diagnosis of SRH is difficult because many benign or malignant lesions can mimic this condition. Although the differential diagnosis of primary retroperitoneal tumors and retroperitoneal hemorrhages can be made by CT or MRI, there are cases in the literature in which surgical excision is made [7].

The management of SRH includes resuscitation, transfusion, reversal of anticoagulation, angioembolization and surgical exploration. The most preferred treatment modality is conservative treatment, with which most cases resolve.

Conclusion

In conclusion, clinicians should pay more attention to SRH, which occasionally mimics other disorders and may cause serious maternal and fetal complications during pregnancy. We recommend that advanced imaging methods be preferred in selected cases.

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Case report
Olgu sunumu

Journal of Surgery and Medicine
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Infantile juvenile polyposis syndrome: A rare cause of protein-losing enteropathy

İnfantil juvenil poliposis sendromu: Protein kaybettiren enteropatinin nadir bir nedeni

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Abstract

Juvenile Polyposis Syndrome (JPS) is a rare autosomal dominant hereditary syndrome affecting 1:100000-160000 individuals. JPS most presents with rectal bleeding, anemia, abdominal pain, obstruction and rarely with rectal prolapsus of the polyp. In this case, we diagnosed Infantile Juvenile Polyposis Syndrome due to protein losing enteropathy, rectal bleeding and extraintestinal manifestations of the syndrome. A 2-year-old male infant was referred to the hospital due to complaints of painless rectal bleeding and rectal prolapsus of the polyp which occurred at 15 months of age. Pathological examination revealed that it was a juvenile polyp. After a short while, the patient was hospitalized due to rectal bleeding, paleness, swelling in both legs and periorbital edema. Physical examination of the patient revealed +3 pretibial, scrotal, periorbital edema, clubbing and pale appearance. The patient had macrocephaly, hypotonicity and neuromotor retardation. Laboratory test results revealed low immunoglobulin levels, hypoalbuminemia, anemia, and electrolyte imbalance. We diagnosed the case with JPS due to protein losing enteropathy with extraintestinal manifestations of the syndrome. Gastroscopic and colonoscopic examinations revealed multiple polyps through the antrum and colon. JPS diagnosis is based on the detection of polyps which are histopathologically defined as juvenile polyps. One of the most common causes of painless, rectal bleeding in children are colorectal polyps. We wanted to emphasize that the sporadic juvenile polyp diagnosis should be made by pathological examination of polypectomy material and clinical exclusion of JPS. In our patient, there were extraintestinal system manifestations such as macrocephaly, congenital heart disease and clubbing, accompanied with protein-losing enteropathy. Awareness of these clinical findings is necessary for the differential diagnosis of protein-losing enteropathy and polyposis syndrome. We would also like to draw attention to the importance of a multidisciplinary approach, early recognition of the syndrome and appropriate referral of the patient.

Keywords: Rectal bleeding, Infantile juvenile polyposis syndrome, Protein losing enteropathy

Öz

Juvenil Polipozis Sendromu (JPS), çok nadir görülen, otozomal dominant geçişli, 1/100000 ile 1/160000 insanı etkileyen, herediter bir sendromdur. JPS sıklıkla rektal kanama, anemi, karın ağrısı, tıkanma ve nadiren polipin rektal prolapsusu ile bulgu verir. Bu olgu ile protein kaybettiren enteropati, rektal kanama ve ekstraintestinal manifestasyonları olan hastamıza JPS tanısı koyduk. 2 yaş erkek hasta ağrısız rektal kanama nedeniyle hastaneye başvurdu. 15 aylık iken rektal polip prolapsusu olmuş ve bu polipin patolojik değerlendirmesi juvenil polip ile uyumlu imiş. Çok kısa süre sonra hasta rektal kanama, solukluk, ayaklarda şişlik ve göz çevresi ödem ile başvurdu. Fizik muayenesinde pretibial +3 ödem, skrotal ödem, göz çevresinde ödem, parmaklarda çomaklaşma ve soluk görünümü mevcut idi. Makrosefali, hipotoni ve nöromotor retardasyonu vardı. Laboratuvar testlerinde: immunglobulinler ve albumin düşük, anemisi mevcut ve elektrolit dengesizliği vardı. JPS tanısı protein kaybettiren enteropatiye eşlik eden ekstraintestinal system bulgularının varlığı ile konuldu. Yapılan gastroskopik ve kolonoskopik incelemesinde antrumdan başlayarak tüm kolon mukozası boyunca yaygın polipler mevcut idi. Histopatolojik incelemesi juvenil polip ile uyumlu idi. Çocuklarda ağrısız rektal kanamaların en sık nedeni kolorektal poliplerdir. Sporadik juvenil polip tanısı, patolojik olarak polipektomi materyalinin incelenmesi ve klinik olarak JPS'nun dışlanması ile konulmalıdır, bunu vurgulamak istedik. Bizim hastamızdaki gibi makrosefali, konjenital kalp hastalığı ve çomak parmak gibi ekstraintestinal bulguların farkındalığı ve protein kaybettiren enteropati ayırıcı tanısında polipozis sendromunun akılda tutulması gerektiğini vurgulamak istedik. Multidisipliner yaklaşım ile erken tanı prognozu iyileştirebilmektedir.

