ISSN 1307 4504

Kafkas J Med Sci

KAFKAS TIP BİLİMLERİ DERGİSİ
Journal of Medical Sciences

http://meddergi.kafkas.edu.tr
e_mail: meddergi@kafkas.edu.tr

Cilt / *Volume* **6**
Sayı / *Issue* **2**
Ağustos / *August* **2016**

KAFKAS TIP BİLİMLERİ DERGİSİ
Journal of Medical Sciences

Cilt / *Volume* **6 • Sayı /** *Issue* **2 • Ağustos /** *August* **2016**

ISSN 1307-4504

Kafkas Tıp Bilimleri Dergisi

Kafkas Tıp Bilimleri Dergisi, Kafkas Üniversitesi Tıp Fakültesi'nin akademik yayın organıdır.

Kuruluş tarihi	:	04.03.2011
Yayın türü	:	Hakemli süreli yayın.
Yayının adı	:	Kafkas Tıp Bilimleri Dergisi, *Kafkas Journal of Medical Sciences.*
Kısaltılmış adı	:	Kafkas J Med Sci.
Yayımlanma ortamları:		Matbu ve elektronik.
Peryodu	:	4 ayda bir (Nisan, Ağustos, Aralık)
Yayın dili	:	Türkçe ve İngilizce.
Yazı içeriği	:	Tıp bilimleri ile ilgili araştırma, kısa bildiri, derleme, editöryal, editöre mektup, çeviri, tıbbi yayın tanıtma vb türlerden yazılar yayımlanır.
DOI numarası	:	Yayımlanan her bir makaleye dijital nesne tanımlayıcı numarası (doi) atanır.
Makale işlemleri	:	Makale toplama ve değerlendirme işlemleri http://194.27.41.48/meddergi/jvi.asp web adresinden online yapılır.

Endekslenme

TÜBİTAK-ULAKBİM
Türkiye Atıf Dizini
Türk Medline

İletişim

Kafkas Tıp Bilimleri Dergisi
Kafkas Üniversitesi, Tıp Fakültesi
36300 KARS - TÜRKİYE
Tel: 474 225 11 96
Fax: 474 225 11 93
E-mail: meddergi@kafkas.edu.tr
Web: http://meddergi.kafkas.edu.tr

Yayın Hizmetleri

Tasarım ve Uygulama
BAYT Bilimsel Araştırmalar Basın Yayın ve Tanıtım Ltd. Şti.
Ziya Gökalp Cad. 30/31, Kızılay - Ankara
Tel: (312) 431 30 62
www.bayt.com.tr

Baskı
Miki Matbaacılık Ltd. Şti.
Matbaacılar Sitesi, 560 Sk. No:27, İvedik - Ankara
Tel: (312) 395 21 28

Baskı Tarihi
29 Ağustos 2016

KAFKAS TIP BİLİMLERİ DERGİSİ
Journal of Medical Sciences

Volume / *Cilt* **6 • Issue /** *Sayı* **2 • August /***Ağustos* **2016**

ISSN 1307-4504

Kafkas Journal of Medical Sciences

Kafkas Journal of Medical Sciences is the official academic publication of Kafkas University School of Medicine.

Founding Date	: March 4, 2011
Type of Publication	: Peer reviewed journal
Name of Journal	: Kafkas Journal of Medical Sciences, Kafkas Tıp Bilimleri Dergisi
Abbrevated Name	: Kafkas J Med Sci
Media of Distribution	: Press and electronic
Period of Publication	: Three issues a year (April, August, December)
Language	: Turkish and English
Contents of Journal	: Articles concerning medical sciences such as original studies, short communications, review articles, editorials, letters to the editor and translated articles et cetera are publicated.
DOI number	: A digital object identifier (doi) number is assigned to all articles accepted for publication.
Manuscript Processing	: Manuscript submission and review procedures are performed online at http://194.27.41.48/meddergi/jvi.asp

Indexed in

TÜBİTAK-ULAKBİM
Türkiye Atıf Dizini
Türk Medline

Administration

Prof. Dr. Sadık Ardıç *(Owner)*
Prof. Dr. Ümit Yener Tekdoğan *(Publishing Manager)*

Editorial Board

The Referees List of This Issue

Esragül Akıncı
Turgut Anuk
Sadık Ardıç
Alican Barış
Çağlar Bülent Bilgin
Alper Bozkurt
Cantürk Çapık
Binali Çatak
Hüsnü Çelik
Bülent Çitgez
Gülfem Ece
Hikmet Fırat
Yusuf Günerhan
Nergiz Hüseyinoğlu
Ahmet Çağkan İnkaya
Şahin Kahramanca
Bahar Kandemir
Yetkin Karasu
Sunay Sibel Karayol
Salih Burçin Kavak
Sezgin Kurt
Aysel Milanlıoğlu
Cengiz Mordeniz
Ercan Olcay
Serkan Özben
Fuat Özkan
Hatice Köse Özlece
Mahfuz Turan
Kahraman Ülker
Ayşe Nur Yeksan
Sema Yıldız

Correspondence

Kafkas Tıp Bilimleri Dergisi
Kafkas Üniversitesi, Tıp Fakültesi
36300 KARS, TURKEY
Phone: +90 474 225 11 96
Fax: +90 474 225 11 93
E-mail: meddergi@kafkas.edu.tr
Web. http://meddergi.kafkas.edu.tr

Publication Services

Graphic Design
BAYT Bilimsel Araştırmalar Basın Yayın ve Tanıtım Ltd. Şti.
Ziya Gökalp Cad. 30/31, Kızılay - Ankara, Turkey
Phone: +90 312 431 30 62
www.bayt.com.tr

Printing
Miki Matbaacılık Ltd. Şti.
Matbaacılar Sitesi, 560 Sk. No: 27, İvedik - Ankara, Turkey
Phone: +90 312 395 21 28

Printing Date
August 29, 2016

KAFKAS TIP BİLİMLERİ DERGİSİ
Kafkas Journal of Medical Sciences

Cilt / *Volume* **6**
Sayı / *Issue* **2**
Ağustos / *August* **2016**

ISSN 1307-4504

İçindekiler / *Contents*

DERLEME / *REVIEW*

OLGU SUNUMU / *CASE REPORT*

KAFKAS TIP BİLİMLERİ DERGİSİ
Kafkas Journal of Medical Sciences

EDİTÖRYAL / EDITORIAL

Kafkas J Med Sci 2016; 6(2):75 • doi: 10.5505/kjms.2016.66587

Oral Status and the Facial Transplant Patient (Letter to the Editor)

Yüz Nakli Hastaları ve Oral Durum (Editöre Mektup)

Hasan Hatipoğlu[1], Müjgan Güngör Hatipoğlu[2]

[1]Dumlupınar University, Faculty of Dentistry, Periodontology, Kütahya, Turkey; [2]Dumlupınar Üniversitesi, Faculty of Dentistry, Dentomaxillofacial Radiology, Kütahya, Turkey

Dear Editor,

Recent developments in plastic surgery are very exciting. Total or partial face transplantation procedures are very difficult and not without complications. We know that the patient selection and planning of the procedures are carefully and very well planned[1]. As a part of the body and face region, we believe that some issues of dental status should be considered before planning and treatment in such a difficult surgery.

A number of dental recommendations are suggested for organ transplant candidates. However, there is not a consensus between organ transplantation centers. It is arguable that dental diseases are sources of infectious complication after the transplantation procedures[2]. Thus a special attention should be given for existing oral-dental statuses for the facial transplantation candidates.

Limited literatures discuss about preliminary dental imaging, examinations and treatments in pre- or post-transplantation period or dental treatment need in this patients[3–5].

Oral cavity, exhibit a close connection with facial transplant area. It is clear that patients are more susceptible to infections and trauma after the transplantation. Infections from oral origin may have negative effects for the immunocompromised patients and recipient transplant area in the post transplantation period. Additionally, oral surgeries (e.g. dental extraction) or prolonged dental procedures can lead to a physical trauma to the transplanted face. The need for dental clinical and radiological evaluations and treatment in the pre transplant phase seems to be more critical especially in this condition.

Even with the limited number of total or partial facial transplant cases, we believe that a treatment protocol should be established for dental therapies in this patient group. With this protocol, possible treatment approaches for dental conditions (in pre- or post-transplantation periods) can be determined. Our belief is that such a crucial and high risk procedure should be supported with a carefully examination and elimination of active dental diseases and potential infection sources of oral origin. The close relationships of the transplant area with the oral cavity need a special cooperation between plastic surgeons and dental health professionals.

Keywords: dentistry; oral health; facial transplantation

References

1. Pomahac B, Nowinski D, Diaz-Siso JR, et al. Face transplantation. Curr Probl Surg 2011;48(5):293–357.
2. Guggenheimer J, Eghtesad B, Stock DJ. Dental management of the (solid) organ transplant patient. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;95(4):383–9.
3. Bueno EM, Diaz-Siso JR, Pomahac B. A multidisciplinary protocol for face transplantation at Brigham and Women's Hospital. J Plast Reconstr Aesthet Surg 2011;64(12):1572–9.
4. Losee JE, Fletcher DR, Gorantla VS. Human facial allotransplantation: patient selection and pertinent considerations. J Craniofac Surg 2012;23(1):260–4.
5. Lantieri L, Meningaud JP, Grimbert P, et al. Repair of the lower and middle parts of the face by composite tissue allotransplantation in a patient with massive plexiform neurofibroma: a 1-year follow-up study. Lancet 2008;372(9639):639–45.

Yard. Doç. Dr. Hasan Hatipoğlu, T. C. Dumlupınar Üniversitesi Diş Hekimliği Fakültesi, Merkez Kampus, Tavşanlı Yolu 10. km Kütahya, Türkiye
Tel. 0274 265 20 31/2502 Email. periohasan@yahoo.de *Geliş Tarihi: 04.09.2014 • Kabul Tarihi: 14.08.2016*

KAFKAS TIP BİLİMLERİ DERGİSİ
Kafkas Journal of Medical Sciences

ARAŞTIRMA YAZISI / ORIGINAL ARTICLE

Kafkas J Med Sci 2016; 6(2):76–80 • doi: 10.5505/kjms.2016.06078

Importance of the Risk Factors for Vancomycin Resistant Enterococcus Infection/Colonization –Development in Tertiary Intensive Care Units

Üçüncü Basamak Yoğun Bakım Ünitesinde Gelişen Vankomisin Dirençli Enterokok Enfeksiyon/Kolonizasyonu İçin Risk Faktörlerinin Önemi

Deniz Erdem[1], Dilek Kanyılmaz[2], Belgin Akan[1], Kevser Dilek Andıç[1], Meltem Arzu Yetkin[3], Hürrem Bodur[3]

[1]Ankara Numune Education and Research Hospital, Department of Intensive Care Unit I, Ankara, Turkey; [2]Ankara Numune Education and Research Hospital, Department of Infection Control, Ankara, Turkey; [3]Ankara Numune Education and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, Ankara, Turkey

ABSTRACT

AIM: *Vancomycin Resistance Enterococci (VRE) infection and/or colonization is a serious problem in intensive care unit (ICU) patients. For this reason, in our study, we aimed to determine the potential underlying risk factors of VRE infection and/or colonization in ICU patients.*

METHODS: *The medical files of the patients that were hospitalized at least 48 hours in intensive care units between January 2012 – July 2013 were retrospectively analyzed. Patients' data on demographic values (age, sex, previous hospitalization, operation history), coexisting diseases (diabetes mellitus, coronary artery disease, malignancy, Alzheimer Disease) prior antibiotic use,the results of rectal swab culture and patient prognosis was collected from the hospital data. Patients were evaluated according to the Centers for Disease Control (CDC). First group was colonisation/ infection group that included the VRE infected and colonized patients according to rectal swab culture results in hospital. The second group was non-infected group that included negative culture results in terms of VRE infection. The risk factors for VRE infection were evaluated.*

RESULTS: *The prevalence of VRE colonization was %10.7 (53 patients of 496). In VRE colonized patients; prolonged hospitalization, malignancy, hemodialysis, Alzheimer Disease and antibiotic usage were assessed as risk factors.*

CONCLUSION: *For preventing the spread of VRE, we should take precaution considering the detected risk factors. Especially, the colonized patients should be isolated, hygiene rules must be exactly performed and the patients should be externed from ICUs as earlier as possible.*

Key words: *vancomycin resistant enterococcus; intensive care unit; rectal colonization*

ÖZET

AMAÇ: *Yoğun bakımda yatmakta olan hastalar için Vankomisin Dirençli Enterokok (VRE) enfeksiyonu ve/veya kolonizasyonu ciddi bir problemdir. Bu nedenle çalışmamızda yoğun bakıma yatmış hastalarda VRE enfeksiyon/kolonizasyonu için olası risklerinin belirlenmesi amaçlanmıştır.*

YÖNTEM: *Ocak 2012 – Temmuz 2013 yılında yoğun bakım ünitesinde enaz 48 saat yatmış olan hastaların dosyaları retrospektif olarak incelenmiştir. Hastaların dosyalarından demografik bilgileri (yaş, cinsiyet, daha önceki başvuru, yatış, ameliyat öyküsü) diabetus mellitus, koroner arter hastalığı, serebrovasküler hastalık, malignite, alzhemier gibi yandaş hastalıklar, daha önce kullandığı antibiyotikler,hastanın kültür sonuçlarına bakılarak VRE üremesi olup olmadığı ve prognozu gibi bilgiler toplanarak kayıt altına alınmıştır. Bu bilgilerden yararlanılarak Centers for Disease Control and Prevantion (CDC) kriterlerine göre VRE ile hastane enfeksiyonu tanısı konulan veya sadece rektal sürüntü örnekleri incelendiğinde kolonizasyon olarak kabul edilen hastalar enfeksiyon ve/veya/kolonizasyon grubunu oluştururken ve yoğun bakımda yattığı süre içinde hiçbir kültüründe VRE üremesi olmayan hastalarda VRE enfeksiyonu gelişmeyen grup olarak değerlendirmeye alınmıştır. VRE enfeksiyonu gelişmesi için risk faktörü olabilecek parametreler değerlendirilmiştir.*

BULGULAR: *Çalışmaya 496 hasta alınmıştır. Hastaların 53'ünde (%10,7) rektal sürüntü örneklerinde VRE üremesi saptanmıştır. Üremelerin hepsi kolonizasyon olarak değerlendirilmiştir. Hastalarda VRE enfeksiyonu ve/veya kolonizasyonu açısından risk faktörleri incelenmiştir. VRE ile enfekte ve/veya kolonize hastalarda uzun yatış, malignite, hemodiyaliz tedavisi ve altta yatan Alzheimer hastalığı varlığı ile antibiyotik (AB) kullanımı risk faktörleri olarak bulunmuştur ($p<0.05$).*

SONUÇ: *VRE gelişimini ve yayılımını önlemek için saptanan risk faktörleri göz önünde tutularak önlemler alınmalıdır. Özellikle kolonize hastalar izole edilmeli, hijyen kurallarına tam uyulmalı ve hastalar mümkün olan en kısa sürede yoğun bakımdan taburcu edilmelidirler.*

Anahtar kelimeler: *vankomisin dirençli enterekok; yoğun bakım; rektal kolonizasyon*

Uzm. Dr. Deniz Erdem, Altındağ, Ulus, Ankara, Türkiye, Tel. 0312 508 42 51
Email. dh2erdem@yahoo.co.uk
Geliş Tarihi: 14.08.2015 • Kabul Tarihi: 16.11.2015

Introduction

Enterococcus spp. is one of the most common infectious agents. These are Gram-positive facultative anaerobic bacteria that live in the gastrointestinal microbiata of humans and animals[1,2]. Among the *Enterococcus* spp., *Enterococcus faecalis* and *Enterococcus faecium* are the most common species that cause infection and *E. faecalis* are the cause of the infection in 90% of cases. However, infections caused by *E. faecium* are increasing recently[3]. *Enterococus* spp., is generally colonized in microbiata of the gastrointestinal system, oral cavity, vagina, gall bladder and urethra as opportunistic pathogens, may sometimes cause urinary system, pelvic infections. They are less frequently localized in the bones, joints and meninges, causing infections[4,5].

Antimicrobial resistance differs among the starins and resistance can ocur in *Enterococcus* spp., by either intrinsic (natural) or extrinsic (acquired) ways. Enterococci are naturally resistant against cephalosporins, antistaphylococcal penicillins, clindamycin and aminoglycosides (low level)[6,7]. *Enterococcus* spp., is sensitive to vancomycin and has been safely used for the treatment of enterococcal infections until 1988. Vancomycin resistant enterococcus (VRE) case in the world has been reported first from United Kingdom, and then from France and United States of America. First VRE case in Turkey has been reported from Akdeniz University, in 1988[5,8]. Today, VRE colonization and infections are being encountered increasingly.

Enterococcus spp. have become one of the causative agents of nosocomial infections. They can transmitted directly from patient to patient as well as by the contaminated hospital equipment and environmental contact, causing nosocomial epidemics[9]. *Enteroccous* spp., have been detected as the causative agents of hospital acquired urinary tract and wound infections. According to SENTRY data of antimicrobial surveillance, blood stream infections have also been added to this rank[10].

In patients, first colonization occurs prior to infection, and in most of the times incidence of infection after the colonization is usually low. In general, the colonized patients are asymptomatic and *Enterococcus* spp., can be detected in stool or rectal swab cultures. The risk factors for VRE infections have been defined as long term stay in hospital or intensive care units, advanced age, being nursing home patient, having intraabdominal or cardiothoracic surgery, organ transplantation, renal failure, persistence of hematologic malignancy, enteral nutrition, high APACHE II score, use of antibiotics especially vancomycin and third generation cephalosporins. Besides these risk factors, poor compliance to hand hygiene was also an important factor for colonization and/infection, as hands of health care personnel may harbor VRE up to 60 minutes after the contact[11–14].

The objective of this study was to investigate persistence and the risk factors of VRE colonization in the patients that were admitted to the intensive care unit in our hospital.

Materials and Methods

After approval by the ethics committee, files of patients who were hospitalized at least for 48 hours in the seven-bed tertiary care Anesthesia Intensive Care Unit of Ankara Numune Training and Research Hospital between January 2012 and July 2013 were retrospectively screened. Files of the patients lost in less than 48 hours after admission to the intensive care unit were not included.

Demographic features (age, gender, history of previous hospitalization, surgery), and data such as underlying diseases (diabetes mellitus, coronary artery disease, cerebrovascular disease, malignancy, Alzhemier disease), previous antibiotic use, presence of VRE growth in the clinical samples and prognosis were recorded on the data collection forms. Based on this information; patients were grouped as infected and/or colonized or controls. Patients who had developed hospital infection with VRE and those have only VRE colonization were accepted to be colonized composed the infection and/or colonization group, while the patients who have not colonized with VRE in any swab culture during study period were considered as the control group.

As a part of our hospital policy active surveillance cultures such as rectal swab cultures have been performed to all the patients at admission to the ICU. Furthermore, rectal swab cultures have been repeated monthly as long as the patients stay in the intensive care unit. If gastrointestinal colonization was detected at admission to the intensive care unit or during their stay, rectal swab sampling had been continued weekly until negative outcome was obtained in successive three samples. Patients with VRE detected in the rectal swabs were isolated and strict isolation measures have been taken.

For the culture of the rectal swabs, Bile Aesculin Azide Agar (Oxoid, England) was prepared in line with the recommendations of the manufacturer, vancomycin 6 μg/mL and ceftriaxone 160 μg/ml were added and

the mixture was put on the sterile plates. Rectal swab samples were directly cultuvated in these plates and incubated for maximal 48 hours at 37°C in the aerobic environment. After gram staining and catalase tests applied on the colonies which were proliferated, forming black color in Bile Aesculin Azide Agar, definition of the colonies at species level and determination of antibiotic sensitivity were carried out using VITEK-2 automated system (bioMérieux-France).

Data obtained in this study were evaluated through licensed SPSS 18.0 package software. Chi-square test was used for two-group comparison as the result of normality tests. Statistical significant level was considered as 0.05 and $p<0.05$ values were accepted as statistically significant.

Results

A total of 515 patients were followed-up during the study period. Of these, 497 patients in whom rectal swab samples collected were enrolled into the study. Among the patients, 48.1% were male with a mean age of 65±19.12. Demographic and clinical features of the patients were shown in Table 1. Cardiovascular disease, cerebrovascular event and malignancy were detected in 50.3%, 31.0%, 18.7% of the patients, respectively. Patients were followed-up in the intensive care unit for average 8.08±11.6 days. Mortality rate was found as 43.9%.

VRE was detected in total 53 patients (10.7%). Patients were divided into two groups based on the presence of VRE colonization and risk factors were investigated between the groups. Although colonized patients were older than those of the non-colonized patients, the difference was not statistically significant ($p>0.05$) (Table 2). Same as mean age, history of previous hospitalization was more detected in the colonized patients compared to the non-colonized patients; the difference was not statistically significant ($p>0.05$). Length of stay in the intensive care unit was statistically significantly longer in the rectal colonization group ($p<0.05$). Among the risk factors defined; coexistence of malignancy, beeing on hemodialysis and Alzheimer disease as an underlying disease were found to be significant in the colonized patients ($p<0.05$) (Table 3).

Rate of the use any antibiotic was significantly higher in the rectal colonization group ($p<0.05$) (Table 3). Among the antibiotics considered as risk factor, use of third generation cephalosporins was found as 35.4% and glycopeptide as 22.5% in the colonized patients. None of the colonized patients developed VRE related infections.

Discussion

There are 16 species in enterococci genus with *E. faecalis* and *E. faecium* are the most common species, while *E.gallinarum* and *E.casseliflavus* less frequently cause infections[15]. Gastrointestinal system is the most common resource of enterococcal infections. First, colonization develops and than the infection occurs. In a study, 40.2% of the bacteria that colonize in the gastrointestinal system were found to be *E.gallinarum,* but no infection was observed due to these bacteria[16]. In our study, 53 of 497 patients developed colonization and the prevalence of VRE colonization in the intensive care unit was found as 10.7%. In their studies performed by Furtado et al. and Pan et al. This rate was found as 32.6% and 11.3%, respectively[17,18]. Whereas Byers et al. found this rate as 6%, Euihan et al. as 7.2% and Pan et al. as 21.9%[19–21]. *E.faecium* ve *E.faecalis*-related infections have been reported in the above mentioned studies, none of the VRE colonized patients developed infection in our study.

It is difficult to distinguish colonization from infection in the patient group with underlying disease. Mortality directly related to VRE is difficult to determine. In our study, we compared the mortality

Table 1. *Characteristics of the patients*

Feature	n	%
1. Age (years)	65±19.12	
2. Hospitalization days (mean)	8.08±11.6	
3. Gender		
Female	258	51.9
Male	239	48.1
4. Reason of hospitalization		
Internal	463	93.1
Surgical	34	6.8
5. Previous hospitalization		
Yes	237	47.7
No	260	52.3
6. Underlying disease		
CVD	250	50.3
CVE	154	31.0
DM	118	23.7
Malignancy	93	18.7
Alzheimer	43	8.7
7. History of antibiotic use		
No	334	67.2
Glycopeptide	12	2.4
Cephalosporin	54	10.8
8. Prognosis		
Discharge	279	56.1
Exitus	218	43.9

Table 2. *Comparison of the colonized and non-colonized patients*

		Colonization patients	Non-colonization patients	p
Age		69.75±17.3	65.4±19.3	>0.05
Gender	Female	28 (52.8%)	230 (51.8%)	>0.05
	Male	25 (47.2%)	214 (48.2%)	
Prognosis	Discharge	28 (52.8%)	251 (56.5%)	>0.05
	Exitus	25 (47.2%)	193 (43.5%)	
Reason of hospitalization	Internal	47 (88.7%)	415 (93.5%)	>0.05
	Surgical	6 (11.3%)	28 (6.3%)	
Previous hospitalization	Yes	30 (56.6%)	229 (51.7%)	>0.05
	No	23 (43.4%)	214 (48.3%)	

Table 3. *Risk factors for VRE colonization*

Risk factor		Colonized patients	Non-colonized patients	p
Hospitalization days		18.4±2.7	6.8±0.5	<0.001
CVD	Yes	33 (62.2%)	217 (48.9%)	>0.05
	No	20 (37.8%)	226 (51.1%)	
CVE	Yes	15 (28.3%)	139 (31.4%)	>0.05
	No	38 (71.7%)	304 (68.6%)	
Malignancy	Yes	3 (5.7%)	90 (20.3%)	<0.05
	No	50 (94.3%)	353 (79.7%)	
Dialysis	Yes	12 (22.6%)	42 (9.5%)	<0.05
	No	41 (77.4%)	401 (90.5%)	
Alzheimer	Yes	17 (32.1%)	26 (5.9%)	<0.05
	No	36 (67.9%)	417 (94.1%)	
Antibiotics	Yes	31 (58.5%)	132 (29.9%)	<0.05
	No	22 (41.5%)	312 (71.1%)	

rates between colonized and non-colonized patients and no statistically significant difference was found in terms of mortality.