Anahtar kelimeler: Rektal kanama, İnfantil juvenil polipozis sendromu, Protein kaybettiren enteropati

Introduction

Juvenile Polyposis Syndrome (JPS) is a rare autosomal dominant hereditary syndrome affecting 1:100000-160000 individuals [1]. It is diagnosed according to the following criteria: a) At least 3 polyps detected on colonoscopy, b) Juvenile polyps in the entire digestive tract (stomach, small bowel, etc.), c) In cases of positive family history of the disease, any number of juvenile polyps [2]. Three subtypes of Juvenile Polyposis Syndrome were defined: 1. Juvenile polyposis coli (JPC), 2. Generalized juvenile polyposis (GJP), and 3. Juvenile polyposis of infancy (JPI) [3]. The first two subtypes are distinguished by the location and extent of polyps along the gastrointestinal tract with polyps located in the colon only in JPC and in the colon and upper gastrointestinal tract in GJP [4].

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JPS most presents with rectal bleeding, anemia, abdominal pain, obstruction and rarely, with rectal prolapsus of the polyp [5]. It is estimated that over 20% patients with JPS have macrocephaly, congenital heart diseases and urogenital system anomalies [6]. Germline mutations which causie JPS in 40–60% of patients have been identified in bone morphogenetic protein receptor type 1A (BMPR1A) and SMAD4 [7,8].

In this case, we diagnosed as Infantile Juvenile Polyposis Syndrome based on protein-losing enteropathy, rectal bleeding and the extraintestinal manifestations of the syndrome.

Case presentation

A 2-year-old male infant was referred to the hospital with complaints of painless rectal bleeding and rectal prolapsus of a polyp, which occurred when was 15 months old. Pathological examination revealed that it was a juvenile polyp. After a short while, the patient was hospitalized due to rectal bleeding, paleness, swelling in both legs and periorbital edema. Physical examination of the patient revealed +3 pretibial, scrotal, periorbital edema, clubbing and pale appearance. The patient had macrocephaly, hypotonicity and neuromotor retardation. Liver and spleen were subcostally palpable at 4 and 2 cm, respectively. We observed the prolapsus of the polyp during rectal examination (Figure 1).

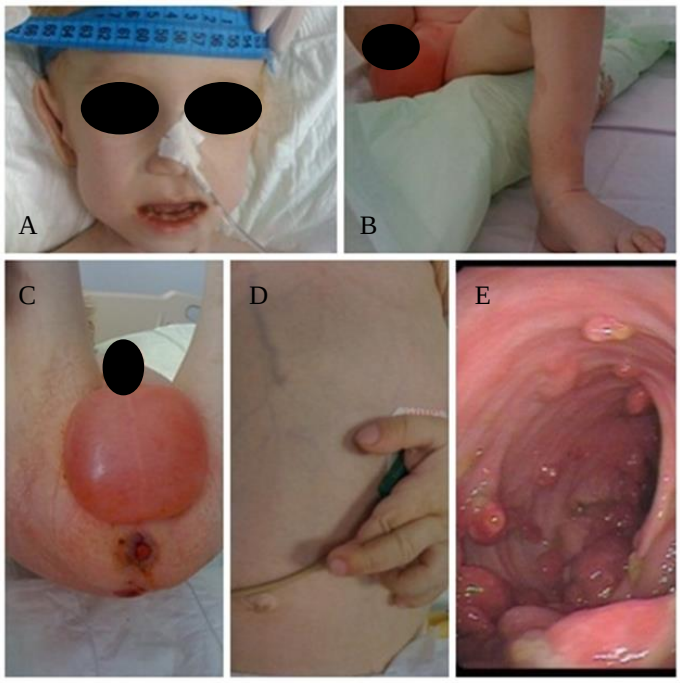

Figure 1: Physical examination of the patient. (A: Macrocephaly, B: Pretibial edema, C: Prolapsus of the polyp and scrotal edema during rectal examination, D: Clubbing, E: Macroscopic appearance of the polyps during colonoscopy)