Since enterococci are the elements of the normal flora of gastrointestinal system, infection due to these microorganisms may occur in case of impaired tissue integrity, perforation, immunosuppression and peritoneal dialysis. In a study performed by Ostrowski et al., prevalence of VRE colonization in surgical intensive care unit was found as 12% and organ transplantation was defined as a risk factor[18]. When reasons of the hospitalization were analyzed in our patient groups; number of the patients who were admitted to the intensive care unit with internal reasons was found to be higher than the other causes. Unlike the above-mentioned study no increase was observed in VRE colonization in the patients who admitted to ICUs after any kind of operation or trauma.

Several studies demonstrated that long hospitalization periods cause increased risk of colonization, higher rates of morbidity and mortality and cost[21–24]. In a study by Pan et al., long stay in the intensive care unit was found as a major risk factor for VRE colonization[22]. Likewise in our study, length of stay in the intensive care unit was found to be significantly longer in the colonization group.

Other risk factors for VRE colonization include underlying diseases such as chronic renal failure, diabetes mellitus, cardiovascular disease and dialysis[25]. Development of VRE colonization can lead to a life-threatening complication especially in the immunosuppressed patients[26]. Similarly to the other studies, in this study we found the risk factors for VRE colonization as the existence of malignancy, renal failure requiring dialysis and concomitant Alzheimer's disease. It was thought that one of the causes increase colonization in the patients having underlying Alzheimer's disease was the lack of self-care.

Antibiotic use seems to be an important risk factor for VRE colonizations and/or infections. Especially wide use of third generation cephalosporins and vancomycin increases the risk[17]. In their studies, Shorman et al. and Saka et al. reported that the use of vancomycin and cephalosporins as well as antimicrobial agents and antianaerobic effect have influence in the development of

VRE colonization[9,25]. In our study, use of antibiotic was found to be significantly higher in the rectal colonization group compared to the non-colonized group. The most common types of antibiotics used were found as glycopeptide and cephalosporins in our study, which was consistent with the literature.

In conclusion; as a result of this study significant risk factors for VRE colonization were found as long hospitalization period, malignancy, being on dialysis, concomitant Alzheimer's disease and excess the use of antibiotics. Since the patients having these risk factors are mainly followed-up and treated in intensive care units, determination of VRE colonization from the rectal swab sampling during the first admission to these unit is crucial. We believe that, rates of VRE colonization and infections would be decreased by the isolation of patients, performing strict infection control implementations and the use of proper antibiotics.

References

1. Schmidt S, Heimesaat MM, Fisher A, et al. Saponins increase susceptibility of vancomycin-resistant enterococci to antibiotic compounds. Eur J Microbiol Immunol 2014;4:204–12.
2. Sievert DM, Ricks P, Edwards JR, et al. National Healthcare Safety Network (NHSN) Team and Participating NHSN Facilities: Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009–2010. Infect Control Hosp Epidemol 2013;34:1–4.
3. Dahlen G, Biomqvist S, Almstahl A, et al. Virulence factors and antibiotic suspectibility in enterococci isolated from oral mucozal and deep infections. J Oral Microbiol 2012;4:10855.
4. Oli AK, Raju S, Rajeshwari, et al. Biofilm formation by Multidrug resistant Enterococcus fecalis (MDEF) originated from clinical samples. J Microbiol Biotechnol Res 2012;2:284–8.
5. Uttley AH, Collins CH, Naidoo J, et al. Vancomycin-resistant enterococci. Lancet 1998;1:57–8.
6. Klare I, Witte W, Wendt C, et al. Vancomycin-resistant enterococci (VRE). Recent results and trends in development of antibiotic resistance. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2012;55:1387–400.
7. Taşbakan MI. Vankomisine dirençli enterokok olguları. ANKEM Derg 2010;24:82–4.
8. Vural T, Şekercioğlu AO, Öğünç D ve ark. Vankomisine dirençli Enterococcus faecium suşu. ANKEM Derg 1999;13:1–4.
9. Atalay S, Ece G, Şamlıoğlu P ve ark. Evaluation of Vankomycin-Resistant Enterococcus Cases at a Tertiary Level Hospital in İzmir. Mikrobiyol Bul 2012;46(4):553–9.
10. Deshpande LM, Fritsche T, Moet G, et al. Antimicrobial resistance and molecular epidemiology of vancomycin-resistant enterococci from North America and Europe: A report from the SENTRY antimicrobial surveillance program. Diagn Microbiol Infect Dis 2007;58:163–70.
11. Çetinkaya Şardan Y. Vankomisine dirençli enterokoklara bağlı hastane enfeksiyonlarının epidemiyolojisi ve kontrolü. Ulusoy S, Usluer G, Ünal S (editörler). Gram Pozitif Bakteri Enfeksiyonları 1. Baskı Ankara: Bilimsel Tıp Yayınevi, 2004:171–85.
12. Katırcıoğlu K, Özkalkanlı MY, Yurtsever S ve ark. Olgu Sunumu: Yoğun bakım ünitesinde vankomisin dirençli enterokok kolonizasyonu ve alınan önlemler. Türk Anest Der Dergisi 2009;37:249–53.
13. Hayden MK. Insights into the epidemiology and control of infection with vancomycin-resistant enterococci. Clin Infect Dis 2000;31:1058–65.
14. Yamazhan T, Ulusoy S. Vankomisine dirençli enterokoklar. Doğanay M, Ünal S, Çetinkaya Şardan Y (editörler). Hastane İnfeksiyonları Kitabı Ankara: Bilimsel Tıp Yayınevi; 2013:355–7.
15. Uttley AH, George RC, Naidoo J, Woodford N, Johnson AP, Collins CH, et al. High-level vancomycin-resistant enterococci causing hospital infections. Epidemiol Infect 1989;103:173–81.
16. Yamazhan T, Ulusoy S. Vankomisine dirençli enterokoklar. Doğanay M, Ünal S, Çetinkaya Şardan Y (editörler). Hastane İnfeksiyonları Kitabı Ankara: Bilimsel Tıp Yayınevi; 2013:251.
17. Furtado GHC, Martins ST, Coutinho AP, Wey SB, Medeiros EAS. Prevalence and factors associated with rectal vancomycin-resistant enterococci colonization in two intensive care units in Sao Paulo, Brazil. Braz J Infect Dis 2005;9:64–9.
18. Kara A, Devrim İ, Bayram N, Katipoğlu N, Kıran E, Oruç Y ve ark. Risk of vancomycin-resistant enterococci bloodsteram infection among patients colonized with vancomycin-resistant enterococci. Braz J Infect Dis 2015;19:58–61.
19. Byers KE, Anglim AM, Anneski CJ, Germanson TP, Gold HS, Durbin LJ, et al. The hospital epidemic of vancomycin-resistant Enterococcus: risk factors and control. Infect Control Hosp Epidemiol 2001;2:140–7.
20. Pan SC, Wang JT, Chen YC, Chang YY, Chen ML Chang SC. Incidence of and risk factors for infection or colonization of vancomycin-resistant in patients in the intensive care unit. PLoS One 2012;7: e47297.
21. Euihan J, Sookjin B, Hojin L, Sang YM, Hyuck L. American Journal of Infection Control, 2014;42:1062–6.
22. Çekin Y, Daloğlu AE, Öğünç D, Baysan BÖ, Dağlar D, İnan D ve ark. Evaluation of vancomycin resistance 3 multiplexed PCR assay for detection of vancomycin-resistant enterococci from rectal swaba. Ann Lab Med 2013;33:326–30.
23. Hayakawa K, Marchaim D, Palla M, Gudur UM, Pulluru H, Bathina P, et al. Epidemiology of vancomycin-resistant Enterococcus faecalis: a case-case-control study. Antimicrob Agents Chemother 2013 Jan; 57(1):49–55.
24. Shorman M, Al-Tawfiq JA. Risk factors associated with vancomycin-resistant enterococcus in intensive care unit setting in Saudi Arabia. Interdiscip Perspect Infect Disease 2013;2013:369674.
25. Whang DW, Miller LG, Partain NM, McKinnell JA. Sistematik review and meta-analysis of Linezolid and Daptomycin for treatment of vancomycin-resistant enterococcal bloodstream infections. Antimicrob Agents Chemother 2013;57:5013–8.
26. Grabsch EA, Mahony AA, Cameron Dr, Martin RD, Heland M, Davey P, et al. Significant reduction in vancomycin-resistant enterococcus colonization and bacteraemia after introduction of a bleach-based cleaning-disinfection programme. J Hosp Infect 2012;82:234–42.

KAFKAS TIP BİLİMLERİ DERGİSİ
Kafkas Journal of Medical Sciences

ARAŞTIRMA YAZISI / ORIGINAL ARTICLE

Kafkas J Med Sci 2016; 6(2):81–87 • doi: 10.5505/kjms.2016.77045

The Results of Retrograd Intramedullary Elastic Nailing in the Treatment of Pediatric Femoral Shaft Fractures

Çocuk Femur Cisim Kırıklarının Retrograd İntramedüller Elastik Çivileme ile Tedavi Sonuçları

Ömer Serkan Yıldız[1], İbrahim Gökhan Duman[1], Emine Ece Yılmaz[2], Raif Özden[1]

[1]Mustafa Kemal University Faculty of Medicine, Department of Orthopaedics and Travmatology, Antakya, Hatay, Turkey; [2]Başkent University Research and Education Hospital of Adana, Department of Physical Medicine and Rehabilitation, Adana, Turkey

ABSTRACT

AIM: *The aim of this study was to evaluate the results of retrograd intramedullary nailing treatment in children with femoral shaft fracture.*

METHODS: *In this study, 20 patients, were included who applied to Mustafa Kemal University Research Hospital and were treated with retrograd intramedullary elastic nailing because of femoral shaft fracture.*

RESULTS: *The mean age of our patients was 14.5 months (9–24 months) and mean follow-up time was 8.3 years (4.5–14 years). The average length of stay in hospital were 3.4 days. The average reunion duration were detected as 7.8 weeks. There was no significant difference between reunion durations of open and closed fractures. Valgus alignment of 7 degrees was observed in one patient and 5 degrees in one other patient. But it did not result any functional or clinical restrictions. There were not any increase of anterior-posterior angle or any rotational deformities observed. Extremity length difference below 1cm was detected in 3 of the patients and length difference between 1–1.5 cm was detected in 2 patients. When patients were evaluated according to Flynn's criteria, the results were excellent in 14 patients (70%), good in 5 patients (25%) and poor in 1 patient (5%).*

CONCLUSION: *Elastic intramedullary nailing treatment of femoral shaft fractures in children between 5–14 years of age is a safe and effective treatment.*

Key words: *femoral fracture; elastic nail; osteosynthesis*

ÖZET

AMAÇ: *Retrograd elastik intramedüller çivileme yöntemi ile tedavi edilen femur cisim kırıklı çocukların sonuçları değerlendirildi.*

YÖNTEM: *Bu çalışmamıza, 2010–2014 yılları arasında Mustafa Kemal Ünviversitesi Araştırma hastanesine başvuran ve femur cisim kırığı tanısı nedeniyle retrograd intramedüller elastik çivileme ile tedavi ettiğimiz 20 (15 erkek, 5 kız) hasta dahil edildi.*

BULGULAR: *Hastalarımızın ortalama takip süresi 14,5 ay (9–24 ay), yaş ortalaması 8,3 (4.5–14 yıl) idi. Olgularımızın 16'sı (%90) kapalı, 4'ü (%10) açık kırık idi. Olgularımızın ortalama yatış süresi ise 3,4 gündür (2–10 gün). Hastalarımızda ortalama kaynama zamanı 7,8 hafta (6–12 hafta) olarak tespit edildi. Açık ve kapalı kırıkların kaynama süreleri açısından anlamlı bir fark saptanmadı. Olgularımızın birinde 5, diğerinde 7 derece valgus dizilimi gözlendi ancak hastalarımızda fonksiyonel ve klinik herhangi bir soruna yol açmadı. Olgularımızın hiç birinde anterior-posterior açılanma ve rotasyonel deformite gözlenmedi. Üç hastamızda 1 cm den az, 2 hastamızda 1–1,5 cm arası extremite uzunluk farkı tespit edildi. Ancak bu uzunluk farkı hastalarımızda klinik ya da fonksiyonel bir sorun yaratmadı. Hastalar klinik ve radyolojik olarak Flynn kriterlerine göre değerlendirildiğinde; 14 hastada (%70) mükemmel sonuç, 5 hastada (%25) iyi sonuç ve 1 hastada (%5) kötü sonuç elde edildi.*

SONUÇ: *Femur cisim kırıklı çocuklarda (5–14 yaş) elastik intramedüller çivi ile osteosentez, güvenilir ve etkin bir tedavidir.*

Anahtar kelimeler: *femur kırığı; elastik çivi; osteosentez*

Introduction

Femoral fractures are leading cause of hospitalization due to fractures in children and constitute 21.7% of total childhood fractures in United States[1]. Femoral fractures are more common in early childhood, when weak trabecular bone turns into hard lamellar bone structure, and also in adolescencents who can be frequently exposed to high-energy traumas[2]. The underlying reason for femoral fractures differ according to the age period. The most common reason before walking age is child abuse (80% of total)[3]. After walking age, child abuse seems to decrease and high-energy traumas are seen as the leading cause. High-energy traumas such as high falls and traffic accidents are responsible 90% of total femoral fractures in that period[4,5].

Uzm. Dr. Ömer Serkan Yıldız, Mustafa Kemal Üniversitesi, Araştırma Hastanesi, 31000 Hatay, Türkiye, Tel. 0505 389 28 56 Email. dromerserkan@mynet.com
Geliş Tarihi: 18.11.2014 • Kabul Tarihi: 04.08.2015

When chosing appropriate method for treatment of childhood femoral fractures, age, growing potential of the epiphysis, length of hospitalization and any other concomittant injuries play important role[6].

In children older than 5 years, closed reduction and pelvipedal casting provide satisfactory outcomes. This method is accepted as the most valuable treatment intervention in femoral fractures of this age group[7–9].

In older children (5–15 years), skeletal traction followed by pelvipedal casting has perfomed but in this age group, skeletal traction has been reported to cause malunions and lengthen the duration of hospitalization[8,10].

Surgical procedures include external fixation, osteosynthesis with plaque nailing and internal fixation with elastic nailing. Although all of these are generally reported to provide good results, while choosing the surgical method facts such as less morbidity, lower financial cost and psychological factors should be considered[11–13].

In this study, we aimed to evaluate and present the clinical and radiological results of patients with femoral shaft fractures between age of 5–15 and treated with intramedullary titanium elastic nailing.

Materials and Methods

20 children (15 male, 5 female) who applied to our clinic between years 2010–2014 and were treated with retrograd intramedullary titanium elastic nailing due to femoral shaft fractures, were included in this study. The mean age of our patients were 8.3 years (4.5–14).

Patients were first evaluated at the emergency room and hospitalized after long leg casting was applied (Fig.1). Time since last food intake and overall condition of the patient and material supplement was considered before admission to the operating room. Under general anestesia and at supin position, mini incisions were applied from median and lateral sides of femoral distal metaphysis, under scopy. After nail insertion points were opened with awl laterally and mediallly, 1 nail per each side were sent retrogradely to trochanteric region, paying attention that elastic nails filled at least 2/3 of the femoral medulla (Fig. 2). Fracture line was reducted with closed reduction. If closed reduction failed, osteosynthesis was provided by open reduction that was performed with a mini incision through lateral side of the fracture line. The nail was cautiously placed as proximal end contacting to the cortex in trochanteric region regarding 3-points- principal but also apophyseal injury of the trochantery was avoided carefully. Distal endings of the nails were cut in appropriate sizes in order to allow future removal. None of our patients needed atele or casting after the surgery. At postoperative first day, patients were allowed to do knee exercises and mobilize without weight-bearing through the operated extremity. After discharge, stiches were removed at day 11 and patients were scheduled for a follow-up visit within post-operative 4th week.

Patients were followed with anterior-posterior and lateral X-rays of both hip and knee.

Observation of callus at at least 3 of 4 cortexes in anterior-posterior and lateral X-rays was considered as radiological reunion and absence of pain and pathological movement was accepted as clinical reunion of the fracture (Fig. 3). Any complications during hospital stay and reunion period were noted. Also, the need for crunches in daily activites, pain during walking and at rest, gait pattern, range of motions of hip and knee were evaluted clinically. Additionally, lower extremity length inequalities and angular deformities were noted for each subject.

Figure 1. *Preoperative radiographs of the patient with elastic nailing we applied to the femoral shaft fracture due to falling.*

Figure 2. *Postoperative radiograph (1. day).*

Figure 3. *Postoperative radiograph (7. month).*

In order to determine functional outcomes, radiological and clinical results were evaluated using Flynn's criteria (Table 1).[14]

Results

Mean follow-up duration for our patients were 14.5 months (9–24 months). Eleven of fractures were at left (55%), and 9 were at the right side (45%). Etiologies of fractures were distrubuted as follows; 13 high-falls (65%), 5 traffic accidents (25%), 1 simple bone cycst (5%) and 1 gun-shot (5%).

16 (90%) of our cases had closed, 4 cases (10%) had open fractures. When closed fractures were graded according to AO classification; 5 patients (25%) were A1, 3 (15%) were A2 and 8 were A3. Open fractures were evaluated using Gustillo-Anderson classification; 2 patients (10%) were Type 1, 1 (5%) was Type 2 and 1 (5%) was Type 3.

Fractures were located at upper 1/3 of femur in 5 subjects (25%), at lower 1/3 of femur in 2 subjects (%10) and at middle 1/3 of femur in 13 (65%) subjects.

Patients were operated within average 0.9 days (0–8 days) after admission to the hospital.

The mean length of hospitalization was 3.4 days (2–10 days). Some of our patients had additional injuries in-conjunction with the femoral fracture. These injuries

Table 1. *FLYNN criteria*

	Perfect result	Good result	Bad result
Limb length discrepancy	<1.0 cm	1–2 cm	>2.0 cm
Angular deformity	<5°	5–10°	>10°
Pain	No	No	Yes
Complication	No	Minor –transitory	Major –permanent

are the major factors that alter duration of hospitalization and prolong the surgical admission period. Two of our patients who had head trauma, were operated after they were followed by neurosurgery department for 1 week. One patient with elevated liver enzymes were followed and treated by paediatrices department and could be operated at day 8 of hospitalization. One patient had ipsilateral, one other patient had contralateral femoral neck fracture. In both cases, femoral neck fractures were stabilized using cannula nails. There was a fracture of mandible in one patient, whom had been followed conservatively by concerning department. One of our patients had ipsilateral humerus fracture which was stabilized with 2 kirschner wires during the same operation session.

Mean union time in our patients was recorded as 7.8 weeks (6–12 weeks). There was no significant difference between open and closed fractures concerning union timing.

There were complete reunion in all of our patients except for one case. In a case of pathologic fracture with underlying simple bony cyst, due to migration of endings from trochanteric area towards posterior region, elastic nails were removed and replaced with plaque nail stabilization.

There was a valgus alignment of 5 degrees in one case, 7 degrees in an other case but neither caused any functional and clinical problems. No anterior-posterior anglings or rotational deformities were noted in any of our cases. There was an extremity length difference less than 1 cm in 3 patients and 1–2.5 cm in 2 patients. However, this length difference did not result any clinical or functional problems. Extreme loss in knee extention was determined in one patient's first follow-up visit. Patient was immediately included in rehabilitation programme and nails were removed after reunion. Loss in knee extention was noted as 5–10 degrees in this case. In 5 patients, there were local tenderness and mild swelling at distal nail endings, that fully recovered after removal of nails. Neither of our patients had superficial or deep infections of any kind. Mean removal time of nails for our patients were approximately 6 months. No recurrent fractures occured following nail removals. There were no abnormal gait, inability to walk without crunches or pain during activity or rest in any of our patients.

When patients were evaluated according to Flynn's criteria[14], 14 patients (70%) had excellent results, 5 patients (25%) had good results and 1 patient (5%) had fair results.

Discussion

Femoral shaft fractures are one of the most common type of injuries in paediatric orthopaedic patient group[15]. It is more frequent during early childhood and adolescence. Also, it is almost 2.5 times common in girls than boys[16,17]. In our study, similar results were found. 15 of our patients were boys and 5 of them were girls and mean age of the patients were 8.3 years.

Femoral shaft fractures are type of fractures that usually happen due to trauma, can be together with other injuries and may result permanent functional damages[18]. They generally occur after high-energy traumas, such as high falls and motor vehicle accidents[16]. In our study, the cause was falls and traffic accidents in 95% of the cases.

In all cases with a femoral fracture, physicians should perform a complete physical examination of the child and bear in mind a type of multiple injury named as the "waddel triad", which consists of traumas of abdomen, thorax and head in addition to the femoral trauma[15]. In our study, 2 patients of total 20 patients had head trauma, 1 patient had humeral fracture, 1 had mandible fracture, 2 head femoral neck fracture and 1 had elevated enzymes due to liver laceration, together with the femoral fracture.

There are various methods for treatment of childhood femoral shaft fractures. When selecting the most appropiate treatment plan, many factors such as age, mechanism of the injury, fracture type, accompanying injuries, social status of the family and treatment costs are considered[15]. In one study, it is reported that surgeons are tend to choose conservative methods before the age of 6, when they are more likely to prefer surgical methods after the age of 6[11].

Conservative methods in treatment include pelvic bandage, pelvipedal casting following traction and immediate pelvipedal casting. In surgical methods, there are options like conventional or biological plaque stabilization, rigid or elastic intramedullay stabilitation and external stabilization[15].

Titanium elastic intramedullary nailing has increasingly become a popular treatment method for childhood femoral fractures in many centers in Europe and Northern America[19].

They are preferred because of early mobilization and early return to daily activities and short-term hospitalization. Also, titanium intramedullary nailing has additional advantages such as being less traumatic, using smaller size nails, absence of drilling, usually being performed with retrograde surgical technique and avoiding epiphyseal damage[20].

There are many studies that compares elastic intramedullay nailing to other alternative treatment methods. In Song et al.'s study that compares the results of retrograd intramedullary elastic nailing to pelvipedal casting following traction, it is reported that there was not any problems such as angular malalignment or inequality of the extremities in elastic naling group, unlike the pelvipedal casting group[21].

Baron et al. compared elastic nailing to external fixation and reported better functional healing and early re-gain of range of motion and early return to school with elastic nailing[22].

Moreover, there were some complications reported with external fixation, such as recurrent fractures, rotational aligment problems and infections of the naling area.

It is reported that duration of hospital stay and related to that, treatment costs decrease with usage of elastic nailing method[14]. In Heybeli et al.'s study[23], they performed retrograde elastic titanium nailing in 34 patients with femoral diaphysis fracture and reported mean duration of hospitalization as 5.5 days.

Mean time of hospital stay was found as 4.2 days by Şükür et al.[24] and as 6 days in another study with 31 patients[25]. Nascimento et al.[26] compared outcomes of intramedullary elastic nailing to pelvipedal casting followed by traction and reported mean time of hospitalization as 9 days in intramedullary nailing group and as 20 days in casting group.

In our study, similar to previous studies in the literature, mean hospitalization time of our patients was 3.4 days (2–10 days).

When mean reunion time for femoral shaft fractures were analyzed, there were different results in different studies. The mean time of reunion was 6.8 weeks in Şükür et al.'s study[24], 7 weeks in Houshian et al.'s study[25] and 7.4 weeks in Heybeli et al.'s study[23].

Mishra et al.[27] reported a mean time of reunion as 9.5 weeks in their study with 30 patients, when a mean time of 6.86 weeks is reported in Jalan et al. 's series[28] and 7.6 ± 1.5 weeks in Assaghir's series[29]. In Nascimento et al.'s[26] study that compared results of titanium elastic nailing to pelvipedal casting following traction, mean reunion time was 7.7 weeks in surgery group and 9.3 weeks in conservative treatment group.

In our study, mean reunion time was detected as 7.8 weeks. There was no significant difference in reunion times between open and closed fractures. Our results were compatible with other studies in the literature.

The most common complication of childhood femoral fractures is inequality of two extremities[23]. Houshian et al.[25] reported an extremity inequality above 1 cm in 6 of 31 children in their study. In Şükür et al.'s study[24], it is found that there was a leg inequality below 1 cm in 5 cases out of 22 patients in total. There were 7 patients with an extremity inequality out of 34 patients in Heybeli et al.'s series[23], 4 out of 30 patients in Jalan et al.'s series[28] and 7 in 59 patients in Assaghir's series[29].

In Nascimento et al.'s study[26] that compared titanium elastic intramedullary nailing to pelvipedal casting following traction, they detected lenghtening in 60% of patients (mean 0.66 cm) and shortening in 6.7% of patients (mean 0.25 cm) in the surgery group. However, in the casting group, they reported shortening in 63.3% of patients (mean 1.14 cm) and shortening in 13.3% of patients (mean 1.06 cm). In our study, out of total 30 patients, we have observed an extremity inequality below 1 cm in 3 patients and 1–1.5 cm in 2 patients. But these inqualities did not cause any clinical or functional problems in none of the cases.

Other common problems related to childhood femoral fractures are malunions and angular deformities[23]. In Şükür et al.'s series[24] including 22 patients, they observed an outer rotation deformity of 10 degrees in one patient and a coronal or sagittal deformity of 5–10 degrees, which does not cause any clinical problems, in 5 of total 22 patients. In a series of Houshian et al.[24], they found an inner rotational deformity of 10 degrees in one of 31 children and no angular deformities. In Heybeli et al.'s study[23] including 34 patients, less than 10 degrees of varus/valgus or anterior/posterior angling were observed in 4 children. In Assaghir's series[29], 5–9 degrees frontal angling has been detected in 6 subjects (10.2%), sagital angling in 7 subjects (11.9%) and 10 degrees rotational deformity in 2 subjects (3.4%). Jalan et al.[28] reported more than 10 degrees rotational deformities in 6 out of 30 patients in their series. In our study, at the last follow-up visits of the 20 patients, we

have detected 5 degree valgus alignment in 1 patient, as well as 7 degree valgus alignment in 1 other patient. Thus, this angling did not lead to any clinical problems. Neither of our patients had anterior/posterior angling or rotational deformities.

Further problems related to elastic intramedullary nailing are pain and skin irritation at nail insertion points, infection and implant failure[15]. In Jalan et al.'s study[28] with 30 patients, they found soft tissue irritation at nail insertion points in 6 patients, superficial infection in 2 patients and skin ulceration in 2 patients. In Assaghir's[29] series with 59 patients, pain in the nail insertion points was reported in 5 patients and superficial infection was reported in 2 patients. In Mishra et al.'s series with 30 patients[27], it is reported that there were 3 irritations but no infections at nail insertion points. Şükür et al.[24] indicated that in 2 of their 22 patients, nails migrated posteriorly and resulted subcutaneous irritation.

In Flynn et al.'s[14] study, only one implant failure was observed and only this one patient out of 234 children who had underewent titanium elastic nailing needed revision. In our study, in 5 of our patients we noted edema and tenderness around nail insertion points, which immediately resolved following nail removal. Also, there were no deep or superficial infections noted. In one patient, who had fracture with an underlying cycst, we had to remove elastic nails due to migration and failure of the implant and then replace it with plaque nailing stabilization. Therefore, we concluded that plaque nailing stabilization is a more convenient option for treatment of femur fractures that developed with an underlying cycst in children.

Different timings for nail removal after titanium elastic nailing has been claimed. Mean time for nail removal is reported as 22 weeks in Houshian et al.'s study[25], 9 months in Şükür et al.'s study[24], 12 months in Heybeli et al.'s study[23] and 20.3±10.2 weeks in Assaghir's study[29]. In our study, we removed the nails approximately at the 6th month. No recurrent fractures have been observed following nail removal. We assume that various numbers have been reported because timing for removals are usually adjusted according to the school breaks of the children.

Today, Flynn's criteria[14] is commonly used to evaluate treatment outcomes of elastic intramedullary nailing. Heybeli et al. reported 71.4% excellent, 25.7% good and %2.9 fair results according to this criteria. Also Jalan et al.[28] reported 66.7% excellent, 33.3% good results as well as Mishra et al.[27] reported 80% excellent, 20% good results. However, Şükür et al.[27] found 68% excellent, 32% good results in their study with 22 patients. In our study, our results were 70% excellent, 25% good and 5% fair, according to Flynn's criteria.

We concluded that our results were similar to previous studies in the literature. Short follow-up time and limited number of patients are the major weaknesses to this sudy. However we believe that this study is a contrubution to the current literature.

Conclusion

In conclusion, in the treatment of femoral shaft fractures, osteosynthesis with elastic intramedullary nailing has many advantages such as less soft tissue and periost damage, less bleeding during surgical procedure, smaller size of scarring, shorter duration of hospitalization, early weight-bearing and early return to school and faster bone healing without damaging the blood flowing of the growing plates.

On the other hand, this method has some disadavateges like causing rotational and angular deformities and resulting extremity inequalities. Despite such disadvantages, osteosynthesis with elastic intramedullary nailing is a safe and affective treatment of children with femoral shaft fracture between the age of 5–14 and it is the first choice treatment method with appropriate indications.

References

1. Galano GJ, Vitale MA, Kessler MW, et al. The most frequent traumatic orthopaedic injuries from a national pediatric inpatient population. J Pediatr Orthop 2005;25:39–44.
2. Viljanto J, Linna MI, Kiviluoto H, et al. Indications and results of operative treatment of femoral shaft fractures in children. Acta Chir Scand 1975;14:366–9.
3. Gross RH, Stranger M. Causative Factors Responsible for Femoral Fractures in Infants and Young Children. J Pediatr Orthop 1983;3:341–3.
4. Gustilo RB, Anderson JT. Prevention of Infection in the Treatment of 1125 Open Long Bone Fractures. J Bone Joint Surg Am 1976;58:453–8.
5. Loder RT. Pediatric Polytrauma: Orthopaedic Care and Hospital Course. J Orthop Trauma 1987;1:48–54.
6. Melisie F, Krug E, Duijff JW, et al. Age specific treatment of femoral shaft fractures in children. Ned Tijdschr Geneeskd 2012;156: A3976.

7. Staheli LT, Sheridan GW. Early spica cast management of femoral shaft fractures in young children. Clin Orthop 1977;126:162–6.
8. Aronson DD, Singer RM, Higgins RF. Skeletal traction for fractures of the femoral shaft in children. J Bone Joint Surg Am 1987;69:1435–9.
9. Newton PO, Mubarak SJ. Financial aspects of femoral shaft fracture treatment in children and adolescents. J Pediatr Orthop 1994;14:508–12.
10. Reeves RB, Ballard RI, Hughes JL. Internal fixation versus traction and casting of adolescent femoral shaft fractures. J Pediatr Orthop 1990;10:592–5.
11. Sanders JO, Browne RH, Mooney JF, et al. Treatment of femoral fractures in children by pediatric orthopedists: Results of a 1998 survey. J Pediatr Orthop 2001;21:436–41.
12. Anglen JO, Choi L. Treatment options in pediatric femoral shaft fractures. J Orthop Trauma 2005;19:724–33.
13. McCartney D, Hinton A, Heinrich SD. Operative stabilization of pediatric femur fractures. Orthop Clin North Am 1994;25:635–50.
14. Flynn JM, Hresko T, Reynolds RA, et al. Titanium elastic nails for pediatric femur fractures: A multicenter study of early results with analysis of complications. J Pediatr Orthop 2001;21:4–8.
15. Çelebi L, Biçimoğlu A. Çocuk femur cisim kırıkları. TOTBİD (Türk Ortopedi ve Travmatoloji Birliği Derneği) Dergisi 2006, cilt 5 sayı:1–2.
16. Hinton RY, Lincoln A, Crockett MM, et al. Fractures of the femoral shaft in children; incidence, mechanisms and sociodemographic risk factors. J Bone JointSurg Am 1999;81:500–9.
17. Daly KE, Calvert PT. Accidental femoral fractures in infants. Injury 1991;22:337–8.
18. Bucholz RW, Jones A. Current concepts review fractures of the shaft of the femur. J Bone Joint Surg 1991;73A(10):1561–6.
19. Pombo MW, Shilt JS. The definition and treatment of pediatric subtrochanteric femur fractures with titanium elastic nails. J Pediatr Orthop 2006;26:364–70.
20. Lascombes P, Bodenreider O, Prevot J, et al. The use of flexible intramedullary pins in the treatment of fractures of the femur in children:250 cases. J Bone Joint Surg [Br] 1993;75(Suppl II):162.
21. Song HR, Oh CW, Shin HD, et al. Treatment of femoral shaft fractures in young children: Comparison between conservative treatment and retrograde flexible nailing. J Pediatr Orthop B 2004;13(4):275–80.
22. Bar-On E, Sagiv S, Porat S. External fixation or flexible intramedullary nailing for femoral shaft fractures in children. A prospective, randomized study. J Bone Joint Surg Br 1997;79:975–8.
23. Heybeli M, Muratli HH, Celebi L, Gülçek S, Biçimoğlu A. The results of intramedullary fixation with titanium elastic nails in children with femoral fractures. Acta Orthop Traumatol Turc 2004;38(3):178–87.
24. Şükür E, Azboy İ, Demirtaş A, Bulut M, Uçar BY, Alemdar C. Çocuk femur diyafiz kırıklarının titanyum elastik intramedüller çivileme ile tedavisi. (Intramedullary Titanium Elastic Nailing in the Treatment of Paediatric Diaphyseal Femur Fractures). İstanbul Med J 2013;14:94–6.
25. Houshian S, Gothgen CB, Pedersen NW, et al. Femoral shaft fractures in children: Elastic stable intramedullary nailing in 31 cases. Acta Orthop Scand 2004 Jun; 75(3):249–51.
26. Nascimento FP, Santili C, Akkari M, et al. Flexible intramedullary nails with traction versus plaster cast for treating femoral shaft fractures in children: Comparative retrospective study. Sao Paulo Med J 2013;131(1):5–12.
27. Mishra AK, Chalise PK, Shah SB, et al. Diaphyseal femoral fractures in children treated with titanium elastic nail system. Nepal Med Coll J 2013 Jun; 15(2):95–7.
28. Jalan D, Chandra R, Sharma VK. Results of titanium elastic nailing in paediatric femoral diaphyseal fractures-report of 30 cases. Chin J Traumatol 2013;16(2):77–83.
29. Assaghir YM. Titanium elastic nail in femur fractures as an alternative to spica cast in preschoolers. J Child Orthop 2012 Dec; 6(6):505–11.

KAFKAS TIP BİLİMLERİ DERGİSİ
Kafkas Journal of Medical Sciences

ARAŞTIRMA YAZISI / ORIGINAL ARTICLE

Kafkas J Med Sci 2016; 6(2):88–93 • doi: 10.5505/kjms.2016.96720

The Evaluation of the Relationships Between Sleep Apnea Syndrome and Depression/Anxiety Disorder

Uyku Apne Sendromu ile Anksiyete ve Depresyon Birlikteliğinin Değerlendirilmesi

Yusuf Ehi[1], Seyho Yücetaş[2], Yelda Yenilmez[3], Serhat Tunç[3], İnan Gezgin[2], Mehmet Yasar Özkul[4]

[1]Kafkas University Faculty of Medicine, Department of Neurology, Kars, Turkey; [2]Kafkas University Faculty of Medicine, Department of Neurosurgery, Kars, Turkey; [3]Kafkas University Faculty of Medicine, Department of Psychiatry, Kars, Turkey; [4]Şifa University of Medicine Faculty, Department of Neurology, İzmir, Turkey

ABSTRACT

AIM: *Sleep apnea syndrome (SAS) is commonly seen disorder in the population. There are many studies using different questionnaires to evaluate the patients who are diagnosed wit SAS and also suffering from depression and anxiety disorder; as there are many different questionnaires to evaluate these patients, the results of these studies have many discrepancies. We aim to research correlation of anxiety and depression with this study.*

METHODS: *134 cases were recruited for the polysomnographic evaluation and these cases are used as the subjects of this study. The participating patients are divided into two main groups: 51 cases with AHI<5 are selected as the control group and the remaining 83 cases with AHI>5 are named as the patient group. Later, these groups are subdivided into 3 more classes; the first one was the mild SAS patients consisting of 27 cases with AHI: 5–14.9, second one was the middle SAS patients consisting of 24 cases with AHI: 15–29.9 and finally the third one was the heavy SAS class which was consisting of 32 patients with AHI≥30. Hospital Anxiety Depression Test (HADT) was applied to all cases.*

RESULTS: *56.7% of the patients participating to the study were male and the remaining 43.3% of the patients were female. The mean age was 48.54±10.59. Control group the mean body mass index (BMI) was 30.11±4.84, patient group the mean BMI was 31.97±5.10. There was no statistically significant correlation between the depression and anxiety scores and AHI scores of the control and patient groups.*

CONCLUSION: *We used the HAD scale to evaluate excessive daytime sleepiness and the concurrence with depression and also to determine whether a correlation was present between the apnea-hypopnea index values and HAS scores in these patients in this study.*

Key words: *sleep apnea syndrome; anxiety; depression*

ÖZET

AMAÇ: *Uyku Apne Sendromu (UAS), toplumda yaygın olarak görülen bir hastalıktır. UAS'lu hastalarda, depresyon ve anksiyete birlikteliğini değerlendirmek farklı ölçeklerin kullanıldığı çalışmalar olmakla birlikte bu konuyla alakalı çelişkili sonuçlar bulunmaktadır. Bu çalışmamızda amaç UAS ile anksiyete ve depresyon korelasyonunu araştırmaktır.*

YÖNTEM: *Çalışmaya polisomnografik inceleme yapılan 134 olgu alındı. Apne-Hipopne İndeksi (AHİ) <5 olan 51 olgu kontrol grubu, AHİ ≥5 olan 83 olgu hasta grubu olarak oluşturuldu. Hasta grubu üç grup şeklinde sınıflandırıldı. 1) AHİ 5–14,9 olan 27 olgu hafif UAS; 2) AHİ: 15–29.9 olan 24 olgu orta düzey UAS; 3) AHİ ≥30 olan 32 olgu ağır UAS idi. Tüm hastalara, Hastane Anksiyete ve Depresyon ölçeği uygulandı.*

BULGULAR: *Çalışmaya dahil edilen hastaların 76 (%56,7)'si erkek, 58 (43,3)'ü ise kadındı. Hastaların yaş ortalaması 48,54±10,59 idi. HAD ölçeğinde kesme puanına göre depresyon tanısı alan olgu sayısı kontrol grubunda 18 (%35,29), hasta grubunda 30 (%36,14) kişiydi. Hasta grubunun alt grupları değerlendirildiğinde, Hafif UAS'de 10 (%37,03), Orta UAS'de 9 (%37,50), Ağır UAS'de 11 (%34,37) olgu olarak bulundu. Kesme puanına göre anksiyete tanısı alan olgu sayısı kontrol grubunda 19 (%37,25), hasta grubunda 27 (%32,53) kişiydi. Hasta grubunun alt grupları değerlendirildiğinde hafif UAS 9 (%33,33), orta UAS 8 (%33,33), ağır UAS 10 (%31,25) olarak bulundu. Kontrol ve hasta grubunun anksiyete ve depresyon skorları ile AHİ karşılaştırıldığında istatistiksel olarak anlamlı korelasyon yoktu (p>0,05).*

SONUÇ: *Çalışmamızda; HAD ölçeği kullanılarak gündüz aşırı uykululuğu, tanıklı apnesi ve horlaması olan hastalarda anksiyete ve depresyon birlikteliğini değerlendirmeyi ve bunun yanı sıra bu hastalarda apne-hipopne endeksi değerleri ile HAD puanlarının arasında korelasyonun olup olmadığını belirlemeyi amaçladık.*

Anahtar kelimeler: *uyku apne sendromu; anksiyete; depresyon*

Yard. Doç. Dr. Yusuf Ehi, Kafkas Üniversitesi Tıp Fakültesi, Kars, Türkiye,
Tel. 0532 664 77 68 Email. yusufehi@windowslive.com
Geliş Tarihi: 20.08.2014 • Kabul Tarihi: 08.06.2015

Introduction

Excessive daytime sleepiness, witnessed apnea and snoring generally suggest two kinds of disorders known as the sleep apnea syndrome (SAS) and the obesity-hyperventilation syndrome[1]. SAS is a common disorder in the population. There are three types named central, obstructive, and mixed and the obstructive type is the most common. Obstructive sleep apnea syndrome (OSAS) is characterized by full (apnea) or partial (hypopnea) upper respiratory tract obstruction attacks and arterial oxygen desaturation during sleep[2]. Central sleep apnea syndrome (CSAS) is characterized by the failure of the respiratory center to send commands to the respiratory muscles during sleep. There is no respiratory effort or intrathoracic change in CSAS in contrast to OSAS. The chest and abdominal movements also stop together with the respiration[3,4]. The airflow is interrupted without respiratory effort at first but this is followed by upper respiratory tract obstruction in mixed apnea. The prevalence of obstructive sleep apnea (OSAS) is 4% in adult males and 2% in adult females[5].

The Obesity-Hypoventilation syndrome is defined as excessive daytime sleepiness and hypoventilation that cause hypercapnia without any other neurological, muscular, mechanic or metabolic cause, generally in patients with a BMI ≥30. OSAS is also present in 90% of these patients[1].

Sleep continuity is disturbed, the superficial sleep duration increases and deep sleep duration decreases in these patients with complaints of excessive daytime sleepiness, witnessed apnea and snoring. These changes in sleep duration lead to neuropsychiatric symptoms such as excessive daytime sleepiness, tiring easily, psychomotor slowness, perception disturbances, forgetfulness, attention deficit, concentration problems, decreased interest, decreased work performance, and sexual problems[6–8].

Some studies have reported depression and decreased quality of life in SAS patients[9]. Depression is the most common mood disorder associated with SAS but most studies have found no such correlation[10]. There is no consensus on whether SAS causes mental changes or psychiatric disorders[11]. Some special scales are used to evaluate mood disorders in SAS patients[12]. The most commonly used scales for this purpose are the Beck Anxiety and Depression Scale and the Hospital Anxiety and Depression Scale (HAD).

We used the HAD scale to evaluate excessive daytime sleepiness and the concurrence with depression and also to determine whether a correlation was present between the apnea-hypopnea index values and HAS scores in these patients in this study.

Materials and Method

We included a total of 134 patients older than 16 years who had presented between June 2009 and July 2010 with one or more of the snoring, excessive daytime sleepiness or relative-reported apnea symptoms, had undergone Polysomnography (PSG), and had fully completed the HAD scale. Permission was obtained from the Harran University Faculty of Medicine Ethics Committee and all patients provided informed consent. Patients who suffered from a chronic pulmonary disorder such as asthma, any disorder that could affect cognitive functions such as bipolar disorder, mental retardation and schizophrenia, or who used any medication that would affect the sleep rhythm were excluded from the study. The Epworth sleep scale score was ≥9 in all patients[13].

The patients were administered the Hospital Anxiety and Depression Scale (HAD) in outpatient conditions before the PSG test. HAD is a four-item Likert-type scale developed by Zigmond and Snaith to determine the anxiety and depression risk of the patient and to measure the level and change in severity[14]. It contains a total of 14 questions with single numbers representing anxiety and even numbers depression. The patients respond by making marks on the scale. The scoring for items 1, 3, 5, 6, 8, 10, 11, 13 is in the form of 3, 2, 1, 0. Items 2, 4, 7, 9, 12, 14 are scored as 0, 1, 2, 3. The Turkish validity and reliability study for the scale has been conducted by Aydemir et al and the scale has been shown to be reliable when screening for depression and anxiety signs in those with a physical disorder[15]. Subscales for anxiety (HAD-A) and depression (HAD-D) are also present. The Turkish study has provided a cutoff point of 10/11 for the anxiety subscale and 7/8 for the depression subscale. Accordingly, patients with higher scores are considered at risk. The lowest score from either scale is 0 and the highest 21.

Our patients were followed up through the night with the Nihon Kohden polysomnography device. The acquired data were analyzed with the Polysmith V 5.0 software. The EEG records during PSG were obtained with four electrodes placed according to the international 10-20 system (C3/A2-C4/A1-O1/A2-O2/

A1). Right and left electrooculography, jaw electromyography and electrocardiography (ECG) were performed. Airflow was monitored with a nasal pressure cannula. Respiratory movements were evaluated with thoracic and abdominal belt measurements. Snoring was recorded with a snoring sensor. Sleep oxygen saturation was measured continuously with pulse oximetry. PSG recording was according to the the American Academy of Sleep Medicine sleep scoring (AASM) standard criteria[16].

The lack of airflow in the mouth and nose for 10 seconds or more following the sleep analyses was defined as apnea. A decrease of more than 30% in the nasal cannula amplitude compared to the baseline or a decrease of more than 4% in saturation for 10 seconds or more compared to the pre-event baseline was defined as hypopnea. The total number of apnea and hypopnea episodes per sleep hour was defined as the Apnea-Hypopnea Index (AHI)[16].

The patients were divided into 2 groups according to their AHI. The 51 cases with AHI <5 made up Group 1 and the 83 cases with AHI ≥5 made up Group 2. Group 2 was subdivided according to the AHI index as follows: The 27 cases with AHI: 5–14.9 were in the Mild group, the 24 cases with AHI: 15–29.9 were in the Moderate group and the 32 cases with AHI: ≥30 were in the Severe Group.

All data were analyzed using the SPSS Version 11.0 (SPSS Inc. Chicago USA) computer software. The arithmetic mean and standard deviation (X±SD) were calculated. The significance of the difference between group means was compared with Student's t test and One-Way ANOVA. The relationship between the parameters was evaluated with Pearson's correlation analysis and a p value >0.05 was considered statistically significant.

Results

The 134 patients included in the study consisted of 76 (56.7%) males and 58 (43.3%) females. Table 1 presents the distribution of the groups by gender, age and body mass index (BMI). There was no significant difference between Group 1 and 2 regarding mean age, BMI, smoking, and alcohol use.

Table 2 presents the comparison of the anxiety and depression scores of the groups. The anxiety and depression scores were lower in Group 2 and its subgroups. However, there was no statistically significant difference.

The number of cases diagnosed with depression according to the cutoff score in the HAD scale was 18 (35.29%) in Group 1 and 30 (36.14%) in Group 2. Evaluation of Group 2 subgroups revealed depression in 10 mild (37.03%), 9 moderate (37.50) and 11 severe (34.37%) cases. The number of cases diagnosed with anxiety according to the cutoff score was 19 (37.25%) in Group 1 and 27 (32.53%) in Group 2. Evaluation of the subgroups revealed anxiety in 9 mild (33.33%),

Table 1. *Demographic features of the groups*

	Group 1 (51) Mean±SD	Group 2 mild (N=27) Mean±SD	Group 2 moderate (N=24) Mean±SD	Group 3 severe (N=32) Mean±SD	p
Gender (M/F)	28/23	15/12	12/12	21/11	0.659
Age (years)	45.41±11.72	46.07±11.98	48.91±10.05	50.34±9.63	0.532
BMI (Kg/m^2)	30.11±4.84	30.88±4.03	31.50±3.59	33.25±6.53	0.498

SD, standard deviation.

Table 2. *Comparison of the anxiety and depression scores between groups*

	Group 1 (N=51) Mean±SD	Group 2 mild (N=27) Mean±SD	Group 2 moderate (N=24) Mean±SD	Group 3 severe (N=32) Mean±SD
Anxiety score	7.66±3.92	6.14±4.02 (p=0.416)	6.50±4.31 (p=0.669)	6.34±4.49 (p=0.492)
Depression score	7.43±3.71	6.66±3.29 (p=0.784)	6.54±2.43 (p=0.720)	6.53±3.67 (p=0.649)

8 moderate (33.33%) and 10 severe (%31.25) SAS cases. There was no statistically significant correlation between the anxiety and depression score and the AHI values of the control and patient groups (p>0.05) (Table 3).

Table 3. *Correlation analysis of SAS severity and anxiety and depression in the groups.*

	Depression r / p	Anxiety r / p
Group 1	0.031 / 0.829	-0.13 / 0.926
Group 2 Mild	0.306 / 0.120	0.312 / 0.113
Group 2 Moderate	0.019 / 0.931	0.149 / 0. 487
Group 3 Severe	0.230 / 0.205	-0.202 / 0.268

Discussion

We did not find a statistically significant correlation between the Apnea-hypopnea index and anxiety and depression scores in patients with symptoms of excessive daytime sleepiness, witnessed apnea and snoring in our study. Several studies have used various scales in various regions to evaluate the concurrence of depression and anxiety in patient groups. Most of these studies have been conducted with SAS patients with symptoms of excessive daytime sleepiness, witnessed apnea and snoring who had AHI values over 5 on polysomnography.