Cardiovascular examination revealed a 1/6 heart murmur. Laboratory test results were as follows: Immunoglobulin (Ig) G: 266 IU/L, Ig A: 69 IU/ml, Ig M: 43 IU/ml, Ig E: 16 IU/ml, Total protein: 2.5 g/dl, Albumin: 1.4 g/dl, Hemoglobin: 6 g/dl, Hematocrit: 18%, Blood Sodium: 125 mmol/L, Potassium: 2.5 mmol/L. Echocardiography reported mitral valve prolapse and mild mitral valve deficiency. Urinary system ultrasonography and cranial magnetic resonance imaging were normal, along with the past medical history of the patient. Two grandfathers had died due to lung cancer and colon cancer. We considered polyposis syndrome in the differential diagnosis of protein-losing enteropathy and diagnosed the case with JPS based on the existence of protein-losing enteropathy with extraintestinal manifestations of the syndrome. Infantile juvenile polyposis syndrome is considered because the symptoms occurred during the first 2 years of age. Gastroscopic examination through the antrum revealed multiple (more than 10), spherical and lobulated, 5-20 cm-sized, pedunculated/sessile polyps. Colonoscopic examination revealed multiple polyps through the colon. JPS diagnosis must be based on histopathological findings coherent with juvenile polyps (Figure 2). We obtained written consents forms from the patient's primary caretakers for this case presentation.

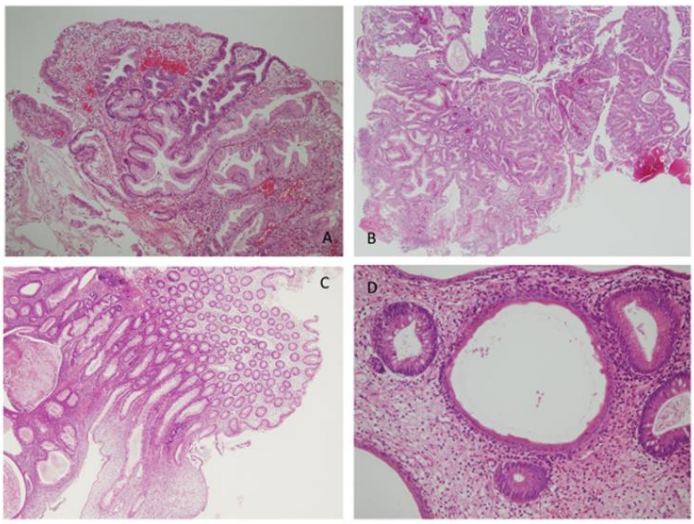

Figure 2: Mucosal pathology (A: Gastric mucosa juvenile poly, Hematoxylin&eosin x40, B: Gastric mucosa juvenile poly, Hematoxylin&eosin x100, C: Colon mucosa juvenile poly Hematoxylin&eosin x40, D: Focal low grade dysplasia, Hematoxylin&eosin x100

Discussion

There are several reasons of rectal bleeding, including infections, medications, and inflammatory bowel disease [9]. One of the most common causes of painless, rectal bleeding in children is colorectal polyps, most of which are sporadic, usually isolated, colorectal juvenile polyps. Sporadic isolated colorectal juvenile polyps are present in as many as 2% of symptomatic children [10]. We want to emphasize that the sporadic juvenile polyp diagnosis should be based on pathological examination of the polyps and clinical exclusion of JPS.

In our patient, extraintestinal system manifestations such as macrocephaly, congenital heart disease and clubbing accompanied protein losing enteropathy. Awareness of these clinical findings is necessary for the diagnosis of polyposis syndrome as the differential diagnosis of protein losing enteropathy. We mentioned the importance of a multidisciplinary approach, early recognition of the syndrome due to the elevated risk of mortality and malignancy development at later stages, and appropriate referral of the patient. This provides the best outcome for patients affected by polyposis syndrome. JPS carries an increased risk of gastrointestinal malignancy (38 % to 68 %) [11].

Conclusion

Our case highlights the importance of combined clinical findings of JPS with extraintestinal system manifestations and endoscopic examination for diagnosis. It is a rare syndrome, requiring more studies in which patients are monitored

prospectively to reach a comprehensive understanding of JPS and make its early diagnosis possible.