Guilleminault et al. have reported high depression scores in sleep apnea patients in their 1977 study[17]. Many later studies have found a positive correlation between the severity of SAS and the intensity of depression and anxiety. Schwartz et al. have found depression in 41% of their SAS patients and have started antidepressant treatment in 39%[18]. Another study evaluating the relationship between quality of life and depression has found worse quality of life in severe SAS patients and depression in half of this group[19]. Aloia et al. have reported that SAS patients suffer from a constant desire to sleep, depression and attention deficit due to the apnea, hypopnea and leg movements[20]. Similarly, Pillar et al. found a higher rate of anxiety and depression in female patients with severe SAS compared to those with mild SAS but they stated that this result was due more to sleeplessness than SAS. They also found that the SAS severity was not correlated with the presence of depression and anxiety in male SAS patients[11]. A study from our country reported interesting results: the lowest depression scores were found in SAS patients and there was a negative correlation between SAS severity and the depression score. The study showed that severe SAS was associated with a low anxiety score. Fidan et al. have associated these results with the effect on the cognitive functions of the patients[21].

There are also some studies stating no relationship between SAS and anxiety and depression as in our study. In other words, many studies have stated that the relationship between SAS and depression is not significant or present except for a few studies reporting their concurrence. Bliwise et al did not find a significant relationship between SAS and depression in their study on 336 subjects[22]. Cassel et al believe that the notion of a relationship between SAS and psychiatric disorders is due to misinterpretation. They have stated that the survey type used could affect the result[23]. Millman et al. found no relationship between the severity of the disorder and the depression score but 45% of SAS patients complained of depression[24]. They also found no relationship between SAS severity and psychological signs in their other study evaluating the relationship between SAS and psychological disorder severity[25]. Two recent studies have found no correlation between anxiety and depression severity in SAS patients[26,27].

There are only a few studies associating SAS and anxiety. Yue et al. have found high anxiety and depression scores in SAS and have suggested that this could be associated with the severely disturbed sleep[28]. Another study found that SAS can cause severe daytime sleepiness due to sleep deprivation, leading to decreased quality of life and increased anxiety and depression in future years[29]. Similarly, Platon and Sierra have reported a weak relationship between SAS and anxiety[30].

Several pathophysiological mechanisms have been suggested to explain the development of depression and anxiety in SAS patients with symptoms of apnea, snoring and excessive daytime sleepiness. The limbic system that contains important neuroanatomical structures such as the thalamus, hypothalamus, hippocampus, pineal gland, the pituitary and amygdala is an important region among the subcortical structures of the brain and is responsible for memory and changes in mood. The amygdala, one of the limbic structures, is a neuroanatomical structure with the most important

role in fear and anxiety development. The lateral hypothalamus, the dorsomedial vagus nucleus, nucleus ambiguus, the parabrachial nucleus, the ventral tegmental area, locus ceruleus, pedinculopontine nucleus, nucleus reticularis and the hypothalamic paraventricular nucleus that have neuronal connections with the amygdala are the main neuroanatomical structures with a role in the development of normal and pathological anxiety signs[31,32]. The depression and anxiety that can develop in the obesity-hypoventilation syndrome can be explained with similar mechanisms. The intermittent hypoxia and the oxygen desaturation that patients with sleep respiration disorders suffer can cause neuronal damage that can result in excessive daytime sleepiness. Subcortical white matter intensity increases indicating advanced damage in the brain parenchyma and especially the structures mentioned above have been found in patients with severe SAS. It is possible that this is correlated with neuropsychological and depression-related scores[20].

Many postmortem and neurological imaging studies also indicate prefrontal cortex and hippocampus atrophy and neuronal loss in patients suffering from anxiety and depression[33]. A model that associates the interrupted sleep and intermittent hypoxemia in SAS patients with prefrontal cortex dysfunction has recently been suggested. This model states that the prefrontal region becomes functional during sleep and is especially sensitive to sleep interruption and that hypoxemia creates a cellular environment that is not conducive for repair processes to take place. This model also postulates that the interruption of sleep and intermittent hypoxemia decrease the efficacy of the sleep-connected repair processes. These changes result in disturbed functional hemostasis in the central nervous system and a change in the survival times of the neurons and glial cells in some parts of the brain[17].

Our study has several limitations. We did not perform capnographic evaluation in Group 1 patients although they had excessive daytime sleepiness, witnessed apnea and snoring and a mean BMI of 30.11 kg/m^2. We therefore felt that the most probable diagnosis was the obesity-hypoventilation syndrome as they were symptomatic and the BMI value was high, even though the AHI index was ≤5. It would also have been more appropriate to use patients with no symptoms and an AHI index ≤5 with PSG in the control group.

In conclusion, we feel studies on larger patient populations that also include non-symptomatic healthy individuals and that take into account all additional risk factors should be conducted although we did not find a statistically significant difference between the patient groups' anxiety and depression values.

References

1. Jay S. Balachandran, Juan Fernando Masa, Babak Mokhlesi. Obesity Hypoventilation Syndrome Epidemiology and Diagnosis. Sleep Med Clin 2014 Sep;9(3):341–7.
2. Köktürk, O. Uykuda solunum bozuklukları. Tarihçe, Tanımlar, Hastalık Spektrumu ve Boyutu. Tüberküloz ve Toraks Dergisi 1998;46:187–92.
3. Cao M, Cardell CY, Willes L, Mendoza J, Benjafield A, Kushida C. A Novel Adaptive Servoventilation (ASVAuto) forthe Treatment of Central Sleep Apnea Associated with Chronic Use of Opioids. J Clin Sleep Med 2014 Aug 15;10(8):855–61.
4. Gupta R, Sindhwani G, Goyal S, Rawat J, Kesarwani V Idiopathic central sleep apnoea: an Indian case with polysomnographic findings. Indian J Chest Dis Allied Sci 2014 Jan-Mar;56(1):41–4.
5. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S, Theoccurrence of sleep disordered breathing among middle-aged adults. N Engl J Med 1993;328:1230–5.
6. Grayburn RL, Kaka Y, Tang WH. Contemporary insights and novel treatment approaches to central sleep apnea syndrome in heart failure. Curr Treat Options Cardiovasc Med 2014 Jul;16(7):322.
7. Sullivan CE, Issa FG. Obstructive sleep apnea. Clin Chest Med 1985;6:633–51.
8. Saunam T, Jehkonen M. Depression and anxiety in obstructive sleep apnea syndrome: a review. Acta Neurol Scand 2007;116:277–88.
9. Harris M, Glozier N, Ratnavadivel R, Grunstein RR. Obstructive sleep apnea and depreesion. Sleep Med Rev 2009;13:437–44.
10. Baran AS, Richert AC. Obstructive sleep apnea and depression. CNS Spectr 2003;8:128–1 34.
11. Pillar G, Lavie P. Psychiatric symptoms in sleep apnea syndrome: effects of gender and respiratory disturbance index. Chest 1998;114:697–703.
12. Andrews JG, Oei TPS. Theroles of depression and anxiety in theunder standing and treatment of obstructive sleep apnea syndrome. Clin Psychol Rev 2004;24:1031–49.
13. Ogeil RP, Phillips JG, Rajaratnam SM, Broadbear JH. Risky drug use and effects on sleep quality and daytime sleepiness. Hum Psychopharmacol 2015 May 25.
14. Zigmond AS, Snaith RP. Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983;67:361–70.
15. Aydemir Ö, Güvenir T, Küey L. Validity and realibility of Turkish version of Hospital Anxiety and Depression Scale. Turkish Journal of Psychiatry 1997;8:280–7.

16. Kothare SV, Rosen CL, Lloyd RM, Paruthi S, Thomas SM, Troester MM, Carden KA. Quality measures for the care of pediatric patients with obstructive sleep apnea. J Clin Sleep Med 2015 Mar 15;11(3):385–404.
17. Guilleminault C, Dement WC. Sleep apnea syndrome due to upper airway obstructin. Arc Intern Med 1977;137:296–30023
18. Schwartz DJ, Kohler WC, Karatinos G. Symptoms of depression in individuals with obstructive sleep apnea maybe amenable to treatment with continuous positive airway pressure. Chest 2005;128:1304–9.
19. Akashiba T, Kawahara S, T. Akahoshi, et al. Relationship between quality of life and mood or depression in patients with severe obstructive sleep apnea syndrome. Chest 2002;122:861–5.
20. Aloia MS, Arnedt JT, Davis JD, Riggs RL, Byrd D. Neuropsychological sequelae of obstructive sleep apnea hypopnea syndrome: a critical review. J Int Neuropsychol Soc 2004;10:772–85.
21. Fidan F, Ünlü M, Sezer M ve ark. Obstruktif uyku apne sendromu ile anksiyete ve depresyon arasındaki ilişki. Toraks Dergisi 2006;7 125–9.
22. Bliwise DL, Yesavage JA, Sink J, et al. Depressive symptoms and impaired respiration in sleep. J Consult Clin Psychol 1986;54 734–5.
23. Cassel W. Sleep apnea and personality cognitive effects and daytime sleepiness –psycho-social sequelae of sleep disordered breathing. Sleep 1993;16:856–8.
24. Millman RP, Fogel BS, McNamara ME, Carlisle CC. Depression as a manifestation of obstructive sleep apnea: reversal with nasal continuous positive airway pressure. J Clin Psychiatry 1989;50:348–51.
25. Macey PM, Woo MA, Kumar R, Cross RL, Harper RM. Relationship between obstructive sleep apnea severity and sleep, depression and anxiet ysymptoms in newly-diagnosed patients. PLoS One 2010 Apr 16;5(4):e10211.
26. Asghari A, Mohammadi F, Kamrava SK, Tavakoli S, Farhadi M. Severity of depression and anxiety in obstructive sleep apnea syndrome. Eur Arch Otorhinolaryngol 2012;269:2549–53.
27. Rey De Castro J, Rosales-Mayor E. Sleep and Breathing 2013;17(2):615–20.
28. Yue W, HaoW, Liu P, et al. A case-control study on psycological symptoms in sleep apnea-hypopnea syndrome. Can J Psychiatry 2003;48:318–23.
29. Şahbaz S, İtil O, İnönü H, Öztura İ, Yemez B, Baklan B, Etikan İ, Seyfikli Z. Obstrüktif Uyku Apne Sendromlu Olgularda Yaşam Kalitesi, Anksiyete ve Depresyon Sıklığı. Türk Toraks Dergisi 2008;9(4):141–5.
30. Ramos Platon MJ, Espinar Sierra J. Changes in psychopathological symptoms in sleep apnea patients after treatment with nasal continuous positive airway pressure. Int J Neurosci 1992;62:173–95.
31. Heilbronner SR, Haber SN. Frontal cortical and subcortical projections provide a basis for segmenting the cingulumbundle: implications for neuroimaging and psychiatric disorders. J Neurosci 2014 Jul 23;34(30):10041–54.
32. Beebe DW, Gozal D. Obstructive sleep apnea and the prefrontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction today time cognitive and behavioral deficits. J Sleep Res 2002;11:1–16.
33. Gorman JM. Comorbid depression and anxiety spectrum disorders. Depress Anxiety 1996;4:160–8.

KAFKAS TIP BİLİMLERİ DERGİSİ
Kafkas Journal of Medical Sciences

ARAŞTIRMA YAZISI / ORIGINAL ARTICLE

Kafkas J Med Sci 2016; 6(2):94–97 • doi: 10.5505/kjms.2016.30301

Acute Gastroenteritis Agents Among 0–5 Years-Old Turkish Children

0–5 Yaş Arası Türk Çocuklarda Akut Gastroenterit Etkenleri

Çiğdem Eda Balkan[1], Murat Karameşe[2], Demet Çelebi[3], Sabiha Aydoğdu[1], Zeki Çalık[2], Yunus Yılmaz[4]

[1]Atatürk University Faculty of Medicine, Department of Microbiology, Erzurum, Turkey; [2]Kafkas University Faculty of Medicine, Department of Microbiology, Kars, Turkey; [3]Atatürk University Veterinary Faculty, Department of Microbiology, Erzurum, Turkey; [4]Kafkas University Faculty of Medicine, Department of Pediatrics, Kars, Turkey

ABSTRACT

AIM: *Acute gastroenteritis outbreaks are the common health problem throughout the world especially in children. Every year, thousands of children die due to the diarrhea caused by bacteria, parasites and viral agents. In this study, we aimed to evaluate the rates of diarrheal agents in 0–5 years-old children's stool samples in terms of seasons.*

METHODS: *In this study, 216 stool samples were taken from 0–5 year-old children. These samples were examined with some tests for Rotaviruses, Adenoviruses, Salmonella, Shigella, Entamoeba, Giardia, Clostridium difficile Toxin A and Toxin B. Clostridium difficile toxins were detected by using ELISA (CerTest, Biotec, Spain). Immunochromatographic tests were used to detect the Rotavirus, Adenovirus, Giardia and Entamoeba antigens. Selenite-F broth and MacConkey Agar mediums were used to find lactose negative colonies for Salmonella and Shigella in stool samples. Confirmation was performed by IMVIC tests.*

RESULTS: *The obtained results showed that the isolated agents were viral (40.74%), bacterial (24.98%) and parasitic (20.82%) respectively. Some agents showed a peak in the cold seasons such as Rotavirus (November, December, January and February). On the other hand, some outbreaks that came out by Salmonella and Shigella were seen most frequent in hot seasons (June, July, and August).*

CONCLUSION: *According to the obtained data, diarrheal infections were mostly identified in February, March and April. Rotavirus infections are more frequent in winter and spring. In conclusion; we believe that analysis of viral antigens, bacteria and the parasites as diarrheal agents in stool sample is important in 0–5 years-old infants to prevent hospitalizations and unnecessary drug use.*

Key words: *children; diarrhea; gastroenteritis; rotavirus; salmonella; giardia*

ÖZET

AMAÇ: *Akut gastroenterit salgınları bütün dünyada özellikle çocuklar için ortak bir sağlık problemidir. Her yıl binlerce çocuk bakteri, parazit ve viral etkenlerin sebep olduğu diyare sonucu hayatını kaybetmektedir. Bu çalışmada, 5 yaş altı çocukların dışkı örneklerinde mevsimlere göre diyare etkenlerinin oranlarının bulunması hedeflenmiştir.*

YÖNTEM: *Bu çalışmada, 0–5 yaş arası çocuklardan 216 gaita örneği toplanmıştır. Bu örnekler; Rotavirus, Adenovirus, Salmonella, Shigella, Entamoeba, Giardia, Clostridium difficile Toksin A ve Toksin B testlerine tabi tutulmuştur. Clostridium difficile toksinleri ELISA metodu ile tespit edilmiştir. Rotavirus, Adenovirus, Giardia and Entamoeba ajanlarına ait antijenlerin tespiti için İmmunkromatografik testler kullanılmıştır. Dışkı örneklerinde Salmonella ve Shigella şüpheli laktoz negatif kolonilerin tespiti için MacConkey Agar ve Selenit-F buyyon kullanılmıştır. Doğrulama için IMVIC testleri yapılmıştır.*

BULGULAR: *Elde edilen sonuçlar, izole edilen ajanların sırasıyla viral (%40,74), bakteriyel (%24,98) ve parazitik (%20,82) ajanlar olduğunu göstermiştir. Rotavirus gibi bazı ajanlar en çok kış aylarında (Kasım, Aralık, Ocak ve Şubat) en yüksek seviyede tespit edilmiştir. Diğer taraftan, Salmonella ve Shigella gibi bazı bakterilerin sebep olduğu salgınlar ise yaz aylarında (Haziran, Temmuz ve Ağustos) daha sık görülmüştür.*

SONUÇ: *Elde edilen verilere göre, diyare enfeksiyonları genellikle Şubat, Mart ve Nisan aylarında görülmektedir. Kış ve ilkbahar aylarında en sık görülen ajan Rotavirus'tur. Sonuç olarak, hastaneye yatış ve gereksiz ilaç kullanımının önüne geçilebilmesi için 0–5 yaş arası çocukların dışkı örneklerinde viral, bakteriyel ve parazitik ajanların diyare etkeni olarak araştırılmasının önemli olduğuna inanmaktayız.*

Anahtar kelimeler: *çocuk; diyare; gastroenterit; rotavirus; salmonella; giardia*

Yard. Doç. Dr. Murat Karameşe, Kafkas University Faculty of Medicine, Department of Microbiology, Kars, Türkiye, Tel. 0554 863 88 53
Email. murat_karamese@hotmail.com
Geliş Tarihi: 15.02.2015 • Kabul Tarihi: 27.07.2015

Introduction

Acute gastroenteritis is one of the most common health problems all over the world[1]. Acute diarrheal infections are also a common disease in children. Estimated incidence rates in developing countries are between 3.5 and 7.0 episodes per child per year during the first 2 years of their life while they are between 2 and 5 episodes per child per year for the first 5 years[2]. Pediatric diarrhea is an important disease and it may lead an emotional trauma for the child and their parents[3].

More than 700 million cases are annually estimated to occur in 0-5 year old children, resulting in few deaths in developed countries. On the other hand, this rate is about 2 million deaths in developing countries. A group of viral, bacterial, and parasitic pathogens cause acute enteric symptoms including nausea, vomiting, abdominal pain, fever, and acute diarrhea. Until the early of 1970s, most viral agents causing gastroenteritis in humans were largely unknown. However, studies using electron microscopy of intestinal contents has been resulted in the discovery of numerous viral enteropathogens such as Rotaviruses, 'enteric' Adenoviruses or other viruses which may cause gastroenteritis[1]. Among them, viral infection is the most common cause, followed by bacterial and parasitic infections[4]. *Giardia lamblia* and *Entamoeba histolytica* are the major parasitic agents for diarrhea[5].

Salmonella spp. and *Shigella spp*. are the bacterial agents which are mostly isolated from stool samples of diarrheal patients, especially in rural areas from developing countries[6,7]. Additionally, *Clostridium difficile*, another bacterial diarrheal agent, is a big threat for children in both community and hospitals[8,9]. *Clostridium difficile* infection has more recently been implicated as dramatically increased prevalent diarrheal pathogen in children[10-12]. Moreover, evidence suggests that a large proportion of pediatric *Clostridium difficile* cases are community-acquired infections[13,14]. In this study, our aim was to detect the prevalence of these gastroenteritis agents in 0–5 year-old children.

Materials and Methods

216 diarrhea-diagnosed children who were admitted to consecutively to the hospital were included to this study. Children who had been treated with antibiotics before the onset of diarrhea were also included. Samples were collected into a sterile sample cup and were transported the same day to hospital laboratories, where they were stored at 4–8°C until they were processed. Specimens for bacteriological culture were inoculated into appropriate media immediately.

Stool specimens from each child with severe gastroenteritis were tested for *Clostridium difficile* by ELISA method to detect Toxin A an Toxin B. *Rotavirus* and *Adenovirus* Card Tests (CerTest, Biotec, Spain), a qualitative immunochromatographic assay were used to detect *Rotavirus* and *Adenovirus* antigens. This immunochromatographic tests were also used for detecting *Giardia* and *Entamoeba* antigens. The stool samples were examined under the microscope after the card test in terms of *Giardia* and *Entamoeba*. Selenite-F broth and MacConkey Agar were used to detect lactose negative colonies for *Salmonella* and *Shigella*. Finally, we performed IMVIC tests to confirm the possible positive samples. "I" is for indole test; "M" is for methyl red test; "V" is for Voges-Proskauer test, and "C" is for citrate test. These tests were performed in the Microbiology Laboratory by using appropriate mediums.

Results

The total number of children was 216 who applied to the hospital in 1 year with the complaints of gastroenteritis. *Rotaviruses* were the most isolated pathogen. According to the seasonal data, the peak incidence occurred in February (n=27) and August (n=28). Additionally, Adenoviruses were detected in 29 of the total samples (13.42%) and *Clostridium difficile* strains isolated from 30 of 216 (13.88%). *Giardia* and *Entamoeba* were identified in 19 (8.79%) and 26 (12.03%) respectively (Table 1).

Some agents are mostly isolated during winter months (December 14.77%, January 13.76%, February 25%) such as *Rotavirus*. Five Adenovirus-Rotavirus mix infections were detected (2 cases in February, 1 case in March, and 3 cases in April). On the other hand, some outbreaks that came out by Salmonella (June 21.42%, July 28.57%, August 35.71%) and Shigella (June 20%, July 20%, August 30%) were seen most frequently in hot seasons (Table 1).

Discussion

Acute gastroenteritis in children continues to be a significant health problem throughout the world. Millions of cases of acute diarrheal disease are estimated to occur annually just in 0–5 year old children[15].

Table 1. *The distribution of isolated diarrheal agents*

	January	February	March	April	May	June	July	August	September	October	November	December	**TOTAL**
Agents	n	n	n	n	n	n	n	n	n	n	n	n	**n**
Giardia spp.	1	0	2	2	1	3	3	4	0	1	2	0	**19**
Entamoeba spp.	0	1	1	3	2	4	5	6	2	0	1	1	**26**
C.difficile	2	2	0	3	2	3	4	7	6	1	3	0	**30**
Salmonella spp.	0	0	0	0	1	3	4	5	1	0	0	0	**14**
Shigella spp.	1	0	0	0	1	2	2	3	0	1	0	0	**10**
Adenovirus	0	2	2	3	2	4	2	2	3	3	2	4	**29**
Rotavirus	12	22	8	4	3	0	0	1	7	8	10	13	**88**
Total number	**16**	**27**	**13**	**15**	**12**	**19**	**20**	**28**	**16**	**14**	**18**	**18**	**216**

African children accounted for the biggest part (42%) of total 10.6 million deaths among 0–5 years-old children in the world[16].

Some studies state that enterotoxigenic *Rotaviruses* predominates in developing areas, cytotoxigenic *Clostridium difficile* are detected with increasing frequency in developed areas; and *Shigella, Salmonella* and *Giardia lamblia* are found whole the world[17]. In Netherlands, viral agents (especially *Rotavirus*) were isolated in the rate of 82% from stool samples while bacterial and parasitic agents were isolated in the rates of 32% and 10% respectively[18]. Our study is consistent with current literature. Rotaviruses were isolated in 40.74% (*Adenovirus* 13.42%, 5 cases are mixed infections) while these rates were 24.98% and 20.82% for bacteria and parasites. Most of the studies have mentioned that mixed infections were less frequent than mono-infections. A study that performed in Spain showed that the most frequent mixed infections were *Rotavirus-Astrovirus* (13 cases) and *Rotavirus-Adenovirus* (10 cases in 820 stool samples) infections[19].

This study found that the highest proportion of dual infections was identified in February, March and April months and seasonal occurrence of some mono-infections such as Rotavirus is more frequent in winter and spring. At the same study that performed in Spain, most of the cases with mixed infection occurred in autumn (26 cases in autumn, 5 in winter, 6 in spring, 2 in summer), and no seasonal differences were detected between the different co-infections[19]. As seen in the present study, *Rotavirus* is the most common isolated viral agent (40.74%) for acute childhood diarrhea. These findings are nearly same with another study performed in İzmir (*Rotavirus,* 39.8% in 920 children)[20]. On the other hand, *Clostridium difficile* infections (CDI) rate were detected as 13.88% in our study. Some researchers have found the incidence of CDI in the pediatric population increased in US hospitals[21].

Entamoeba histolytica, *Giardia lamblia* and *Cryptosporidium parvum* are considered to be the most important diarrheal agents[22-26]. We tried to identify *Entamoeba* and *Giardia* infections in our study. *Giardia lamblia* infections are very common throughout the world and are considered one of the main non-viral causes of diarrhea in industrialized countries[26]. For many years, microscopic examination of stool samples has been considered as "gold standard" for diagnosis of *Entamoeba histolytica*, *Giardia lamblia* and some parasites. Recently, more specific and sensitive alternative methods (PCR, ELISA) have been introduced for all these parasitic infections. We have detected these parasites with microscopic examination and according to the obtained data, *Giardia spp.* and *Entamoeba spp*. were detected in the rate of 8.79% and 12.03% of all samples respectively. These rates show us that parasitic infections are incontrovertible cause of acute diarrhea.

As a conclusion, we believe that analysis of viral antigens, bacteria and the parasites as diarrheal agents in stool sample is important in 0–5 years-old infants to prevent hospitalizations and unnecessary drug use.

References

1. Mahy BW, Van-Regenmortel M, Walker P, et al. Encyclopedia of Virology (Third Edition), Enteric Viruses, Elsevier Ltd, Oxford, London, 2008;116.
2. Black RE. Epidemiology of diarrheal disease: implications for control by vaccines. Vaccine 1993;11(2):100–6.
3. Graeme LB, Eric U, Kerrie BS, et al. Bishop Etiology of Acute Gastroenteritis in Hospitalized Children in Melbourne, Australia, from April 1980 to March 1993. J Clin Microbiol 1998;36(1):133–8.
4. Jeong WH, Su GM, Young HL. Survey of Intestinal Protozoan Infections among Gastroenteritis Patients during a 3-Year Period (2004–2006) in Gyeonggi-do. South Korea Korean J Parasitol 2009;47(3):303–5.
5. Aranda-Michel J, Giannella RA. Acute diarrhea: a practical review. Am J Med 1999;106(6):670–6.
6. Okeke IN, Ojo O, Lamikanra A, et al. Etiology of acute diarrhea in adults in southwestern Nigeria. J Clin Microbiol 2003;41(10):4525–30.
7. Vargas M, Gascon J, Casals C, et al. Etiology of diarrhea in children less than five years of age in Ifakara, Tanzania. Am J Trop Med Hyg 2004;70(5):536–9.
8. Langley JM, LeBlanc JC, Hanakowski M, et al. The role of Clostridium difficile and viruses as causes of nosocomial diarrhea in children. Infect Control Hosp Epidemiol 2002;23(11):660–4.
9. Klein EJ, Boster DR, Stapp JR, et al. Diarrhea etiology in a children's hospital emergency department: a prospective cohort study. Clin Infect Dis 2006;43(7):807–13.
10. Denno DM, Shaikh N, Stapp JR, et al. Diarrhea etiology in a pediatric emergency department: a case control study. Clin Infect Dis 2012;55(7):897–904.
11. Kim J, Smathers SA, Prasad P, et al. Epidemiological features of Clostridium difficile-associated disease among inpatients in the United States, 2001–2006. Pediatrics 2008;122(6):1266–70.
12. Zilberberg MD, Shorr AF, Kollef MH. Increase in Clostridium difficile-related hospitalizations among infants in the United States, 2000–2005. Pediatr Infect Dis J 2008;27(12):1111–3.
13. Toltzis P, Kim J, Dul M, et al. Presence of the epidemic North American pulsed field type 1 Clostridium difficile strain in hospitalized children. J Pediatr 2009;154(4):607–8.
14. McFarland LV, Brandmarker SA, Guandaline S. Pediatric Clostridium difficile: a phantom menace or clinical reality? J Pediatr Gastroenterol Nutr 2000;31(3):220–31.
15. Snyder JD, Merson MH. The Magnitude of the Global Problem of Acute Diarrheal Disease: A Review of Active Surveillance Data. Bull World Health Org 1982;60(4):605–13.
16. Bryce J, Boschi PC, Shibuya K, et al. WHO Estimates of the Causes of Death in Children? The Child Health Epidemiology Reference Group. Lancet 2005;365(9465):1147–52.
17. Guerrant R, Hughes J, Lima N, et al. Diarrhea in developed and developing countries: magnitude, special settings, and etiologies. Rev Infect Dis 1990;1:41–50.
18. Friesema IH, de-Boer RF, Duizer E, et al. Etiology of acute gastroenteritis in children requiring hospitalization in the Netherlands. Eur J Clin Microbiol Infect Dis 2012;31(4):405–15.
19. Roman E, Wilhelmi I, Colomina J, et al. Fauquier Acute viral gastroenteritis: proportion and clinical relevance of multiple infections in Spanish children. J Med Microbiol 2003;52(5):435–40.
20. Kurugol Z, Geylani S, Karaca Y, et al. The Rotavirus gastroenteritis among children under five years of age in İzmir, Turkey. Turkish Journal of Pediatrics 2003;45(4):290–4.
21. Zilberberg MD, Tillotson GS, Mcdonald CL. Clostridium difficile infections among Hospitalized Children, United States. Emerg Infect Dis 2010;16(4):604–9.
22. Amin OM. Seasonal prevelance of intestinal parasites in the United States during 2000. Am J Trop Med Hyg 2002;66(6):799–803.
23. Current, WL, Garcia S. Cryptosporidiosis. Clin Microbiol Rev 1991;4(3):325–58.
24. De-Wit MA, Koopmans MP, Kortbeek LM, et al. Etiology of gastroenteritis in sentinel general practices in the Netherlands. Clin Infect Dis 2001;33(3):280–8.
25. Nichols GL. Food-borne protozoa. Br Med Bull 2000;56(1):209–35.
26. Ece G, Samlioglu P, Ulker T, Kose S, Ersan G. Rotavirus and adenovirus prevalence at Tepecik education and research hospital (Turkey). Infez Med 2012 Jun;20(2):100–4.

KAFKAS TIP BİLİMLERİ DERGİSİ
Kafkas Journal of Medical Sciences

ARAŞTIRMA YAZISI / ORIGINAL ARTICLE

Kafkas J Med Sci 2016; 6(2):98–101 • doi: 10.5505/kjms.2016.53215

İkinci Basamak Sağlık Kurumuna Müracaat Eden Kuduz Şüpheli Temas Vakalarının Değerlendirilmesi*

*The Evaluation of Rabies-Suspicious Cases Admitted to Second Step Health Institution***

Emsal Aydın[1], Yunus Yılmaz[2], Sergülen Aydın[3], Hatice Özlece[4], Ayten Kadanalı[1], Esragül Akıncı[1], Hürrem Bodur[1]

[1]Kafkas Üniversitesi Tıp Fakültesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, Kars; [2]Kafkas Üniversitesi Tıp Fakültesi, Çocuk Sağlığı ve Hastalıkları Anabilim Dalı, Kars; [3]Kafkas Üniversitesi Tıp Fakültesi, Aile Hekimliği Anabilim Dalı, Kars; [4]Kafkas Üniversitesi Tıp Fakültesi, Nöroloji Anabilim Dalı, Kars

ABSTRACT

AIM: *In this study, our aim was to evaluate the general characteristics and prophylaxis of rabies cases, admitted to the emergency department of the Kars State Hospital.*

METHODS: *Descriptive research data were obtained from records of emergency department of Kars State Hospital. A total of 1070 evaluation forms of patients were obtained between June 2011 and May 2014. The evaluation forms include some information such as; demographic characteristics of patients, contact type, animals and prophylactic application state. Data were analyzed by using SPSS 20.0 package program.*

RESULTS: *Seventy-five percent (75%) of rabies-suspicious cases were male and 28.6% of them were in the 10-19 age group. Additionally, more than half of cases (51.0%) live in rural areas. 84.7% of contacted-animals were dogs and 3.0% were wild animals. Only vaccination was performed of 72.8% of cases, while both vaccination and immunoglobulin were performed to 27.2%. Single dose was performed to 28.1% of total cases and five doses were performed to 22.5% of total cases, when the study was evaluated in terms of vaccine dose.*

CONCLUSION: *In this study, we wanted to point out that rabies prophylaxis was not applied in our region in accordance with the rabies prevention and control guidelines. Therefore, Board of State Hıfzıssıhha should meet and make the necessary decisions about the stray animals. Health personnel should take an in-service training about rabies prophylaxis.*

Key words: *rabies-suspicious cases; prophylaxis; immunoglobulin*

ÖZET

AMAÇ: *Kars Devlet Hastanesi acil servisine kuduz şüpheli temas nedeniyle başvuran vakaların genel özellikleri ve profilaksi durumlarının değerlendirilmesi amaçlanmıştır.*

YÖNTEM: *Tanımlayıcı tipte yapılan araştırmanın verileri Kars Devlet Hastanesi acil servis kayıtlarından elde edilmiştir. Çalışmada, Mayıs 2011 ve Haziran 2014 tarihleri arasında, acil servise kuduz şüpheli temas ile başvuran toplam 1070 hasta formu değerlendirmeye alınmıştır. Değerlendirme formları, hastaların demografik özellikleri, temas tipi, temasta bulunan hayvan ve profilaksi uygulanma durumu gibi bilgileri içermekte idi. Veriler SPSS 20.0 paket programında analiz edilmiştir.*

BULGULAR: *Kuduz şüpheli temas vakalarının %75,0'i erkek, %28,6'sı 10–19 yaş grubundandır. Ayrıca vakaların yarısından fazlası (%51,0) kırda yaşamaktadır. Temas eden hayvanların %84,7'si köpek iken, %3,0'ü yabani hayvanlar oluşturmuştur. Vakaların %72,8'ine sadece aşı, %27,2'ine ise aşı ve immünglobülin yapılmıştır. Doz açısından incelendiğinde vakaların %28,1'ine tek doz, %22,5'ine 5 doz aşı yapılmıştır.*

SONUÇ: *Bu çalışmada, bölgemizde yapılan kuduz profilaksisinin kuduz korunma ve kontrol yönergesine uygun yapılmadığı tespit edilmiştir. Bu nedenle, başıboş hayvanlar ile ilgili il Hıfzıssıhha Kurulu toplanmalı ve gerekli kararlar alınmalıdır. Hizmet sunan sağlık personeli kuduz ve profilaksi konusunda hizmet içi eğitime alınmalıdır.*

Anahtar kelimeler: *kuduz şüpheli temas; profilaksi; immünglobülin*

Giriş

Kuduz günümüzde önemli bir halk sağlığı sorunu olarak devam etmektedir. Kuduz insanlar ve hayvanlar için öldürücü ensefalit oluşturan zoonotik bir viral hastalıktır[1]. Kuduz hastalığı çoğunlukla tükürük bezlerinde bulunan ve salyadan yaraya bulaşan kuduz virüsünün meydana getirdiği viral bir ensefalittir[2]. Virüs insana en fazla hayvan ısırması, tırmalaması, yara ve mukozalarla temas sonucu bulaşmaktadır[1].

**Bu çalışma EACID (The 6th Eurasia Congress of Infectious Diseases) 24–27 Eylül 2014 Belgrad, Sırbistan'da poster olarak sunulmuştur.*

***This study was presented as a poster in EACID (The 6th Eurasia Congress of Infectious Diseases) 24–27 September 2014 Belgrad, Serbia.*

Yard. Doç. Dr. Sergülen Aydın, Kafkas Üniversitesi Tıp Fakültesi, Kars, Türkiye, Tel. 0505 586 04 59 Email. dr.sergulenaydin@hotmail.com
Geliş Tarihi: 29.09.2014 • Kabul Tarihi: 16.05.2015

Dünya Sağlık Örgütü verilerine göre her yıl yaklaşık 55 bin insan köpek kaynaklı kuduz nedeniyle hayatını kaybetmektedir[3]. Ülkemizde 1987 yılına kadar kuduza bağlı ölümler yüksek olmasına rağmen, modern aşıların kullanılmaya başlanması ve alınan önlemler ile ölümler çok azalmış hatta bazı yıllarda rastlanmamıştır[4]. Türkiye'de yapılan bir çalışmada 1992–2007 yılları arasında 39 kuduz vakası olduğu saptanmıştır. Bu vakaların 29'unun köpek kaynaklı, kalan vakaların ise yaban hayvanları tarafından meydana getirildiği gösterilmiştir[5].

Türkiye'de Sağlık Bakanlığına yaklaşık 175 bin kuduz şüpheli temas vakası bildirilmekte ve 1–2 kuduz vakası ortaya çıkmaktadır[6]. Kuduz hastalığı mutlak öldürücü olduğundan, korunma ve hastalık etkeniyle karşılaşmayı takiben enfeksiyonun durdurulması önem taşımaktadır. Bu nedenle kuduz şüpheli temas durumlarında profilaksi uygulanması önemlidir[2].

Bu çalışmada, Kars Devlet Hastanesi Acil servisine kuduz şüpheli temas nedeniyle başvuran vakaların genel özellikleri ve profilaksi durumlarının değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem

Tanımlayıcı tipte yapılan araştırmanın verileri Kars Devlet Hastanesi acil servisi kuduz şüpheli temas vaka inceleme formlarından (Form 1) elde edilmiştir. Form vakaların adı, soyadı, yaşı, cinsiyeti, şüpheli temas tipi, temasa sebep olan hayvan ve mevcut durumu, kişinin daha önceki şüpheli teması ve profilaksi uygulanma durumu, uygulanan tedavi şeması gibi bilgileri içermektedir.

Araştırmada mayıs 2011 ile haziran 2014 dönemlerine ait 1093 formdan, bilgileri eksik olan 23 form değerlendirme dışı bırakılarak toplam 1070 form değerlendirmeye alınmıştır.

Çalışmanın veriler SPSS 20.0 paket programında analiz edilmiştir. Analizlerde tanımlayıcı ölçütlerden frekans ve yüzde kullanılmıştır.

Bulgular

Kuduz şüpheli temas vakalarının %75,0'i erkek, %28,6'sı 10–19 yaş grubundan ve vakaların yarısından fazlası (%51,0) kırda yaşamaktadır (Tablo 1).

Araştırmada vakaların %84,7'si köpekler tarafından ısırılmış iken, %3,0'ü yabani hayvanlar (20 fare, 2 böcek) ile temasa maruz kalmıştır. Hayvanların %56,3'ü sahipli, %11,6'sı ise aşılıdır (Tablo 2).

Tablo 3'te kuduz riskli temas vakalarının tedavi şeması ve aşı dozları gösterilmiştir. Vakaların %1,1'ine sadece immünglobülin, %26,1'ine ise aşı ve immünglobülin yapılmıştır. Doz açısından incelendiğinde vakaların %28,1'ine tek doz, %22,5'ine 5 doz aşı yapılmıştır.

Tablo 1. *Kuduz şüpheli teması olan kişilerin demografik özellikleri (Kars, 2011–2014)*

Demografik özellikler		Sayı	%
Cinsiyet	Erkek	803	75,0
	Kadın	267	25,0
Yaş grupları	0–5	42	3,9
	6–15	337	31,5
	16–30	293	27,4
	31–45	193	18,0
	46 ve üzeri	205	19,2
Yaşadığı yer	Kır	546	51,0
	Kent	486	45,4
	Eksik veri	38	3,6
Toplam		1070	100,0

Tablo 2. *Kuduz şüpheli temas eden hayvanların özellikleri (Kars, 2011–2014)*

Temas eden hayvanın özellikleri		Sayı	%
Cinsi	Köpek	906	84,7
	Kedi	88	8,2
	Sığır	27	2,5
	Diğer evcil*	12	1,1
	Yaban hayvanı	32	3,0
	Eksik veri	5	0,5
Sahiplilik durumu	Sahipli	602	56,3
	Sahipsiz	458	42,8
	Eksik veri	10	0,9
Aşılanma durumu	Aşılı	124	11,6
	Aşısız	464	43,4
	Bilinmiyor	475	44,4
	Eksik veri	7	0,7
Toplam		1070	100,0

*Diğer evcil: at, eşek, koyun

Tablo 3. *Kuduz şüpheli temas vakalarında hikâye, tedavi şeması ve aşı dozu (Kars, 2011–2014)*

Tedavi ve aşı dozu		Sayı	%
Tedavi şeması	Aşı	779	72,8
	Aşı + Ig*	291	27,2
Yapılan aşı dozu	1	308	28,8
	2	160	15,0
	3	242	22,6
	4	107	10.0
	5	241	22,5
Toplam		1070	100,0

*İmmünglobülin

Tartışma

Bu çalışmada, Kars Devlet Hastanesi Acil servisine kuduz şüpheli temas nedeniyle başvuran vakaların genel özellikleri ve proflaksi durumları değerlendirildi.

Çalışmamızda kuduz şüpheli temas vakalarının %75,0'i erkektir. Ülkemizde yapılan benzer çalışmalarda erkeklerin oranı %67,0–78,6 arasında değişmektedir[7-12]. Gerek bizim çalışmamızda ve gerekse diğer çalışmalarda erkek oranın yüksek olmasının muhtemel nedeni; erkeklerin iş, oyun ve diğer aktivitelerinde açık alanı daha fazla kullanması, köpeklerle daha fazla temas etmesine ve bunun sonucunda ısırılma riskinin daha fazla olabileceği düşünülmektedir.

Araştırmamızda kuduz şüpheli temas vakalarının %35,1'ini 6–15 yaş grubu oluşturmaktadır. Gerek Dünya Sağlık Örgütü'nün verilerinde[13] ve gerekse ülkemizde yapılan çalışmalarda kuduz şüpheli temas vakalarının en fazla görüldüğü yaş grubu 6–15 yaş grubudur (%28,4–43,7)[7,9-11]. Bu yaş grubunda kuduz şüpheli temas vakalarının daha fazla olmasının muhtemel nedeni, bu vakaların oyun, spor gibi aktivitelerini sokak, cadde ve oyun alanı gibi açık alanlarda gerçekleştirmesi olabilir.

Bu çalışmada kuduz şüpheli temas vakalarının %51,0'i kırsal alanda ikamet etmektedir. Ülkemizde yürütülmüş diğer çalışmalarda riskli temasta bulunan vakaların %29,3–47,0 arasında kırsalda ikamet ettikleri tespit edilmiştir[7-11]. Literatürün aksine, araştırmamızda kırsal alanda yaşayan kişilerin daha fazla olmasının muhtemel nedeninin, merkeze bağlı köy sayısının fazla olmasından kaynaklanabileceği düşünülmektedir.

Çalışmamızda kuduz şüpheli temas vakalarının %84,7'si köpek ısırması ile meydana gelmiştir. Gerek ülkemizde (%61,3–77,4) ve gerekse farklı ülkelerde yapılan çalışmalarda (%66,7–86,0) kuduz şüpheli temas vakalarının çoğunluğu köpekler tarafından meydana getirilmiştir[7-12,14,15]. Diğer yandan bu çalışmada köpeklerin yarıdan fazlasının sahiplidir (%56,3). Ülkemizde özellikle Güneydoğu Anadolu Bölgesinde yapılan çalışmalarda köpeklerin sahiplilik düzeyi %68,7–75,4 arasında iken[7,8,11], kent merkezinde yapılan çalışmalarda sahiplilik düzeyi %23,6–46,2 arasında değişmektedir. Gerek bu çalışmada ve gerekse Güneydoğu Anadolu çalışmalarında sahipli köpek sayısının fazla olması, o bölgelerde hayvancılığın yaygın olması ve köpeklerin de hayvanları koruma amaçlı kullanılmasından kaynaklanabilir. Ayrıca bu çalışmada hayvanların %11,6'sı aşılıdır. Ülkemizde yapılan diğer çalışmalarda da aşılı hayvan oranın düşük olduğu bildirilmektedir[9,16,17]. Aşılanma oranlarının düşük olmasının muhtemel nedeni, hayvan sahiplerinin aşılanma konusunda yeterli bilgiye sahip olmamasıdır.

Araştırmada tüm vakalara profilaksi yapılmıştır. Sağlık Bakanlığı "Kuduz Korunma ve Kontrol Yönetmenliği" de (KKKY) fare gibi hayvanların ısırıkları ve sahipli hayvanların ısırıklarını profilaksi gerektirmeyen durum olarak tanımlamıştır. Bu araştırmada vakaların 20 si fare, 2'si böcek ve 1 vaka da insan ısırığıdır. Diğer yandan sahipli hayvanlar toplam vakaların %56,3'ünü oluşturmuştur. Tüm bunlar göz önüne alındığında vakaların yarısından fazlasına yönergeye uymayan şekilde profilaksi yapıldığı söylenebilir. Diyarbakır'da yapılan bir çalışmada çalışmamızla benzer biçimde vakaların yarısına yakın kısmına yönergeye uymayan şekilde profilaksi yapıldığı belirtilmektedir[9].

Araştırmada saptanan diğer önemli bir nokta ise aşılama yapılan kişilere immüngolbülin yapılmamasıdır. KKKY'de "Bütün kuduz şüpheli temas sonrası bağışıklama yaklaşımları, aradan geçen süre ile ısırık veya ısırık dışı temas olup olmadığına bakılmaksızın kuduz immünglobülinin ve kuduz aşısının birlikte verilmesini kapsamalıdır." denilmektedir. Gerek bu araştırmada ve gerekse ülkemizde yapılan diğer araştırmalarda aşı yapılan vakalara aynı zamanda immünglobülin yapılma oranı istenilen düzeyin oldukça altındadır[1-3,16]. Bu durumun hizmet veren personele eğitim seminerleri verilerek düzeltilebileceği kanaatindeyiz.

Aşı dozu açısından da KKKY'ye uyulmadığı görülmektedir. Yönergede hayvan sahipli ise ve 10 günlük gözlem sonucunda kuduz olduğu görülmedi ise aşının sonlandırılması, bir diğer deyişle 3 doz aşı yapılması önerilmektedir. Temasta bulunan hayvan gözlem altına alınamamış ve takip edilememiş ise aşının 5 doza tamamlanması istenmektedir. Araştırmada yaklaşık her 5 vakadan birine 3 doz, yine her 5 vakadan 1'ine ise 5 doz aşı yapılmıştır. Ancak temasta bulunan hayvanların takibinin yapılıp yapılmadığına ilişkin herhangi bir bilgi bulunmamaktadır. Bu durum ise kuduz şüpheli vakalara profilaksi yaklaşımının hizmet veren sağlık personelinin doğrudan bilgi ve donanımı ile ilgili olduğu gibi, vatandaşın bu konuda yeterince bilgi sahibi olmadığını da göstermektedir. Bu nedenle özellikle acilde çalışan sağlık personeline ve hayvanlarla teması yüksek olan risk grubundaki kişilere düzenli aralıklarla eğitim verilmelidir.

Arşiv kayıtları incelenerek yapılan çalışmamızda bazı kısıtlılıklar mevcuttur. Bunların genellikle formların

eksik doldurulması ve düzenli olarak arşivlenmemesinden kaynaklandığı görülmüştür. Bu nedenle daha sonra yapılacak çalışmaların ileriye dönük olarak tasarlanması bu kısıtlılığı ortadan kaldıracaktır.

Sonuç olarak araştırmada kuduz şüpheli temasın en sık kaynağı köpeklerdir. Vakaların çoğunluğunu erkekler, kırsalda yaşayanlar, 6–15 yaş grubundan olan kişiler oluşturmuştur. Hayvanların yarıdan fazlası sahiplidir, hayvanların aşılanma düzeyi düşüktür. Profilaksinin genelgeye uygun biçimde yapılmadığı saptanmıştır.

Bu bağlamda; il hıfzıssıhha kurulunda alınacak kararlar ile kurumlar arası iletişim arttırılabilir ve bu yolla sahipsiz köpeklerin kontrolü sağlanabilir. Hizmet sunan sağlık personeli kuduz ve profilaksi konusunda hizmet içi eğitime alınmalı ve bu eğitimler periyodik olarak yinelenmelidir.

Teşekkür

Katkılarından dolayı Yard. Doç. Dr. Binali Çatak'a teşekkür ederiz.

Kaynaklar

1. Warell Mj, Warrell DA. Rabies and other lyssa virus diseasse. Lancet 2004;363(9413):959–69.
2. T. C. Sağlık Bakanlığı Temel Sağlık Hizmetleri Genel Müdürlüğü Kuduz Korunma ve Kontrol Yönergesi. (http://www.saglik.gov.tr/SHGM/belge/1-15918/kuduz-korunma-ve-kontrol-yonergesi.html)
3. World Health Organization. Weekly epidemiological record Releve epidemiologique hebdomadaire. WHO, Geneva 2010;85(32):309–20.
4. Büke M, Büke AÇ. Kuduz. İçinde: Topçu AW, Söyletir G, Doğanay M, editörler. İnfeksiyon Hastalıkları ve Mikrobiyoloji 3. baskı. Nobel Tıp Kitabevleri, Nobel Matbaacılık, Cilt 1. 2008;1453–67.
5. Buzgan T, Irmak H, Yılmaz GR, Torunoğlu MA, Safran A. Epidemiology of human rabies in Turkey: 1992–2007. Turk J Med Sci 2009;39(4):591–7.
6. Temel Sağlık Hizmetleri Genel Müdürlüğü Çalışma Yıllığı 2003 Ankara: Sağlık Bakanlığı Yayınları 2004, s.105.
7. Temiz H, Akkoç H, Diyarbakır Devlet Hastanesi Kuduz Aşı Merkezine Başvuran 809 Olgunun Değerlendirilmesi. Dicle Tıp Dergisi 2008;35(3):181–4.
8. Yılmaz F, Akbulut AS, Taş M, Kavalcı C, Arslan ED, Sönmez M. Acil Servise Başvuran Kuduz Riskli Olguların Değerlendirilmesi. J Clin Anal Med 2014:5(1):8–11.
9. Gülaçtı U, Üstün C, Gürger M, Şahan M, Satıcı Ö. Kuduz Şüpheli Vakaların Epidemiyolojisi ve Kuduz Proflaksisi Uygulamasının Değerlendirilmesi. Türkiye Klinikleri J Med Sci 2012:32(3):759–65.
10. Gülaçtı U, Büyükaslan H, İçer M, Şahan M. Acil Servisite Uygulanan Kuduz Şüpheli Temas Sonrası Proflaksi ile Dünya Sağlık Örgütü'nün Önerdiği Proflaksi Uygulamasının Karşılaştırılması. Düzce Tıp Dergisi 2013;15(1):46–9.
11. Sögüt Ö, Sayhan MB, Gökdemir MT, Kara HP. Türkiye'nin Güneydoğusunda Önlenebilir Bir Halk Sağlığı Sorunu: Kuduz Riskli Temas Olguları. JAEM 2011;10:14–7.
12. Karadağ M, Çatak B, Baştürk S, Elmas Ş. Bursa Yıldırım İlçesinde Kuduz Riskli Temas Bildirimlerinin Değerlendirilmesi. Türk Aile Hek Derg 2014;18(3):116–20.
13. Rabies vaccine WHO position paper: WHO Weekly Epidemiological Record 2010;85(32):309–20.
14. Sriaroon C, Sriaroon P, Daviratanasilpa S, Khawplod P, Wilde H. Retrospective: animal attacks and rabies exposures in Thai children. Travel Med Infect Dis 2006;4:270–4.
15. Roseveare C, Goolsby WD, Foppa IM. Potential and actuel terrestrial rabies exposures in people and domestic animals. Upstate South Carolina, 1994–2004. BMJ Public Health 2009;9:1–6.
16. Göktaş P, Ceran N, Karagül E, Çiçek G, Özyürek S. Evaluation of 11,017 cases applicated to a rabies vaccination center. Klimik Dergisi 2002;15(1):12–5.
17. Şengöz G, Yaşar KK, Karabela SN, Yıldırım F, Vardarman FT, Nazlıcan O. Evaluation of cases admitted to a center in İstanbul, Turkey in 2003 for rabies vaccination and three rabies cases followed up in the last 15 years. Jpn J Infect Dis 2006;59(4):254–7.