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Case report
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Primary mediastinal hydatid cysts

Primer mediastinal kist hidatikler

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Abstract
Hydatid cysts are a parasitic disease caused by *Echinococcus granulosus*, and 0.5 to 2.6% of all hydatid cysts are in the mediastinum. In this study, we presented primary mediastinal hydatid cysts. All patients underwent chest X-ray and thoracic computed tomography (CT), and only one patient underwent thoracic magnetic resonance imaging (MRI) due to the association with spinal cord. All lesions removed through thoracotomy were confirmed pathologically, and no postoperative complications were observed, except for one patient. Anthelmintic treatment was started in one patient with vertebral involvement. No recurrence was observed in any of the patients. Although mediastinal hydatid cysts are rarely encountered, it is difficult to differentiate mediastinal hydatid cysts from other mediastinal diseases. However, the diagnosis is often made intraoperatively. Despite being a benign disease, mediastinal hydatid cysts should be removed surgically, as they may lead to serious complications due to deformation.
Keywords: Mediastinum, Hydatid cyst, Echinococcosis, Ekstrapulmonary

Öz
Hidatik kist, Echinococcus granulosus'un neden olduğu paraziter bir hastalıktır. Tüm kist hidatik vakalarının %0.5-2.6'sı mediastinal yerleşimlidir. Çalışmamızda primer mediastinal kist hidatikleri sunduk. Bütün hastalarda akciğer grafisi, toraks bilgisayarlı tomografi (BT) çekildi. Bir olguda spinal kordla ilişkisi nedeniyle toraks manyetik rezonans görüntüleme (MR) çekildi. Torakotomi ile çıkarılan bütün lezyonlar patolojik olarak doğrulandı. Postoperatif bir hastada dışında komplikasyon gelişmedi. Vertebra tutulumu olan bir olguda antihelmitik tedavi başlandı. Hiçbir olguda nüks gözlenmedi. Mediastinal kist hidatikler nadir görülmekle beraber diğer mediastinal hastalıklardan ayrımı zordur. Çoğu zaman cerrahi sırasında tanı konulur. Benign bir hastalık olmasına rağmen dektrüksiyona yol açarak ciddi komplikasyonlara neden olabileceğinden cerrahi olarak çıkarılmalıdır.
Anahtar kelimeler: Mediasten, Hidatik kist, Ekinokokkoz, Ektrapulmoner

Introduction

Hydatid cysts are a parasitic disease caused by the larvae of *Echinococcus granulosus*, and are endemic in some regions. Although very rare, intrathoracic extrapulmonary hydatid disease may occur in the pleural space, pleural fissure, chest wall, mediastinum, pericardium, myocardium and diaphragm. Of all hydatid cyst cases, 0.5 to 2.6% were in the mediastinum [1]. Here, we present the cases with primary mediastinal hydatid cysts we operated between 2009 and 2019 to contribute to the literature.

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Case presentation

We reviewed 254 patients operated on due to intrathoracic hydatid cysts between 2009 and 2019. Of 254 patients, four (1.6%) were mediastinal hydatid cyst. All patients underwent chest X-ray and computerized tomography (CT), while magnetic resonance imaging (MRI) was performed in only one patient to determine the relationship between neural foramen and the lesion. All cases were operated on, and the lesions were completely removed. Pathological examination revealed hydatid cysts. Of all patients, three were female and one was a male. Their ages ranged between 47-74 years, with a mean value of 59 years. Except for one, all patients were symptomatic. Two patients displayed coughing, while one had dyspnea and back pain. Radiologically, three of the hydatid cysts were located in anterior mediastinum, and one was posteriorly located. Thoracic CT revealed diaphragm paralysis in one of the cases with anteriorly located hydatid cysts (Figure 1, 2). Except for one of the hydatid cysts located in the anterior mediastinum, no distinction could be made from pericardial cysts. MRI was performed to differentiate from neurogenic tumors in the posteriorly located lesion. The defined mass extended into the neural foramen, and due to the destruction of the vertebral corpus and posterior components, the patient was radiologically pre-diagnosed with a neurogenic tumor and underwent surgery (Figure 3). Thoracotomy was performed to remove all lesions totally in all cases. The drains were drawn in a mean of 4 days postoperatively (ranging 2-5 days). Mean hospital stay was 5 days (ranging between 3-6 days). Postoperative complications developed in one patient (Table 1) in the form of diaphragmatic eventration, in whom diaphragm plication was performed six months later due to dyspnea. No recurrence was witnessed in the patients during the mean 88-month follow-up period (range: 42-126 months).