KAFKAS TIP BİLİMLERİ DERGİSİ
Kafkas Journal of Medical Sciences

ARAŞTIRMA YAZISI / ORIGINAL ARTICLE

Kafkas J Med Sci 2016; 6(2):102–109 • doi: 10.5505/kjms.2016.00821

Comparison of Larger Diameter and Multiple Cysts in the Treatment of Giant Hydatid Cysts of Liver

Karaciğer Dev Kist Hidatiklerinin Tedavisinde Büyük Çaplı ve Multipl Kistlerin Karşılaştırılması

Mehmet Aziret[1], Hilmi Bozkurt[2], Hasan Erdem[2], Şahin Kahramanca[1], İlhan Bali[3], Enver Reyhan[2], Safa Önel[2], Kenan Binnetoğlu[4], Ali Cihat Yıldırım[1], Oktay İrkörücü[2]

[1]Kars State Hospital, Department of General Surgery Kars, Turkey; [2]Adana Numune Training and Research Hospital, Department of General Surgery, Adana, Turkey; [3]Fırat University Faculty of Medicine, Department of General Surgery, Tekirdağ, Turkey; [4]Fırat University Faculty of Medicine, Department of General Surgery, Elazığ, Turkey

ABSTRACT

AIM: *Hepatic hydatidosis is a benign, chronic parasitic disease that can affect many organs. The disease is usually asymptomatic, but the cysts that develop as a result of the disease can reach large sizes. We aimed to compare large hydatid cysts (>10 cm) and multiple cysts (>4) in giant hydatid cysts of liver in terms of demographic structure, recurrence, complications, diagnosis and treatment.*

METHODS: *A total of 15 out of pool of 62 patients were enrolled in the study and placed into two groups: Group 1 included patients with a cyst diameter larger than 10 cm (n=12) and Group 2 included patients with more than 4 cysts (n=3). The two groups were retrospectively compared in terms of age, sex, demographic structure, recurrence, complications, morbidity and mortality, diagnosis and treatment.*

RESULTS: *In Group 1, the patients' mean age, BMI, diameter of cyst and hospitalization time, were 39.5 years, 25.5 kg/ m2, 11.75 cm, 9.8 days and 21.4 months, respectively. In Group 2, the patients' mean age, BMI, number of cysts and hospitalization time were 44.7 years, 27.7 kg/m2, 8.3 cysts, 8.6 days and 17.1 months, respectively (p>0.05). In Group 1, 1 patient had a wound infection (1.6%) and 1 patient had an intraoperative hemorrhage (1.6%). In Group 2, 2 patients had recurrence (3.2%). A significant difference was detected between groups in terms of recurrence (p=0.029).*

CONCLUSION: *Rarely seen, giant hydatid cysts may cause secondary infection or fistulization into several organs, and it can open into the peritoneal cavity or place pressure on adjacent organs and structures, which leads to obstructive jaundice. Morbidity, mortality and cost can increase should these potential results of giant hydatid cysts occur. This study demonstrated the resulting high rate of cure and low morbidity and complications that were able to be achieved using conservative surgical treatment methods for hydatid cysts.*

Key words: *giant hydatid cyst; echinococcus granulosus; conservative surgical treatment*

ÖZET

AMAÇ: *Karaciğer kist hidatiği benign, kronik ve birçok organı etkileyebilen paraziter bir hastalıktır. Çoğunlukla asemptomatiktir ve büyük boyutlara ulaşabilir. Dev karaciğer kist hidatiklerinde büyük çaplı (>10 cm) ve multipl sayıda (>4) hastaların tedavi, nüks, morbidite ve mortalite, sosyodemografik yapı ve komplikasyonlarını karşılaştırmayı amaçladık.*

YÖNTEM: *Toplam 62 hastanın 15 tanesi çalışmaya dahil edildi. Çalışmada iki grup oluşturuldu. Grup 1, kistin çapı 10 cm'den büyük hastalar (n=12); Grup 2, kist sayısı 4'ten fazla hastalardı (n=3). İki grup, komplikasyon, nüks, sosyodemografik açıdan, tanı ve tedavileri açısından istatistiksel olarak karşılaştırıldı. Çalışma retrospektif olarak planlandı.*

BULGULAR: *Grup 1'de hastaların sırasıyla ortalama yaş, vücut kitle indeksi, kist çapı, hastanede kalma süresi, takip süresi; 39, 5 yıl, 25, 5 kg/ m2, 11, 75 cm, 9,8 gün, 21, 4 aydı. Grup 2'de hastaların sırasıyla ortalama yaş, vücut kitle indeksi, kist sayısı, hastanede kalma süresi, takip süresi; 44,7 yıl, 27,7 kg/m2, 8,3 adet, 8,6 gün, 17,1 aydı (p>0,05). Grup 1'de, 1 hastada yara enfeksiyonu, 1 hastada intraoperatif kanama ve Grup 2'de 2 hasta da nüks görüldü. Nüks açısından iki grubun karşılaştırmasında anlamlı farklılık tespit edildi (p=0,029).*

SONUÇ: *Dev kist hidatikler toplumda nadir görülmektedir. Çevre organ ve yapılara bası, safra yollarına veya peritona açılma ve anafilaktik şoka neden olabilmektedir. Ayrıca morbidite, mortalite ve hastane maliyelerini arttırabilmektedir. Çalışmamızdaki bulgular sonucunda dev kist hidatiklerine konservatif cerrahi yöntemleriyle, yüksek kür ve düşük morbidite ve komplikasyon oranlarıyla etkin tedavi edilebilmektedir.*

Anahtar kelimeler: *dev kist hidatik; ekinokokus granulosus; konservatif cerrahi tedavi*

Uzm. Dr. Mehmet Aziret, Sakarya Üniversitesi Eğitim ve Araştırma Hastanesi, Genel Cerrahi Kliniği, Sakarya, Türkiye, Tel. 0506 305 73 17
Email. mhmtaziret@gmail.com
Geliş Tarihi: 22.10.2014 • Kabul Tarihi: 23.07.2015

Introduction

A hydatid cyst (HC) is produced from hepatic hydatidosis, aparasitic disease caused by the cestoda *Echinococcus granulosus* (EG)[1–3]. HCs are mostly seen in the liver (70%) in humans[3,4]. Dogs and wolves are the primary hosts for EG, while humans, sheep and cattle are intermediate hosts[5]. Cases of hydatid cyst are usually found in South Australia, New Zealand, Africa, Greece, Spain, and the Middle East. Its annual incidence is 2–6% in endemic regions[6].

Because hydatid cystsare generally asymptomatic, diagnosis often comes late, usually not until the cyst grows and increases in diameter. Significant complications are associated with giant HCs, such as the cyst's penetration into other organs, cholangitis and anaphylactic shock. High morbidity and mortality may result from these complications[2–4,6].

Serologic tests, such asthe enzyme-linked immunosorbent assay (ELISA) and the indirect hemagglutination test (IHA), can be used for diagnosis of HC. Additionally, abdominal ultrasonographies (USG), computer tomographies (CT) and magnetic resonance imaging (MRI) are quite sensitive for detecting hydatid cysts[7,8]. A sonography classification of the cyst can greatly aid the diagnosis and treatment of HC. Over time, the classification of HC has changed, with the most recent one being issued by the WHO-IWGE (World Health Organization-Informal Working Group on Echinococcosis), which classifies HC stages as active (CE1 and CE2), transitional (CE3) and inactive (CE4 and CE5) (Fig. 1)[9–11].

In this study, we aimed to compare large hepatic hydatid cysts (diameter ≥10 cm) and multiple cysts (>4) in giant hydatid cysts in terms of diagnosis, treatment, complications and recurrence rates.

Materials and Methods

Ethics Statement and Patients

All patients gave their written informed consent to data treatment and the study was approved by the Ethics Committee. The sixty-two patients who were diagnosed with HC in the liver and underwent surgical treatment for it between January 2012 and September 2014 at the Adana Training and Research Hospital and the Kars state hospital, department of general Surgery were analyzed to determine recurrence, complications and socio-demographic data and followed up. Forty-seven patients were excluded from the study due to diameter of their cysts being <10 cm or their number of cysts being <4. As a result, fifteen patients were included in study. The study was retrospective in design, with no randomization. The 15 patients who had been treated with surgery for HC were divided into the following two groups for treatment: Diameter of cysts larger than 10 cm (larger diameter cysts) (Group 1) (n=12) and number of cysts >4 (multiple cysts) (Group 2) (n= 3) (Table 1). All cases were evaluated in terms of gender and age, location of liver, postoperative length of hospital stay, postoperative complications (wound dehiscence, infection, hematoma, seroma) and recurrence. Before the treatment, all the diagnoses were confirmed by radiological examinations (ultrasonography and/or computed tomography or MRI) and indirect hemagglutination (IHA) with antigen test. In cases of suspicion of a cystobiliary fistula (CBF), a magnetic resonance cholangiopancreatography (MRCP) or endoscopic retrograde cholangiopancreatography (ERCP) was performed to investigate the biliary duct obstruction. All of the patients were treated with albendazol before (10–15 mg/kg/day for 3 weeks) and after (10–15 mg/kg/day in a

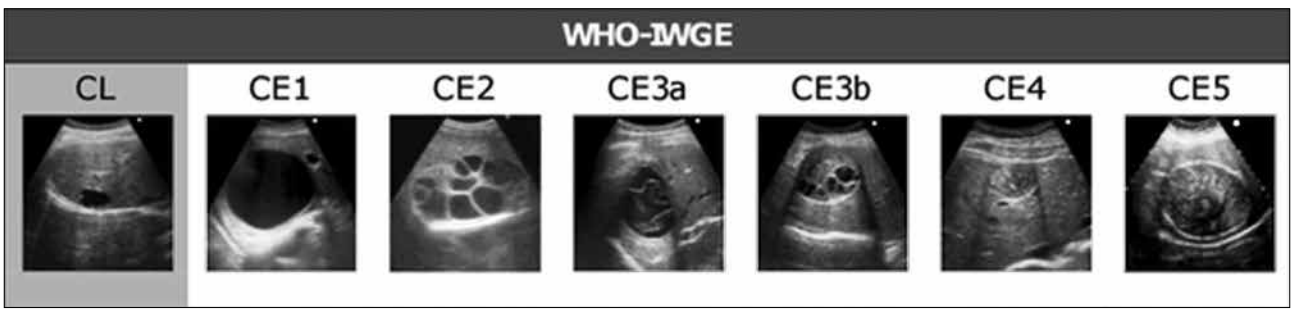

Figure 1. *WHO-IWGE ultrasound classification of echinococcal cysts. CE1 and CE2 (active cysts), CE3A and CE3B (transitional cysts), and CE4 and CE5 (inactive cysts)[9]. doi:10.1371/journal.pntd.0003057.g001*

course of 6 months, separated by intervals of 1 week) the invasive approaches. The patients' liver functions were evaluated every month.

Inclusion Criteria

1- Patients willing to give written informed consent.
2- Adult patients (over 18 years of age) undergoing surgery for HC.
3- Diameter of cysts >10 cm.
4- Number of cysts >4.
5- Active period for the HC (CE1, CE2 and CE3).
6- International normalizing ratio (INR) <1.5.
7- Prothrombin time (PT) should be <15 s.
8- Partial thromboplastin (PTT) time should be near normal.
9- Platelet count should be >50,000/mm^3 to limit the risk of bleeding.

Table 1. *Patients and cyst characteristics*

Characteristics	Diameter of cysts >10 cm (n=12)	Number of cysts >4 (n=3)	p value
Gender M/F	6/6	1/2	1
Mean age (years)	39.5	44.60	0.563
BMI (kg/m^2)	25.5	27.6	0.384
Symptoms			
Abdominal pain (%)	44	54	-
Nausea (%)	18	10	-
Nonspecific (%)	15	7	-
Asymptomatic	33	29	-
Mean cyst size (cm)	11.75	-	
Mean number of cysts	-	8.3	
Side			
Left	3	0	
Right	8	0	
Bipolar	1	3	
IHA (%)	68.4	72.5	0.343
Mean hospital stay (day)	9.8	8.6	0.767
Follow up (months)	21.4	17.1	0.248

BMI, body mass index; IHA, indirect hemagglutination test.

Exclusion Criteria

1- Patients not willing to give informed consent
2- <16 years of age.
3- Diameter of cysts <10 cm.
4- Number of cysts <4.
5- No active period for the HC (CL1, CE4 and CE5) and emergency cases.
6- Uncontrolled diabetes mellitus, renal failure, coagulation and immunosuppression disorders.

Surgical Technique

All patients were operated on under general anesthesia in the operating room. After administration of anesthesia, standard aseptic procedures were performed before the laparotomy.In most patients, entry was made into the abdomen through a right subcostal incision, with the incision having to be extended in only few patients. Hypertonic saline gas compresses (3 % NaCl) or povidone-iodine 10% solution was prepared before surgery. The hypertonic solution was injected into cysts according to their diameter. The cyst was opened after approximately 15 minutes. Total/partial pericystectomy, cystotomy and drainage, T tube or simple suture, unroofing, introflexion, capitonnage and/or omentoplasty were the preferred procedures, and the appropriate technique was performed according to the characteristics of patient's cyst. Drain was placed according to the state of cyst after washing with 0.9% NaCl. Abdomen was closed anatomically (Fig. 2 and Fig. 3).

Serology

The indirect hemagglutination test (IHA) performed on all of our patientswas made in the laboratory of our hospital, according to the manufacturer's instructions. IHA was also performed to evaluate recurrence and to conduct postoperative follow up.

Postoperative Follow-up

The patients were evaluated using serological tests and either USG, CT scan or MRI at intervals of three months in the postoperative first year. Complete blood count (CBC) and liver function tests were performed every month for the first 6 months. In cases when high liver function tests were administered, Albendazol or Mebendazol was stopped. All patients were provided with the hospital telephone numbers to call in case of emergency.

Figure 2. *Appearance of large diameter cysts and multiple cysts in computed tomography scan. Multiple cysts in different sections (left and middle) of the same patient. Giant hydatid cyst (right).*

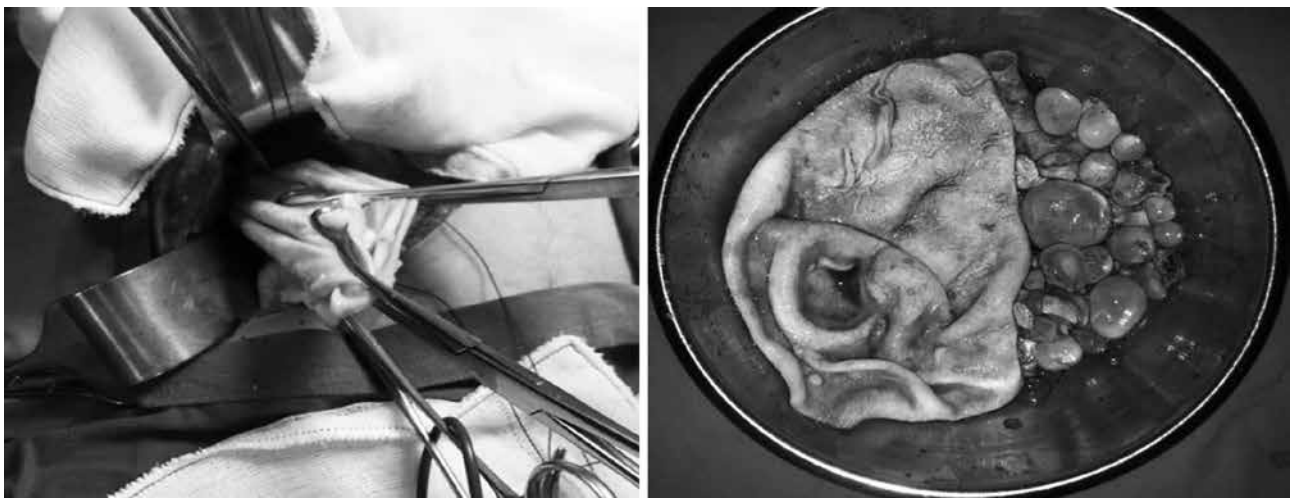

Figure 3. *Appearance of cyst at removal and daughter cysts, cyst wall and germinal membrane.*

Statistical Analysis

The data compiled in this study were analyzed through SPSS 20 software package (Statistical Package for the Social Sciences ver. 20.0, SPSS Inc, Chicago, Illinois, USA). Chi-square analysis was used for assessment of frequency distributions, and the Mann-Whitney U and Fisher's Exact tests were used for comparisons of mean values. For all statistical analyses $p<0.05$ was accepted as significant.

Results

There was no mortality in any of our patients. A total of 7 (46.7%) patients were male and 8 (53.3%) female in this study, and no statistically significant differences were found between the two groups in terms ofgender ($p>0.05$). The mean age of the patients was 41.05±4.3 years, withthe minimum and maximum ages being 19 and 70 years old. In Group 1, the mean age of the patients was 39.5 years, and in Group 2, it was 44.7 years.The patients in Group 2 were older than those in Group 1, but no statistically significant differences were found between the groups in terms of age ($p>0.05$). In Group 1, 12 patients had cysts with a diameter larger than 10 cm (80%), and 3 patients in Group 2 had more than 4 cysts (20%). The body mass index (BMI) was 25.5 and 27.7 kg/m^2 in Group 1 and Group 2, respectively ($p>0.05$). Patients from both groups experienced pain in the upper right quadrant – 44% in Group 1, and 54% in Group 2 – while some patients had multiple complaints. In Group 1, 33% of the patients were asymptomatic and in Group 2, 29% were asymptomatic. Most of the cysts were located in the right hepatic lobe (55.4%), 4 of the patients had multiple and bilobar cysts and 1 patient had a cyst in the left lobe (Table 1). The mean cyst size in Group 1 was 11.75 cm and the mean number of cysts in Group 2 was 8.3.

The mean hospitalization time was similar between each group (9.8 and 8.6 days, respectively), and no statistically significant differences were found between the two groups in terms of mean hospitalization time (p>0.05). The median follow-up time of patients was 25.6 months (total 9,250 days) (Table 1). Intraoperative massive hemorrhage occurred in one of the patients when removing the cyst from the left hepatic vein. The patient was administered 8 units of erythrocyte suspension and 8 units of fresh frozen plasma intraoperatively. The patient was taken to the intensive care unit with a mechanic ventilator. Wound infection also occurred in the same patient.

During the follow-up period, 2 recurrences (13.3%) occurred in Group 2. No recurrences, however, occurred in Group 1, and significant differences were found between the groups in terms of recurrence (p=0.029). Wound infection occurred in 1 patient in Group 1 and in 2 patients in Group 2. No significant differences werefound between the groups in terms of wound infection (p>0.05). Perihepatic abscess, incisionel hernia, postoperative biliar fistula and mortality did not occur in any patients (Table 2).

All of the cysts were classified according to both the WHO-IWGE classification of HC and the Gharbi classification. One patient had CE1, 7 patients had CE2, 5 patients had CE3a, 1 patient had CE4 and 4 patients had CE3b. Two patients had both CE2 and CE3a in Group 2 and one patient had CE3a and CE4 at the same time in Group 2. CL1 and CE5 were not determined in either of the two groups' patients who underwent a laparotomy (Table 2).

Conservative surgical treatments were performed in the two groups. Onepatient underwent drainage and omentoplasty, 3 patients underwent drainage and cysto-pericystectomy, four patients underwent drainage, cysto-pericystectomy and omentoplasty, two patients underwent drainage, cysto-pericystectomy and capitonnage, one patient underwent drainage, cysto-pericystectomy and introflexion, one patient underwent drainage, cysto-pericystectomy and simple suture and two patients underwent drainage, cysto-pericystectomy and T-Tube drainage (Table 3).

Table 2. *Complications*

	Group 1	Group 2	P value
Wound infection	1	2	0.224
Hemorrhage	1	0	0.056
Recurrence	0	2	0.029
Mortality	0	0	

Table 3. *WHO-IWGE classification and surgical methods*

Diagnosis and treatment	Diameter of cysts >10 cm	Number of cysts >4
WHO-IWGE classification		
CE1	1	0
CE2	5	2
CE3a	3	2
CE3b	3	1
CE4	-	1
Surgical methods		
Drainage + O	1	0
Drainage + C-p	2	1
Drainage + C-p + O	4	-
Drainage + C-p + C	1	1
Drainage + C-p + I	1	-
D + C-p + Simple sutur	1	-
D + C-p + T-Tube drainage	2	-

D, drainage; O, omentoplasty; C-p, cysto-pericystectomy; C, capittonage; I, introflection

Discussion

Hepatic hydatidosis, which is responsible for producing hydatid cysts in the host, is known as one of the oldest diseases and was referred to as 'liver filled with water' by Hippocrates[12]. The Turkana region of Kenya features the most cases of hydatid cysts (200/100.000) in the world[13]. The annual incidence rate in Turkey is 4.4–6.5/100,000 and giant hydatid cysts are rarely seen[14]. HC is observed slightly more in women than in man (female ≥ man)[15]. In our study, the rate of women with HC was 53.3%.

HC results from a chronic disease caused by infection from *Echinococcus granulosus, Echinococcus multilocularis, Echinococcus vogeli, and Echinococcus oligarthrus*. Echinococcus granulosus (EG) is the most common cause of HC and is largely localized in the liver[14,15]. It can also be found, less frequently, in the lung, spleen, kidney and brain[16]. HC often occurs with uncontrolled slaughter and is taken by directly or indirectly diseased organs[17]. Our study was in agreement with the clinical picture described above.

The majority of HC cases are asymptomatic, but when symptoms do appear, they include upper right quadrant pain, nausea, vomiting, jaundice and fever[18]. Because of the slow growth rate of cysts (1–2 cm/year) in the host and the lack of symptoms accompanying them, cysts can reach to large sizes before being diagnosed and possibly fistulize into the bile ducts when the diameter of the cyst increases[18,19]. The incidence of asymptomatic patients in various series is 8–75%. In our patients, the primary symptom seen was upper right quadrant pain. Additionally, the mean diameter of cysts in patients was 11.3 cm and in three patients biliary fistulas developed.

Imaging techniques and serology can help in the diagnosis of HC. The sensitivity of an enzyme-linked immunosorbent assay (ELISA) is 64–100%[20]. In the study carried out by Piccoli et al. the rate of negative sensitivity was detected to be 70% for ELISA in diagnosis[9]. The sensitivity of the indirect hemagglutination test (IHA) was 64–100%[7,20]. In our patients, the sensitivity of IHA was approximately 70% and no significant difference was found between the two groups in terms of this test ($p>0.05$).

Ultrasonography is frequently used in the diagnosis, treatment and follow-up of HC, with rates of correct diagnosis at 90%[8, 21]. CT scan and MRI are effective in terms of identifying hydatid disease, detecting complications and determining non-liver HC locations[22]. CT scan and USG were used in the diagnosis of all our patients, while MRI was used in only some of them.

The Gharbi and WHO-IWGE classifications are used for the management of diagnosis and treatment of HC. The Gharbi classification shows the natural course of the disease and the WHO-IWGE determines activity and viability of cyst (Fig. 1)[10,11]. All of our patients had classification of active period HC (CE1, CE2 and CE3).

The treatment course for HC includes medical treatment, follow-up, percutaneous aspiration and drainage and laparoscopic and open surgery[22,23]. The most important issue to address when dealing with HCs involves determining which cysts to treat. Medical treatment can vary depending on the unique circumstances of each patient. For example, non-surgical treatment is preferred in patients who are older or pregnant, when co-morbidities are present or when the cyst is located in a hard to reach locationfor the performance of surgical or percutaneous treatment[23,24]. Additionally, the treatment is not generally recommended in Type 5 or CE4 and CE5 classifications. Albendazol (10–15 mg/kg/day) or Mebendazol (35–50 mg/kg/day) may be administered to patients as treatment for a period of 4–6 months but patients should be monitored with liver function tests. However, inpatients with symptomatic and active period cysts, treatmentshould be given due to risk of severe complications[24]. The goal of treatment is to prevent secondary infection as well as to prevent the cyst from fistulizing into other organs, opening into the peritoneal cavity and putting pressure on adjacent organs and structures, which leads to obstructive jaundice[25,26].

PAIR (puncture, aspiration, injection and re-aspiration), which was defined by Amour in 1986, is usually recommended in Type 1 and 2, and some Type 3 classification cysts [27]. In a meta-analysis conducted on PAIR, it was reported that the rates of cure were 95%, mortality 0.1%, recurrence 1.6%, minor complications 13.1% and major complications 7.9%[28]. Although the use of PAIR was encouraged in the Cochrane systematic review, the review also indicated that there was insufficient evidence to support its effectiveness and that there was a need for well-designed randomized controlled trials to further confirm its validity[29].

Laparoscopic surgery is used in the treatment of HC. As this surgery is minimally invasive and low cost, is can be used as a viable option. However, it should be noted that there are limitations associated with this option, namely, the possibility of contamination of the cyst into the abdominal cavity[30].

Radical surgical procedures, such as lobectomy or hepatectomy, have recently been increasingly used in the treatment of hepatic HC, and it has been reported that these procedures have low recurrence, morbidity and mortality rates[31,32]. For example, in the meta-analysis conducted by Buttenscho et al. the rates of mortality were reported to be 1.2%, morbidity 11.7% and recurrence 2%[25]. However, many researchers argue that it is unnecessary to perform radical interventions forbenign diseases. Therefore, we chose to perform conservative surgery in our patients (Fig. 3).

Conservative surgical approaches include drainage of cavity, cyst-pericystectomy, omentoplasty, capitonnage or introflexion, T-Tube drainage and simple suture for biliary fistula[16,21,26,29,32]. Jerraya et al. reported rates of cure to be 90%, mortality 0.7% and recurrence 6% with conservative approaches for HC[32]. In our

study, the conservative surgery methods we usedon patients resulted in rates of recurrence of 3.2%, cure 95%, mortality 0% and morbidity 9.6%. The data from our study are similar with the data found in the literature [25,28,32]. In Group 2, 2 cases of recurrence occurred, with statistically significant differences found between large cysts and multiple cysts groups in terms of recurrence ($p<0.05$). These results suggest that conservative treatment may be limited in cases of multiple HC. However, in 1 of our patients who had a giant cyst, a left hepatectomy was planned, but massive intraoperative hemorrhaging occurred, and therefore, drainage of cavity, cyst-pericystectomy and omentoplasty were performed on the patient. As a result, in patients with giant cysts, radical surgery combined with a multidisciplinary approach should be considered, particularly in high volume centers.

When the number of HC or the diameter of HC increases, the rate of complications tends to increase with time. In a study by Milicevic et al. conducted onthe connected biliary ducts of patients, it was reported that 70% of the biliary ducts were connected and that they were controlled with simple suture[18]. In the same study, T-tube drainage was performed on 16% of the patients and a Roux-en-Y cystojejunostomy on 2% of the patients. Gonzales et al. suggested that a Roux-en-Y cystojejunostomy and sphincteroplasty should be performed for large hydatid cysts (>20 cm) in cases of biliary fistulas[19]. Darakdeh et al. reported that surgical treatment had negative effectsin cases when the diameter of cyst was wider than 10 cm, the patient was older than 40 years of age and preoperative complications were present[31]. In our study, the biliary fistula was found in 3 patients, 1 of the them was treated with a primary suture and other two patients were treated with T-tube drainage. In follow-ups on these patients, no biliary fistula was present and recurrence did not occur. Finally, Elber et al. demonstrated in their study comparing T-tube drainage and choledochoduodenostomy that tube drainage was more effective[33]. With these results, it can be suggested that primary suture and T-tube drainage are effective treatments for biliary fistula.

Our study did include some limitations. Firstly, because giant HCs are rare, we had an insufficient number of patients and therefore, randomization was unable to be achieved. Secondly, since the literature lacks evidence from high-value studies, adequate comparisons were unable to be made. Lastly, our follow-up period was not long enough to clearly evaluate recurrence.

Conclusion

Giant hydatid cysts are rare and benign cysts of liver. They should be treated early to prevent the onset of fatal complications. In our study, giant hydatid cysts were successfully treated with conservative surgical methods and our results were similar to those found in the literature.

Acknowledgments

This study was not supported by any company and it was presented as the oral presentation at the 3th National Surgery of Gastroenterology congress.

Conflicts of Interest

There are not any conflicts of interest.

References

1. Fernández-Martínez D, Alvarez-Pérez JA, Granero-Castro P, et al. Giant hepatic hydatid cyst with mediastinal extension. Rev EspEnferm Dig 2013;105(6):367–8.
2. Rinaldi F, De Silvestri A, Tamarozzi F, et al. Medical treatment versus "Watch and Wait" in the clinical management of CE3b echinococcal cysts of the liver. BMC Infect Dis 2014;14:492.
3. Craig PS, Larrieu E. Control of cystic echinococcosis/ hydatidosis: 1863–2002. Adv Parasitol 2006;61:443–508.
4. Akalin S, Kutlu SS, Caylak SD, et al. Seroprevalence of human cystic echinococcosis and risk factors in animal breeders in rural communities in Denizli, Turkey. J Infect Dev Ctries 2014;8(9):1188–94.
5. Moro PL. Epidemiology and control of echinococcosis. Waltham, USA. UpToDate. Available: http://www.uptodate.com/contents/epidemiology-and-control-of-echinococcosis. Accessed: August 2013.
6. King CH, Fairley JK. Cestodes (Tapeworms). In: Mandell GL, Bennett JE, Dolin R, editors. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 7th edition. Philadelphia: Churchill Livingstone; 2010. p.3607–16.
7. Brunetti E, Kern P, Vuitton DA. Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans. Acta Trop 2010;114:1–16.
8. Stojkovic M, Rosenberger K, Kauczor HU, et al. Diagnosing and staging of cystic echinococcosis: how do CT and MRI perform in comparison to ultrasound? PLoS Negl Trop Dis 2012;6(10):e1880.
9. Piccoli L, Tamarozzi F, Cattaneo F, et al. Long-term Sonographic and Serological Follow-up of Inactive Echinococcal Cysts of the Liver: Hints for a "Watch-and-Wait" Approach. PLoS Negl Trop Dis 2014 Aug 14;8(8):e3057.

10. Gharbi HA, Hassine W, Brauner MW, et al. Ultrasound examination of the hydatic liver 1981 May;139(2):459–63.
11. WHO Informal Working Group. International classification of ultrasound images in cystic echinococcosis for application in clinical and field epidemiological settings. Acta Trop 2003;85:253–61.
12. Saidi F. How to manage asymptomatic liver hydatids. Arch Iran Med 2006 Apr;9(2):173–4.
13. Smith SA, Richards KS. Ultrastructure and microanalyses of the calcareous corpuscles of the protoscoleces of Echinococcus granulosus. Parasitol Res 1993;79(3):245–50.
14. Yazar S, Ozkan AT, Hökelek M, et al. Cystic echinococcosis in Turkey from 2001–2005. Turkiye Parazitol Derg 2008;32(3):208–20.
15. Kayaalp C, Bzeizi K, Demirbag AE, et al. Biliary complications after hydatid liver surgery: incidence and risk factors. J Gastrointest Surg 2002 Sep-Oct;6(5):706–12.
16. Akkucuk S, Aydogan A, Ugur M, et al. Comparison of surgical procedures and percutaneous drainage in the treatment of liver hydatide cysts: a retrospective study in an endemic area. Int J Clin Exp Med 2014;7(8):2280–5.
17. Carabin H, Balsera-Rodríguez FJ, Rebollar-Sáenz J, et al. Cystic Echinococcosis in the Province of Alava, North Spain: The Monetary Burden of a Disease No Longer under Surveillance. PLoS Negl Trop Dis 2014 Aug 7;8(8).
18. Milicevic MN. Hydatid Disease, In: Blumgart LH, Fong Y, editors. Surgery of Liver and Biliary Tract. 3rd edition. London: WB Saunders Company; 2000. p.1167–204.
19. Moreno Gonzales E, Loinaz Sequrola C, Garcia Urena MA, et al. Liver transplantation for Echinococcosis granulosus hydatid disaese. Transplantation 1994;58:797.
20. Liance M, Janin V, Bresson-Hadni S, et al. Immunodiagnosis of Echinococcus infections: confirmatory testing and species differentiation by a new commercial Western Blot. J Clin Microbiol 2000 Oct;38(10):3718–21.
21. Safioleas M, Misiakos E, Manti C, et al. Diagnosis and treatment of hepatic hydatid disease of the liver. World J Surg 1994;18:859–63.
22. Adán Merino L, Alonso Gamarra E, Gómez Senent S, et al. Hidatidosis hepática: manejo actual de una entidada únpresente. Rev Esp Enferm Dig 2008;100:1130–48.
23. Salemis NS. Giant hydatid liver cyst. Management of residual cavity: A case report. Ann Hepatol 2008;7:174–6.
24. Giorgio A, de Stefano G, Di Sarno A, et al. Clinical and sonographic management of viable hydatid livercysts. J Ultrasound 2008 Sep;11(3):107–12.
25. Buttenschoen K, Schorcht P, Reuter S, et al. Surgicaltherapy of alveolar echinococcosis and long-term outcome. Chirurg 2001 May;72(5):566–72.
26. Sayek İ. Temel Cerrahi, 4. Baskı, Güneş Tıp Kitabevleri, Ankara 2010, Bölüm 136, s.1571–83.
27. Ben Amor N, Gargouri M, Gharbi HA, et al. Trial therapy of inoperable abdominal hydatid cysts by puncture. Ann Parasitol Hum Comp 1986;61(6):689–92.
28. Smego RA Jr, Sebanego P. Treatment options for hepatic cystic echinococcosis. Int J Infect Dis 2005 Mar;9(2):69–76.
29. Nasseri-Moghaddam S, Abrishami A, Taefi A, et al. Percutaneous needle aspiration, injection, and re-aspiration with or without benzimidazole coverage for uncomplicated hepatic hydatid cysts. Cochrane Database Syst Rev 2011 Jan 19;(1):CD003623.
30. Busić Z, Cupurdija K, Servis D, et al. Surgical treatment of liver echinococcosis –open or laparoscopic surgery? Coll Antropol 2012;36(4):1363–6.
31. Daradkeh S, El-Muhtaseb H, Farah G, et al. Predictors of morbidity and mortality in the surgical management of hydatidcyst of the liver. Langenbecks Arch Surg 2007 Jan;392(1):35–9.
32. Jerraya H, Khalfallah M, Osman SB, et al. Predictive factors of recurrence after surgical treatment for liver hydatid cyst. Surg Endosc 2014 Jun 25. [Epub ahead of print]
33. Elbir O, Gundogdu H, Caglikulekci M, et al. Surgical treatment of intrabiliary rupture of hydatid cysts of liver: comparison of choledochoduodenostomy with T-tube drainage. Dig Surg 2001;18(4):289–93.

KAFKAS TIP BİLİMLERİ DERGİSİ
Kafkas Journal of Medical Sciences

ARAŞTIRMA YAZISI / ORIGINAL ARTICLE

Kafkas J Med Sci 2016; 6(2):110–114 • doi: 10.5505/kjms.2016.58070

Anestezi Teknikerlerinin SHMYO Eğitimiyle İlgili Görüşleri ve Mesleki Beklentileri: Anket Çalışması

Opinions and Occupational Expectations of Vocational Academy of Health Related Professions' Students: A Survey Study

Ahmet Şen[1], Başar Erdivanlı[1], Ürfettin Hüseyinoğlu[2], Ersin Köksal[3], Muhammet Bilal Çeğin[4], Emin Sılay[5], Yakup Tomak[6]

[1]Recep Tayyip Erdoğan Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Rize; [2]Kafkas Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Kars; [3]On Dokuz Mayıs Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Samsun; [4]Van Yüzüncü Yıl Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Van; [5]Kayseri Eğitim ve Araştırma Hastanesi, Anesteziyoloji ve Reanimasyon Kliniği, Kayseri; [6]Sakarya Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Sakarya

ABSTRACT

AIM: *Vocational Academy of Health Related Professions (VAHRP) is founded to train qualified technicians to work in the health sector and resolve deficits in education. In this study, we investigated the occupational expectations, approaches and productiveness of students, currently studying in VAHRP Department of Anesthesia.*

METHODS: *Students studying in VAHRP Department of Anesthesia were asked to fill a questionnaire with 23 questions, in writing and witout mentioning their names. We analysed the answers and investigated the relationship between students' demographics and their educational and occupational expectations.*

RESULTS: *A total of 286 completely fulfilled questionnaires were analysed. We found that students, who chose Anesthesia Department at their own will or due to their parents are older (p=0.012 and 0.045, respectively), whereas students, who chose due to their friends are younger (p=0.02). Ninety six (33%) students stated that they chose Anesthesia Department because of their interest in the subject, 154 (54%) of them due to economical concerns. We found that students graduating from a vocational school of health trust themselves more on bedside (p<0.01), and care about team work (p<0.03). Ninety (90%) of vocational school of health graduates and 138 (75%) of other students stated that graduation from a ocational school of health is an advantage.*

CONCLUSION: *Health related professions should not be chosen due to economical concerns. We are in opinion that VAHRPs should be educational facilities that are chosen by students, who have a basic training in health sector and wish to improve their knowledge.*

Key words: *Vocational School of Health related professions; anesthesia technician; education; occupational expectations*

ÖZET

AMAÇ: *Sağlık Hizmetleri Meslek Yüksekokulları (SHMYO) nitelikli yardımcı sağlık personeli yetiştirmek ve eğitimdeki eksiklikleri gidermek için kurulmuştur. Çalışmamızda, SHMYO Anestezi Teknikerliği Bölümü'nde eğitim gören öğrencilerin mesleki beklentileri, yaklaşımları, ve verimlilikleri değerlendirildi.*

YÖNTEM: *SHMYO Anestezi Teknikerliği Bölümü'ne yeni başlayan öğrencilere, isimleri kaydedilmeksizin, yazılı olarak, 23 soruluk anket doldurtuldu. Cevap dağılımları incelenerek, öğrencilerin sosyokültürel özellikleri ile eğitim ve mesleki beklentileri arasındaki ilişkiler incelendi.*

BULGULAR: *Eksiksiz doldurulan 286 anket değerlendirildi. Okulu kendi istekleriyle tercih edenler ve ebeveyn tavsiyesini dikkate alanların yaşları daha ileri (sırasıyla p=0,012 ve 0,045), arkadaş tavsiyesi ile yönelenler daha genç (p=0,02) bulundu. Öğrencilerin 96'sı (%33) anestezi teknisyenliğini sevebileceği düşüncesiyle tercih ettiğini, 154'ü (%54) ekonomik kaygılarla tercih ettiğini belirtti. Sağlık meslek lisesi mezunlarının hasta başında kendine daha çok güvendiği (p<0,01), takım çalışmasını önemsedikleri (p<0,03) saptandı. Sağlık meslek lisesi mezunlarının 90'ı (%90), diğer öğrencilerin 138'i (%75), sağlık meslek lisesi mezunu olmayı mesleki bir avantaj olarak gördüğünü belirtti.*

SONUÇ: *Sağlık sektörü ekonomik beklentiler ve işsizlik korkusuyla tercih edilecek kadar hafife alınmamalıdır. SHMYO'ların, sağlık alanında temel eğitim almış, ve eğitimini ilerletmeyi hedefleyen öğrencilerin girebildiği eğitim kurumları olması gerektiği kanaatindeyiz.*

Anahtar kelimeler: *Sağlık Hizmetleri Meslek Yüksekokulu; anestezi teknikeri; eğitim; mesleki beklenti*

Yard. Doç. Dr. Başar Erdivanlı, İslampaşa Mahallesi, Şehitler Cad., Rize, Türkiye, Tel. 0505 780 07 30 Email. berdivanli@gmail.com
Geliş Tarihi: 28.02.2014 • Kabul Tarihi: 07.12.2015

Giriş

Sağlık hizmetleri, geniş kapsamlı ve multidisipliner yaklaşımla karşılanabildiğinde hedeflerine yaklaşabilmektedir. Anestezi uygulamalarında da ameliyathane hizmetlerinin tek bir anestezi uzmanı ile yürütülemeyeceği muhakkaktır. Yakın geçmişte sayılı merkezlerde anestezi uzmanları çalışmaktayken, birçok il ve ilçe hastanelerinde aynı işi cerrahın sorumluluğunda anestezi teknisyenleri yürütmekteydi. Her zaman sağlık sektörünün nitelikli yardımcı eleman gereksinimi önemli bir konu olmuştur. Bu nedenle nitelikli eleman yetiştirmek üzere Sağlık Hizmetleri Meslek Yüksekokulları (SHMYO) kurulmuş ve eğitimdeki eksiklikleri giderme noktasında gayretler gösterilmiştir.

Anket çalışmamızda, SHMYO Anestezi teknikerliği bölümünde eğitim gören öğrencilerin mesleki beklentilerini, yaklaşımlarını, iş ve gelecekle ilgili beklentilerine bağlı olarak verimliliklerini değerlendirmeyi, sağlık meslek lisesi (SML) ve diğer liselerden (DL) mezun olan öğrenciler arasında fark olup olmadığını incelemeyi amaçladık.

Yöntem

Yerel etik kurul onayı (04/01/2013: 2013/03) alındıktan sonra Eylül 2013 tarihinde Kahramanmaraş, Kars, Rize, Sakarya, Samsun, Urfa, ve Van illerinde bulunan yedi farklı SHMYO Anestezi Teknikerliği okulunun birinci sınıf öğrencilerden, kendi rızaları ile isimlerini belirtmeden, 23 soruluk anket formunu doldurmaları istendi. Seçilen öğrenci kitlesi, Öğrencilere, ankette istenen bilgilerin ne amaçla kullanılacağının anlatıldığı onam formu imzalatılarak, anket sorularını okumaları ve anladıkları şekilde cevap vermeleri istendi.

Anket, eğitim-öğretim yılı başlangıcındaki ilk hafta içerisinde, henüz teorik ve uygulama dersleri başlamadan önce uygulandı. Anketin ilk bölümü yaş, cinsiyet, ebeveynlerin eğitim düzeyi, meslek ve gelir gibi bilgilerden oluşurken, ikinci bölüm öğrencilerin okul tercih sebebi, beklentileri, umutları gibi mesleki tatmini ortaya koymaya çalıştığımız sorulardan oluştu.

İstatistiksel Analiz

Elde edilen veriler SPSS 12 programıyla (Statistical Package For Social Sciences, Chicago, IL, USA) analiz edildi. Tanımlayıcı istatistiklerde sınıfsal değişkenlerin sayıları ve yüzdeleri verildi. İstatistiksel anlamlılık için ki-kare ve t-testi kullanıldı, $p<0,05$ anlamlı olarak kabul edildi.

Bulgular

Toplam 300 anketten, soruların eksiksiz cevaplandığı 286 anket değerlendirildi. Demografik özellikler Tablo 1'de özetlendi. Öğrencilerin beklenti ve yaklaşımlarıyla ilgili sorulara verdikleri cevaplar Tablo 2'de verildi. Farklılıkların direkt olarak gruplarla ilişkili olmadığı bir takım cevaplar aşağıda özetlenmiştir.

Okul tercihini öğrencilerin çoğunluğunun kendi isteğiyle yaptığı, ve öğrencilerin çoğunluğunun çekirdek ailesinin 4–8 kişiden oluştuğu saptandı. Ebeveyn tavsiyesini dikkate alanların daha yaşlı, arkadaş tavsiyesini dikkate alanların daha genç olduğu ($p=0,032$, $t=-2,15$)

Tablo 1. *Ankete katılan öğrencilerin demografik özellikleri*

Yaş (yıl)	18 (19–20)
Cinsiyet (K/E)	127/160
İkamet	
Devlet yurdu	108 (%37,63)
Arkadaşla ortak ev	71 (%24,74)
Özel yurt	44 (%15,33)
Ailesiyle	32 (%11,15)
Diğer	32 (%11,15)
Ailedeki toplam birey sayısı	6 (5–8)
Ailenin toplam aylık geliri (YTL)	1225 (900–2000)
Aylık harçlık (YTL)	260 (200–365)
Mezun olduğu lise	
Düz lise	128 (%44,6)
Sağlık Meslek Yüksekokulu	112 (%39)
Diğer	47 (%16,4)
Anestezi teknikerliğine yönlendiren	
Kendi tercihi	212 (%73,9)
Sağlıkçı akraba tavsiyesi	28 (%9,75)
Anne ve babanın tavsiyesi	27 (%9,4)
Arkadaşları	20 (%6,95)
Anestezi teknikerliğini tercih nedeni	
Erken yaşta iş hayatına başlamak	106 (%36,93)
Sevebileceği bir iş olabilir düşüncesi	96 (%33,45)
Ekonomik beklentiler	47 (%16,38)
Daha iyi bir okul kazanamamak	38 (%13,24)
Birinci derece sağlık çalışanı akraba	
Hemşire	69 (%24)
Doktor	45 (%15,7)
Sağlık memuru	36 (%12,5)
Teknisyen	32 (%11,2)
Memur	22 (%7,7)
Laborant	17 (%5,9)
Yok	66 (%23)
Daha önce ameliyathaneye girdi mi?	
Hayır	163 (%56,8)
Merakı nedeniyle	47 (%16,4)
Ameliyat olmak için	47 (%16,4)
Hasta yakını olarak	30 (%10,4)

Veriler sayı, sayı (%) ve ortanca (%25–75 çeyrek değerler) olarak gösterilmiştir.

Tablo 2. *Sağlık Meslek Yüksekokulu mezunları ile diğer lise mezunlarının karşılaştırması*

	Sağlık Meslek Lisesi (n=112)	Diğer liseler (n=175)	İstatistik*
Hasta başında yalnızken kendime güvenirim	88 (%78,57)	103 (%58,86)	p<0,001, x^2=11,05
Nerede çalışmalıyım:			
Ameliyathanede	78 (%44,57)	97 (%86,6)	p=0,022, x^2=5,21
Ameliyathane ve yoğun bakımda	32 (%18,28)	76 (%67,86)	p=0,016, x^2=5,81
Kiminle çalışmalıyım:			
Anestezi uzmanıyla	103 (%91,43)	160 (%91,96)	p>0,05
Cerrah ile	0 (%0)	8 (%7,14)	p>0,05
Tek başına	9 (%8,03)	5 (%2,86)	p>0,05
Kapalı ortamda çalışabilirim	90 (%80,36)	129 (%73,71)	p>0,05
Steril giysilere uyum sağlayabilirim	96 (%85,71)	135 (%77,14)	p<0,1, x^2=2,67
Anestezik gazları sağlığıma tehdit olarak görmüyorum	31 (27,67)	64 (36,57)	p>0,05
Mesleğim ile mutlu olabileceğimi düşünüyorum	97 (%86,61)	150 (%85,71)	p>0,05
Takım çalışması:			
önemli	69 (%61,61)	81 (%46,28)	p=0,016, x^2=5,83
önemsiz	26 (%23,21)	63 (%36)	p=0,03, x^2=4,64
İki yıllık eğitim süresi:			
yeterli	47 (%41,96)	55 (%31,43)	p>0,05
yetersiz	64 (%57,14)	116 (%66,28)	p>0,05
SML çıkışlılar, bu meslekte avantajlıdır	101 (%90,18)	127 (%72,57)	p<0,001, x^2=11,91

Veriler sayı (%) olarak gösterilmiştir.
*Karşılaştırmada ki-kare testi kullanılmıştır.

saptandı. Sağlıkçı bir yakın tavsiyesini dikkate alanların aile gelirinin, diğerlerine göre daha düşük olduğu (p=0,019, t=2,43) saptandı.