Table 1: General characteristic of the patients

Cases	Age	Gender	Location	Surgical procedure	Postoperative drain removal time	Postoperative complications
1	59	F	Anterior mediastinum	Thoracotomy excision	5th day	Diaphragm eventration
2	56	F	Anterior mediastinum	Thoracotomy excision	2nd day	No
3	74	F	Posterior mediastinum	Thoracotomy excision	2nd day	No
4	47	M	Anterior mediastinum	Thoracotomy excision + Diaphragm plication	5th day	No

F: Female, M: Male

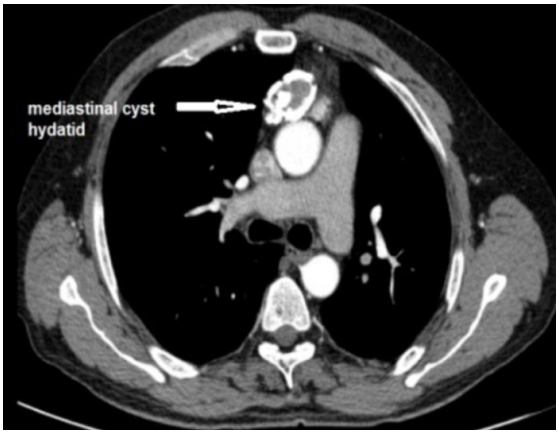

Figure 1: Thoracic Computed Tomography showing the lesion

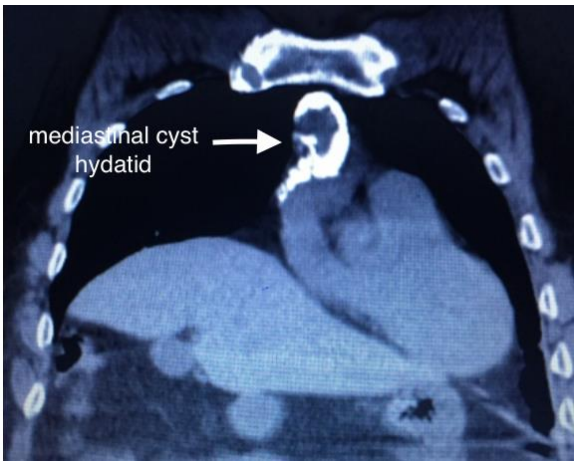

Figure 2: Eventration of diaphragm on the right

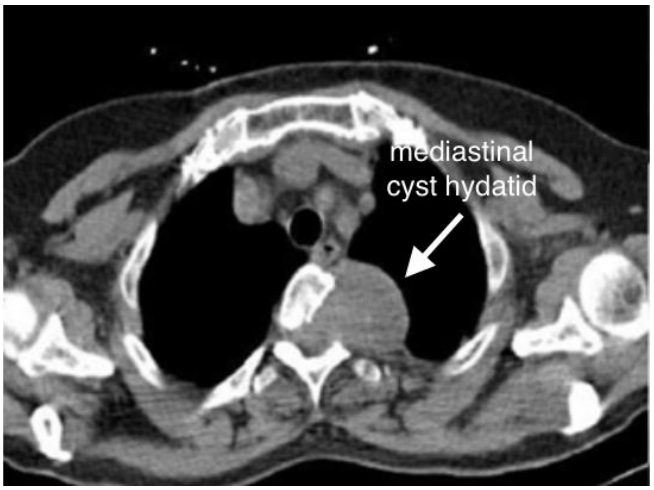

Figure 3: Vertebral invasion thorax Computed Tomography image

Discussion

Hydatid cysts are rarely observed in mediastinum. The parasite possibly migrates to the region through the arterial branches of the thoracic aorta or lymphatics after passing through the hepatic and pulmonary filters. The symptoms are caused by cyst size, location, mediastinal pressure, and degree of erosion. Among the symptoms commonly witnessed are chest pain, cough, dyspnea and recurrent nerve palsies [2]. As consistent with literature, cough, dyspnea and back pain were also observed in our study.

Today, many serological tests are recommended to diagnose hydatid cysts; however, most are not performed routinely in clinical practice due to their low diagnostic value, variable sensitivity, and specificity [3]. In our study, we also did not routinely use any serological tests.

In a study performed by Rakower and Milwidsky [4], primary mediastinal hydatid cysts were located most in posterior, anterior and middle mediastinum, respectively. In our study, however, hydatid cysts were more frequently located in anterior mediastinum.

In general, mediastinal hydatid cysts cannot be distinguished clinically and radiologically from other mediastinal cystic lesions. Radiological examinations, such as chest radiography, thoracic CT and MRI facilitate the diagnostic procedure. Although the diagnostic procedure involves taking all clinical, radiological, laboratory and historical data into consideration, the diagnosis of mediastinal hydatid cysts is usually made during the surgery [5]. In all our patients, chest X-

ray and thoracic CT were performed; in addition, MRI was performed to determine the association with spinal nerves in a patient with a posteriorly located cyst. Despite these procedures, all but one case was diagnosed during surgery in our study.

Mediastinal hydatid cysts may lead to complications such as rupture, fistulas, embolism, and pressure on vital organs [6-7]. Posteriorly located hydatid cysts may destruct the vertebrae, compress on the spinal nerve, and be confused with neurogenic tumors [8]. In our case with the posteriorly located cyst, the lesion extended into the neural foramen, causing a destruction of the vertebral corpus and posterior elements; therefore, the case was pre-diagnosed as a neurogenic tumor and operated. During the surgery, it was considered as a daughter vesicle and the case was diagnosed with a hydatid cyst. The lesion was totally excised with the simultaneous participation of neurosurgery. The diaphragmatic paralysis is an exceedingly rare entity in primary mediastinal hydatid cysts, and as its treatment modality, simultaneous diaphragmatic plication is also performed during surgery [9]. We detected diaphragmatic eventration in a case with an anteriorly located cyst but did not evaluate the diaphragmatic paralysis was due to the hydatid cyst because the location of the lesion was far from the phrenic nerve. We also performed the diaphragm plication simultaneously during the surgery. A variety of techniques have been described to treat hydatid cysts, such as percutaneous drainage and capitonnage. However, when the hydatid cysts are strongly associated with vital mediastinal structures, total excision may not be possible, and partial excision is achieved (9). During surgery, dissemination or seeding of the cysts, and anaphylactic reaction may occur [10]. In such cases, anti-helminthic drugs are administered in the postoperative period [9]. In our case, we administered the treatment of andazol for 12 months only to the case with vertebra dextration, and observed no recurrence during the follow-up.

Conclusion

Although mediastinal hydatid cysts are rarely encountered, it can be difficult to differentiate them from other mediastinal lesions, and the diagnosis can be made during the surgery. Despite being a benign disease, because they may cause serious complications due to destructions and pressure on the surrounding tissues, the mediastinal cysts must be operated and removed totally, if possible. In addition, long-term anthelmintic treatment should be started in patients with bone involvement.

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Case report
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May Covid-19 cause intracerebral hemorrhage in patients with cavernous malformation?

Covid-19, kavernöz malformasyonlu hastalarda intraserebral kanama'ya neden olabilir mi?

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Abstract
Coronavirus disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, has become a global health threat. COVID-19 often involves the respiratory tract, however, it is also associated with several neurological conditions (seizures, convulsions, changes in consciousness, encephalitis, cerebral hemorrhage, and cerebral thrombosis). Cavernous malformations (CMs) are vascular lesions that occur in the central nervous system and the body. Symptomatic CMs most manifest through headaches, seizures, hemorrhage, or focal neurological deficits. The co-occurrence of COVID-19 and cavernous hemangioma hemorrhage has not been reported in the literature. The association between COVID-19 and intracerebral hemorrhage remains controversial. However, a relationship with COVID-19 infection in patients with intracerebral hemorrhage should always be considered during this pandemic. The case of a 37-year-old female patient is reported here. The patient presented to the emergency room with a headache that persisted for 2 days along with cavernous hemangioma hemorrhage and tested positive for COVID-19.
Keywords: COVID-19, Hemangioma, Cavernous

Öz
SARS-CoV-2 virüsünün neden olduğu Coronavirus hastalığı 2019 (COVID-19), küresel bir sağlık tehdidi haline geldi. COVID-19 genellikle solunum yolunu tutar; bununla birlikte çeşitli nörolojik durumlarla (nöbetler, konvülsiyonlar, bilinç değişiklikleri, ensefalit, serebral hemoraji ve serebral tromboz) ilişkili olduğu da bulunmuştur. Kavernöz malformasyonlar (KM), merkezi sinir sisteminde ve vücutta meydana gelen vasküler lezyonlardır. Semptomatik KM'ler en yaygın olarak baş ağrısı, nöbetler, kanama veya fokal nörolojik defisitlerle kendini gösterir. Literatürde COVID-19 ile kavernöz hemanjiyom kanamasının birlikte görülmesi bildirilmemiştir. COVID-19 ile intraserebral hemoraji arasındaki ilişki tartışmalıdır. Bununla birlikte, intraserebral hemorajili hastalarda COVID-19 enfeksiyonu ile bir ilişki bu pandemi sırasında her zaman dikkate alınmalıdır. 37 yaşında bir kadın hastanın vakası burada bildirilmektedir. Hasta kavernöz hemanjiyom kanaması ile birlikte 2 gün süren baş ağrısı ile acil servise başvurdu ve ayrıca COVID-19 testi pozitif çıktı.
Anahtar kelimeler: COVID-19, Hemanjiom, Kavernöz

Introduction

Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2 virus, was first described in Wuhan, China in December 2019 and has become a global health threat. Most patients with COVID-19 manifest respiratory tract symptoms; however, extrapulmonary manifestations have also been reported. Fever, cough, myalgia, weakness, shortness of breath, headache, nausea, vomiting, diarrhea, and anosmia are common symptoms [1]. Patients may develop pneumonia, acute respiratory distress syndrome and multiorgan failure in severe cases.

COVID-19 has been associated with several neurological pathologies (seizures, convulsions, changes in consciousness, encephalitis, intracerebral hemorrhage [ICH] and cerebral thrombosis) [2].

Cavernous malformations (CMs) are vascular lesions in the central nervous system (CNS) and the body. CMs are also referred to as cavernomas, cavernous angiomas or cavernous hemangiomas. Their prevalence ranges from 0.4% to 0.6% [3]. They can be observed anywhere in the CNS. They usually are not symptomatic. Symptomatic CMs are most often manifested by headaches, seizures, hemorrhage, or focal neurological deficit [4].

Here, the case of a 37-year-old female patient is reported. The patient presented to the emergency room with a persistent headache for 2 days and had a hemorrhage of the cavernous hemangioma and tested positive for COVID-19.

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Case presentation

A 37-year-old female patient presented to the emergency room with a severe headache that persisted for 2 days. The results of neurological examination were normal. She had no history of trauma and no additional diseases. She had no history of use of anti-aggregates or anticoagulants. Her blood pressure was 120/80 mm Hg. C-reactive protein was 9 mg/L, and D-dimer was 480 µg/L. Liver function test results were normal. No hematological abnormalities such as thrombocytopenia or hemorrhagic diathesis were found. As a large number of patients with COVID-19 report headache as a key symptom, a throat swab was taken from the patient. Real-time polymerase chain reaction (PCR) test was performed with the throat swab sample, which confirmed COVID-19. Ground-glass opacity was seen in the lower left lobe of the lung that could be consistent with COVID-19 on computed tomography (CT) of the thorax (Figure 1). On the brain CT performed to exclude neurological pathologies, an ICH sized 1 × 1 cm^2 was seen in the right frontal region (Figure 2a) and the hemorrhage in the right frontal region was consistent with a cavernous hemangioma in the magnetic resonance imaging (Figure 2b, 2c). The patient's general condition was good, and her neurological examination was normal. Therefore, she was not considered for any surgical intervention and admitted to the pandemic ward. Treatment was initiated for COVID-19. However, she did not need treatment in the intensive care during her hospitalization. The patient's follow-up PCR on the fifth day was positive. Follow-up CT performed on the 10^{th} day revealed that the bleeding was resorbed. The patient's condition improved, and she was discharged after 11 days of hospitalization with an advice to isolate herself at home to prevent the spread of infection among family members.

Written informed consent was obtained from the patient for this case report.

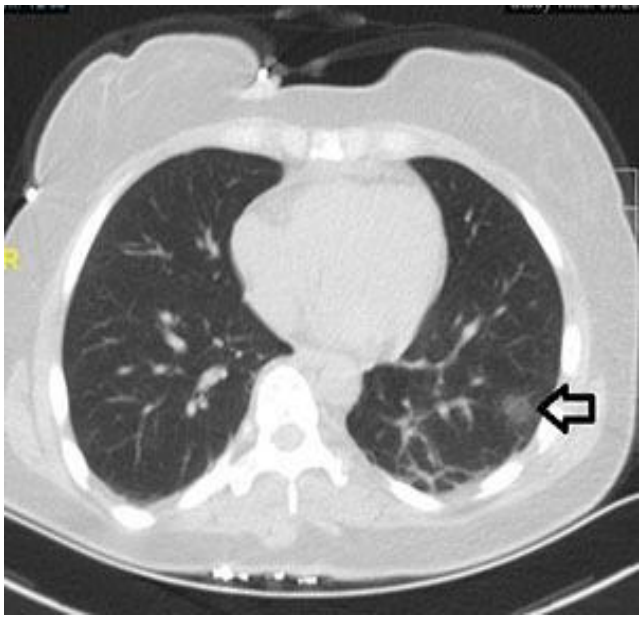

Figure 1: Axial non-contrast–enhanced thoracic computed tomography image in the parenchyma window shows area of infiltration with ground-glass density at the lower lobe of the left lung.

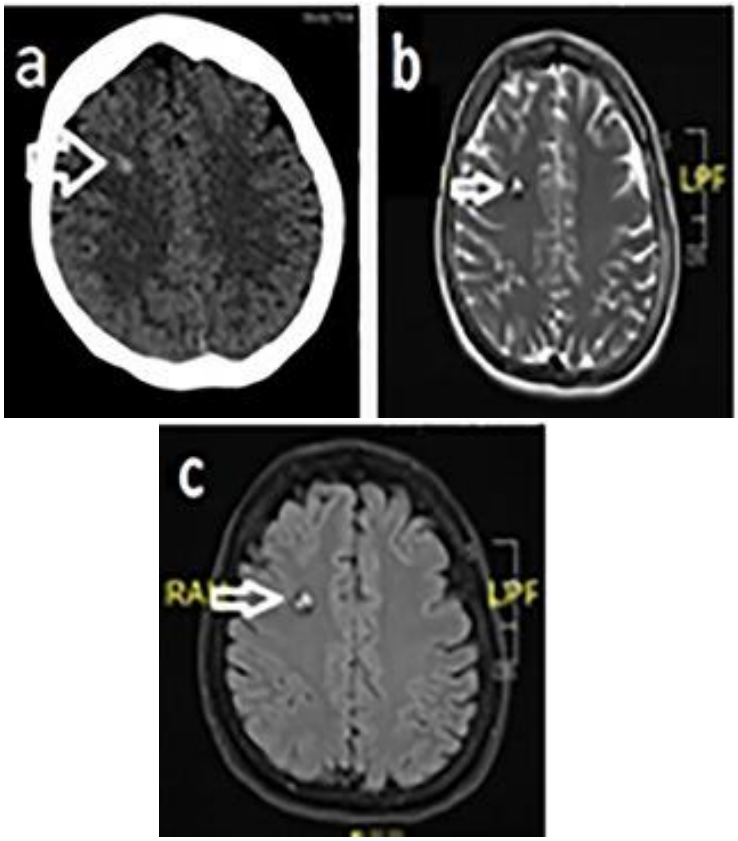

Figure 2: (a) CT brain showing hemorrhage in the right frontal region. T2 axial (b) and FLAIR axial (c) section of MRI brain showing hemorrhage related with cavernous hemangioma in the right frontal lobe.

Discussion

COVID-19 has affected individuals worldwide. However, individuals also have to cope with financial and social disturbances during this period [5]. Its clinical manifestations vary; it can be asymptomatic, mild or severe.

Respiratory involvement is very common in patients with COVID 19, and patients often present with typical symptoms such as fever, cough, weakness and diarrhoea [1]. Some patients may exhibit neurological symptoms only, without the typical symptoms of COVID-19. Dizziness and headache are the most common neurological symptoms [2]. Our patient had severe headaches with no other additional symptoms.

Our patient was young, aged 37 years. As morbidity and mortality increase with advanced age in COVID-19, our case was found to be interesting in this regard [6].

Cavernous haemangiomas are usually located in the supratentorial region. The rate of occurrence of haemorrhage varies between 2.6% and 3.1% annually [3]. CM was supratentorial and located in the right frontal region in our patient.

Lobar ICH occurs in 15%–30% of conventional cases and is predominantly associated with an underlying vascular anomaly [7]. Cavernous haemangiomas, which are among vascular malformations, comprise enlarged blood vessels that do not have smooth muscle cells or elastic fibres in their walls and are covered only by a single layer of epithelium, and there is no normal neural tissue between these vessels. Therefore, it is considered that they can easily bleed [4]. There may also be lobar haemorrhages in COVID-19, and anterior circulation and frontal lobe may be affected [8]. The haemorrhage occurred in

the right frontal lobe, and a concomitant cavernous malformation was observed in our patient.

The association between COVID-19 and ICH is controversial. However, it is established that the virus can directly reach the CNS through the olfactory receptors of the cranial nerve I in the nasal cavity cell membrane and cause neurological problems in patients [9,10].

Some publications support the association of COVID-19 with ICH and indicate possible mechanisms. Sharifi-Razavi et al. [9] and Md Noh et al. [11] reported that COVID-19 acts through angiotensin-converting enzyme (ACE) II receptors, filling ACE II receptors and may reduce the expression of ACE II and increase the risk of cerebral haemorrhage owing to high blood pressure. Levi et al. [12] reported that the risk of cerebral haemorrhage, elevated D-dimer and coagulopathy may increase secondary to prolonged prothrombin time in patients with COVID-19. Benger et al. [8] reported that COVID-19–mediated ICH was caused by endothelial damage and indicated that both direct and indirect endothelial toxicity and renin–angiotensin system disruption were possible mechanisms.

Conclusion

Although headache is a common symptom in patients with COVID-19, our case is interesting because she also had haemorrhage of cavernous haemangioma. To our knowledge, the co-occurrence of COVID-19 and cavernous haemangioma haemorrhage has not been reported in the literature. The relationship between COVID-19 and ICH remains controversial. To date, the evidence obtained shows a fairly low prevalence of cerebral haemorrhage in infected patients. However, a relationship with COVID-19 infection should always be considered in patients presenting with ICH during this pandemic.

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