SML mezunlarının %44'ünün okul tercihini, erken yaşta iş hayatına başlamak için yaptığı, ve genç öğrenciler olduğu saptandı (p=0,0016, t=-3,17). Sevebilecekleri bir iş olabilir düşüncesini taşıyanların çoğunluğu ise daha yaşlı öğrencilerdi (p=0,013, t=-2,51).

Tüm öğrencilerin 2/3'ü ameliyathaneye hiç girmemiş ya da eğitim harici, hasta yakını olarak girmişti. Ameliyathaneyi merak ederek ziyaret edenlerin çoğunluğunu SML mezunları oluşturmaktaydı (p<0,0001, x^2=15,63). Ameliyathaneye en az girmiş olanların DL mezunları olduğu saptandı (p<0,0001, x^2=19,23).

Anestezi teknikerliği bölümünde okurken SML mezunu olmanın avantaj olduğunu 228 (%79), avantaj olmadığını 20 (%7), avantaj olarak fark etmediğini 38 (%13) öğrenci ifade etti. SML mezunlarının 90'ı (%90), diğer öğrencilerin 138'i (%75), SML mezunu olmayı mesleki bir avantaj olarak görmekteydi.

Ankete katılanların 191'i (%66,8) ameliyatta hasta başında kaldığında kendine güveneceğini ifade etti. Bu kişilerin 173'ü (%90,6) anestezi teknikerliğini kişisel veya ekonomik nedenlerle tercih eden öğrencilerdi (p=0,014, x^2=6,04). Hasta başında kendine güvenmenin, mesleğe yönlendiren kişilerle veya SML bitirmeyi avantaj olarak görmekle bir ilişkisi yoktu (sırasıyla p=0,26, x^2=1,26 ve p=0,1, x^2=2,67). Öğrencilerin 150'si (%48) daha önce bir takım çalışmasında bulunduğunu, 85'i (%30) bulunmadığını, 78'i (%27) ise takım çalışmasının önemli olmadığını belirtti. Takım çalışmasına verilen önemle hasta başında kendine güven arasında ilişki saptanmadı (p=0,11, x^2=2,53). Hasta başında kendine güvenenlerin büyük çoğunluğu (159, %83.2), kapalı ortamda uzun süre kalabileceğini ifade etti (p=0,0003, x^2=13,17).

Ankete katılan 175 (%61) öğrenci anestezi teknikerinin çalışma ortamının ameliyathane olduğunu, 108 (%38) öğrenci hem ameliyathane hem de yoğun bakımda çalışıldığını belirtti. Öğrencilerin 263'ü (%92) anestezi uzmanıyla, 14'ü (%5) tek başına, 8'i (%3) cerrah ile çalışacağını düşündüğünü ifade etti.

Ameliyathane kıyafetleri, maske, bone, sterilizasyon kuralları gibi kavramlar 231 (%81) öğrencide bir tereddüt oluşturmazken, 41 (%14) öğrenci için fark etmemekteydi. Anestezik gazları 80 (%28) öğrenci mesleki

açıdan bir tehlike, 111 (%39) öğrenci kısmen tehlike olarak görürken, 95 (%33) öğrenci için tehlike değildi.

Anestezi teknikerliği ile bir meslek ya da hayat tarzı olarak 98 (%34) öğrenci mutlu olacağını, 149 (%52) öğrenci ise mutlu olmayı umduğunu belirtti.

Öğrencilerin 102'si (%36) SHMYO'nda geçirecekleri iki yıllık eğitim süresinin yeterli olacağını belirtirken, yeterli olmayacağını belirtenler 88 (%31) kişiydi.

Tartışma

Bu çalışmanın yapıldığı tarih itibariyle anestezi teknikerliği eğitimi 16 adet eğitim kurumunda verilmekteydi. Çalışmamız 7 kurumu kapsadığından öğrencilerin önemli bir kısmı örneklenmiş oldu. Anestezi teknikerliğine giriş için ya yükseköğretime geçiş sınavını kazanmak, ya da SML mezunu olmak gereklidir. Dolayısıyla anestezi teknikerliği bölümünde büyük oranda SML mezunlarının bulunması beklenebilir. Çalışmamıza katılan öğrencilerin %39'unun SML mezunu, %44,6'sının düz lise mezunu, %16,4'ünün diğer liselerden mezun olduğu göz önüne alındığında, örneklemimizin evreni temsil edebilecek genişlikte olduğu kanaatindeyiz.

SHMYO bilgi, beceri ve takım uyumunu öğretme amacıyla kurulmuşlardır. Bu nedenle teknikerlere tıbbi gelişmeleri aktarırlar, hasta ve yakınları ile iletişim kurma tekniklerini öğretirler[1]. Anketimize katılan öğrencilerin yarısı daha önce takım çalışması içinde bulunmamıştı. Özellikle genç öğrencilerin takım çalışmasını önemsiz görmesi dikkat çekiciydi. Ameliyathanelerde kişisel iletişim ve hastaya yaklaşım açısından takım uyumu gereklidir ve eğitimler daha çok uygulamaya yönelik olmalıdır. Anketimize cevaplayan tüm öğrencilerin %79'u (SML mezunlarının %90'ı, DL mezunlarının ise %75'i) SML mezunu olarak bu okullarda okumanın avantaj olduğunu belirttiler. Lise tahsili boyunca temel sağlık dersleri ve uygulama pratikleri SML mezunları için SHMYO eğitiminde avantaj oluşturmaktaydı. Dolayısı sağlıkla ilgili temel derslerin öğretildiği lise eğitimini alanların SHMYO'na gelmesi daha uygun görünmektedir.

Bilimsel gelişimin hızlı olduğu sağlık bilimlerinde teknikerler klinik ve teknik bilgilerini sürekli yenilemeli ve geliştirmelidirler. Yüksek okullardan mezun olan öğrenciler meslek hayatına adım atacak ve hasta güvenliğinden direkt olarak sorumlu olacaklardır. Bunun için eğitimler iyi ve eksiksiz planlanırken, teknikerler de gerekli bilgi ve donanımla mezun olmaya gayret etmelidirler[2].

Okul tercihini kendi isteği ile yapan öğrenciler ve SML mezunları özgüvenleri ve hasta başında kendilerine daha çok güvendiklerini belirttiler. DL mezunları hasta başında yalnız kalmak konusunda kendilerine güvenmiyorlardı. Hem SML mezunu olmayı avantaj olarak gören öğrenciler, hem de kapalı ortamda uzun süre çalışmayı problem etmeyen öğrenciler hasta başında kendilerine güvenmekteydiler.

Ulusal toplantılarda, SML çıkışlı öğrencilerin dahi mesleksel bilgiler, genel kültür, gözlem ve inceleme yeteneklerinin zayıf olduğu, öğrenme meraklarının geliştirilmemiş olduğu belirtilmektedir. Böylece öğrencilerin kişisel gelişimleri eksik olduğu için okul süresinin uzatılması da önerilmektedir[3]. Başka bir toplantıda ise, yüksek öğretim veren kurumların, öğrenci gereksinimlerine göre, eğitimdeki yeterli ve eksik durumların tespit edilmesini ve dikkatli davranılmasını tavsiye etmektedir[4]. Bu durum, temel sağlık eğitimi almayan DL mezunları açısından daha önemli gözükmekte. Çünkü anket cevaplarında büyük oranda iki yıllık eğitim süresinin yetersiz olduğu görüşü yer aldı.

Sağlık hizmetlerine insan kaynağı yetiştirmek SHMYO'larının en önemli görevlerindendir. Bu nedenle eğitimi daha dikkatli, kapsamlı ve nitelikli olmalıdır[5]. Okul tercihinde SML mezunları erken yaşta iş hayatına atılmayı, DL mezunları ise ekonomik beklentilerini karşılamayı ön planda tutmuşlardır. Okul tercihini kendi isteği ile yapan öğrencilerin aile nüfusu az iken, okul tercihinde ekonomik beklentileri öne çıkaran öğrencilerin aile nüfusu daha fazlaydı.

SHMYO'ları yardımcı sağlık personelleri için mesleki yönelim, bilgi, beceri geliştirmek ve iş hayatına atılmadan önce kişisel ve mesleki gelişimlerini tamamlamaları için son aşama konumundadır[6]. Değişik çalışmalarda; farklı eğitim, bilgi ve beceri düzeyine rağmen aynı ünvan verilen kişilerin sağlık sektörünün kalitesini düşüreceği belirtilmektedir[5,7]. SML öğrencilerinin DL'den mezun öğrencilere göre bilgi ve deneyimleri daha çok olacaktır. Elde ettiğimiz sonuçlarda SML mezunları ve kendi isteğiyle okul seçimi yapan öğrencilerin hasta başında kendilerine daha çok güvendiğini saptadık. Bu güven ve becerinin sağlık hizmetine kalite olarak geri döneceği kanaatindeyiz.

Anestezi teknikerinin çalışma ortamı, kapalı ortamda uzun süre kalabilme, ameliyathane kıyafetleri ve sterilizasyon kuralları gibi kavramların oluşturduğu endişeler, anestezik gazların tehlikesi ve anestezi teknikerliğine mesleki bakış ile ilgili sorulardan alınan

cevaplar incelendiğinde baskın bir cevabın olmadığı ve öğrencilerin aslında başlamış oldukları bu eğitim ve sonrası hakkında tam bir bilgi sahibi olmadıkları görülmektedir.

Çalışma Kısıtlılıkları

Ana kısıtlılık, örneklemin belirli bölgelerdeki okulları içermesidir. Mevcut şartlarda sınıf başına düşen öğrenci sayısı düşük olduğundan, ankete katılan okullarda, sınıflar içinde rastgele öğrenci seçimi yapılmayarak tüm öğrencilerin ankete katılımı hedeflendi. Bu yöntemin öğrenciler arasında kendi fikirlerini ifade etmek açısından bir eşitsizliğe neden olmadığı kanaatindeyiz. Örneklemin sadece bir bölgeyi içermesi de diğer bir kısıtlılıktır. Bu çalışmanın diğer bölgelerde de tekrarlanması halinde, bölgesel farklılıkları ortaya koymak ve ayırımları yapmak mümkün olacaktır. Ayrıca tüm ülkeden gelen verilerin toplanması halinde, bölgesel şartların ve farklılıklarının çalışma sonuçlarını etkilemeyeceğini, ve sonuçların tüm ülkeyi yansıtır nitelik kazanacağını düşünüyoruz.

Diğer kısıtlılık ise, anketin henüz yüksekokula yeni başlamış olan öğrencilere uygulanmış olmasıdır. Bu öğrenciler katıldıkları eğitimin önemini henüz kavramamış olabilirler. Belki takibeden iki yıl içinde görüşleri değişecektir. Veya çalışmanın yapıldığı dönemdeki tüm öğrenciler benzer fikirde olabilir. Bu ve benzeri durumların öğrenilebilmesi için anketin diğer sınıf düzeylerine de uygulanması ve periyodik olarak tekrarlanması gerektiğini düşünüyoruz.

Sonuç

Anketimizden elde ettiğimiz görüşlere göre, SHMYO eğitiminin, lisede temel sağlık eğitimi almış olan sağlık lisesi öğrencilerine daha uygun olduğu kanaatindeyiz. Öğrencilerin beklentilerinin ve görüşlerinin, SHMYO eğitimi sırasında ne şekilde değiştiğini görmek, ve eğitime yön vermek açısından, anketin düzenli olarak tekrarlanması gerektiği düşüncesindeyiz.

Teşekkür

Halk Sağlığı Anabilim Dalı'ndan Prof. Dr. Leyla Karaoğlu'na, anket sorularının hazırlanmasındaki yardımlarından dolayı teşekkür ederiz.

Kaynaklar

1. Yurt A, Manisalıgil A, Güneli E, et al. Sağlık Sektörünün Radyoloji Teknikerlerinden Beklentileri. Fırat Sağlık Hizmetleri Dergisi 2009;4(10):60–70.
2. Ballack S, Botes A. Profile of baccalaureate curriculum graduate students in 1997. Curationis 2003;26(3):60–8.
3. Kocaeli Üniversitesi, Sağlık Hizmetleri Meslek Yüksekokulu. Sınavsız geçiş sisteminin sağlık hizmetleri meslek yüksekokullarında yol açtığı eğitsel, yönetsel sorunlar ve çözüm önerileri, 2008; Available from: http://www.4myomt.ktu.edu.tr/komisyon1/1.komisyon.rtastan.doc.
4. Ege Öğretim Elemanları Derneği. Nasıl Bir Eğitim Reformu? 2008; Available from: http://egoder.org.tr/bilgi/egitim_reformu.pdf.
5. Van Yüzüncü Yıl Üniversitesi, Sağlık Hizmetleri Meslek Yüksekokulu. III. Ulusal Sağlık Hizmetleri Meslek Yüksekokulları Sempozyumu, 2008. Available from: http://shmyo.yyu.edu.tr/GirisveIcindekiler.pdf.
6. Suna TY, Aysel K. Sağlık hizmetleri meslek yüksek okullarının durumu ve çözüm önerileri. Ankara Üniversitesi Dikimevi Sağlık Hizmetleri Meslek Yüksekokulu Dergisi 2008;7(2):37–40.
7. Akyurt N, Şahin H, Demirbaş B, et al. Marmara Üniversitesi Sağlık Hizmetleri Meslek Yüksekokulu'na Sınavlı ve Sınavsız Geçiş ile Kayıt Yaptıran Öğrencilerin Mezuniyet Başarılarının Karşılaştırılması. Fırat Sağlık Hizmetleri Dergisi 2008;7(2):156–69.

KAFKAS TIP BİLİMLERİ DERGİSİ
Kafkas Journal of Medical Sciences

ARAŞTIRMA YAZISI / ORIGINAL ARTICLE

Kafkas J Med Sci 2016; 6(2):115–120 • doi: 10.5505/kjms.2016.65002

Evaluation of Lung Cancer Patients with Distant Organ Metastasis*

*Uzak Organ Metastazlı Akciğer Kanseri Hastalarının Değerlendirilmesi***

Pınar Acar[1], Meftun Ünsal[1], Nejat Altıntaş[2]

[1]On Dokuz Mayıs University Faculty of Medicine, Samsun; [2]Namık Kemal University Faculty of Medicine, Tekirdağ

ABSTRACT

AIM: *Cancer is the leading cause of death in economically developed countries and the second leading cause of death in developing countries. The aim of the study was to evaluate distant organ metastasis in patients with lung cancer and the effect of metastasis on survival rates.*

METHODS: *Lung cancer patients with distant organ metastasis were enrolled to the study. Localization of primary tumors and metastasis, histological types of the metastasis, clinical symptoms and signs, the interaction of tumor and lymph nodes, the effects of metastasis on survival rates were evaluated.*

RESULTS: *174 patients were included in the study. Cytologic subgroups of patients were subdivided as non-small cell lung cancer (NSCLC) (75.3%) and small cell lung cancer (SCLC) (24.7%). The most frequent metastatic sites were bone (41.4 %), contralateral lung (32.8%), liver (23.9%) brain (27%), adrenal gland (19,5%), pleura (9.2%). The most common metastasis sites for NSCLC and SCLC were bone and liver respectively. Squamous cell carcinoma was the most common type of metastases in brain, bone, adrenal and contralateral lung metastasis. Metastatic pleural effusions mostly originated from adenocarcinoma and liver metastasis generally originated from small cell lung cancer. Having specific symptoms related to bone and brain were powerful predictors for metastasis.*

CONCLUSION: *Cytological types of the cancer, number of metastasis, weight loss, poor performance status, the absence of symptoms in SCLC with bone and brain metastasis, and presence of the symptoms in liver metastases had adverse effects on survival rates. Evaluation of patients with combination of clinical symptoms, laboratory and radiological findings as whole it may be helpful in predicting metastasis and may prevent unnecessary surgery.*

Key words: *lung cancer; metastasis; symptoms; laboratory; survival*

ÖZET

AMAÇ: *Kanser ekonomik olarak gelişmiş ülkelerde önde gelen ölüm nedenidir ve gelişmekte olan ülkelerde ikinci önde gelen ölüm nedenidir. Çalışmanın amacı, uzak organ metastaz olan akciğer kanserli hastaların ve metastazların sağkalım oranları üzerine etkisinin değerlendirilmesidir.*

YÖNTEM: *Uzak organ metastazı olan akciğer kanserli hastalar çalışmaya alındı. Primer tümörlerin lokalizasyonu ve metastaz, metastaz histolojik tipleri, klinik belirti ve bulgular, tümör ve lenf nodlarının etkileşimi, sağkalım oranları üzerindeki metastazların etkisi değerlendirildi.*

BULGULAR: *Çalışmaya 174 hasta dahil edildi. Hastaların sitolojik alt gruplarının küçük hücreli dışı akciğer kanseri (KHDAK) (%75,3) ve küçük hücreli akciğer kanseri (KHAK) (%24,7) olarak iki alt gruba ayrıldı. En sık metastaz bölgleri kemik (%41,4), kontralateral akciğer (%32,8), karaciğer (%23,9) beyin (%27), böbreküstü bezi (%19,5), plevra (%9,2) idi. KHDAK ve KHAK için en sık metastaz yerleri sırasıyla kemik ve karaciğer idi. Skuamöz hücreli karsinom beyin, kemik, böbreküstü ve karşı akciğerde metastaz en yaygın türü oldu. Metastatik plevra sıvıları çoğunlukla genellikle adenokarsinom ve karaciğer metastazları ise küçük hücreli akciğer kanserlerinde kaynaklanmıştır. Kemik ve beyin ile ilgili spesifik semptomların varlığı metastaz için güçlü belirleyicilerdi.*

SONUÇ: *Kanserin tipi, metastaz sayısı, kilo kaybı, kötü performans status, kemik ve beyin metastazı yapan KHAK'lerinde semptomların olmamasının, karaciğer metastazında ise semptomların olmasının sağkalım oranları üzerine ters etkisi vardı. Hastaların klinik laboratuvar ve radyolojik bulguları bir bütün incelenmesi metazların tahmininde faydalı olurken, gereksiz cerrahiyi önlemiş olur.*

Anahtar kelimeler: *akciğer kanseri; metastaz; semptomlar; laboratuvar; sağkalım*

Introduction

Cancer is the leading cause of death in economically developed countries and the second leading cause of death in developing countries[1]. In over two-thirds of patients, lung cancer is diagnosed at an advanced stage[2]. This may reflect the aggressive biology of the disease, the frequent absence of symptoms until locally advanced or metastatic disease is present, and the lack, of an effective screening test. Symptoms may result

**Accepted as a poster presentation in ERS 2014 Munich/Germany congress.*
***ERS 2014 Kongresinde (Münih/Almanya) sunulan bir poster.*

Yard. Doç. Dr. Nejat Altıntaş, Namık Kemal University, Department of Pulmonary, Critical Care and Sleep Medicine, Tekirdağ, Türkiye
Tel. 0282 500 00 00 Email. nejataltintas@gmail.com
Geliş Tarihi: 22.09.2015 • Kabul Tarihi: 26.11.2015

from local effects of the tumor, from regional or distant spread. Distant metastatic disease is present at the time of initial diagnosis of lung cancer in approximately 43% of patients[3]. Brain, bones, liver, contralateral lung, adrenal glands are the most common sites of metastasis, but it can occur all over the body. It has been reported that the frequencies of extrathoracic metastasis of lung cancers are 54% in squamous cell carcinoma, 86% in large-cell and 82% in adenocarcinomas[3].

Better understanding of the lung cancers' nature might help in two ways. First lung cancers may be identified early which is an important issue as treatment options change[4]. Secondly unnecessary surgery can be avoided since many patients have undetected disseminated disease at the time of thoracotomy, and this is the most likely cause of treatment failure and ultimate death[5].

In this study, we investigated distant metastasis areas and the correlation of these metastases with cell type, organ-specific symptoms, physical examination and radiological findings and laboratory results in patients with lung cancer. With regard to these results, we evaluated the role of clinical assessment in predicting the distant organ metastases and also investigated the effect of metastases on life expectancy.

Materials and Methods

A retrospective computerized search of our center's clinical database for cases from January 2009 to September 2013 was used to identify 405 patients with a diagnosis of lung cancer as determined by means of cytologic and/or histopathologic analysis of material. We excluded patients who did not have definitive histopathological diagnosis, or distant metastasis, patients whose staging tests were not completed and whose symptoms, signs and laboratory results could not be obtained. Final 174 patients with distant organ metastasis were chosen for the study. The tumor stage was defined according to the seventh revision of the tumor–node–metastasis classification[6]. Thoracic, cranial and abdominal computerized tomography (CT) and bone scintigraphy were used for staging. Symptoms, physical examination, radiological and laboratory findings associated with distant organ metastasis sites were evaluated.

Organ specific findings; in brain metastases, the presence of headache, dizziness, hemiparesis, gait and balance disorder, disturbance of consciousness, dysarthria, ptosis; in bone metastasis, localized pain, pathological fractures, dysfunction, hypercalcemia and high levels of ALP; in liver metastasis, hepatomegaly, elevated liver enzymes (AST, ALT, GGT), right upper quadrant pain, jaundice and ascites were evaluated.

Impact of cell type, location, number of metastasis, the presence of symptoms, weight loss, performance status, TNM stage on survival were evaluated.

Ethical Concerns

This retrospective study was approved by XXXX university Ethic Committee (2013.9.25) who waived the need for informed consent.

Statistical Analysis

The statistical analysis of the data were done by SPSS (Statistical Package for Social Sciences (SPSS) version 15.0 Chicago, Illinois). Defining characteristics of data were expressed as mean±standard deviation, numbers and percentages. Chi-square test was used for comparisons. Sensitivity, specificity, positive predictive values (PPV), negative predictive values (NPV) and likelihood ratios for bone, liver, brain metastases were calculated. Survival rates were calculated by Kaplan-Meier survival analysis of the groups. $P<0.05$ was considered statistically significant.

Results

The study was performed on 158 (90.8%) males and 16 (9.2%) females who had lung cancer with distant metastasis at initial diagnosis. Mean age was 62.6±9.2 years (range: 33–81 years). Demographic and clinical characteristics of patients with distant organ metastasis are shown in Table 1.

Squamous cell carcinoma (SCC) was the most common cell type (41.9%). Distant metastases were most commonly found in bone (41.4%). Bones in NSCLC and liver in SCLC were the most common sites of metastasis. The vertebrae (66.7%) and then the ribs (50%) were the most frequent bone metastasis sites. Adenocarcinomas for brain and bone, SCC for adrenal glands had predilection. While adrenal and brain metastasis were solitary, bone and liver metastases were often more than one. The frontal lobe was the most frequent (59.1%) site of metastasis in the brain. Brain metastases tended to be solitary in NSCLC, while it was multiple in SCLC. The most frequent malignant pleural effusions were observed in adenocarcinomas. The breakdown in frequency of metastatic disease to specific sites according to histology was given in Table 2.

Organ-specific symptoms and signs were not observed in 40.4%, 15.9%, 13.9%, of patients with liver, brain

and bone metastases respectively. Headache and dizziness for brain, localized pain for bone metastasis were the most common complaints. ALP levels were high in 73.6% of cases and it was significantly associated with the presence of bone metastasis (p=0.007). Hepatomegaly (57.4%) was observed in patients with liver metastases, 70.2% of these cases had higher liver enzyme levels. AST, ALT and GGT elevation was significantly correlated with liver metastases, (p=0.0001). There were no organ specific symptoms in patients with adrenal metastasis.

The presence of bone and brain-specific symptoms were shown to be more powerful in predicting metastasis than any other organ specific symptoms**.** The absence of specific symptoms was not convenient for assessing the presence of liver metastasis. Weight loss of more than 10% was significant in the presence of bone and pleural metastasis (p=0.042, p=0.034 respectively).

Predicting the metastasis with presence of organ-specific symptoms in patients with bone, liver and brain metastases were shown in Table 3.

While primary lung tumors in the left upper lobe had predilection for brain metastasis, right upper lobe tumors had predilection for bone, liver, and adrenal metastases. In addition, central lung localization was accounted for the majority of metastases.

The median survival of all patients was calculated to be 198 days in the study. The longest median survival was in NSCLC with contralateral lung metastasis, the shortest was in SCLC with liver metastasis. The median survival according to localization of metastasis was shown in Table 4.

The survival time was 246 days in patients with single organ metastasis and 110 days in patients with multiple organ metastases (p=0.003). The survival time in patients with NSCLC was 248 days in single organ metastasis and 120 days in multiple organ metastases and these figures were only 175 days and 81 days in patients with SCLC respectively. Relationship between survival and organ specific symptoms were shown in Table 5.

The survival was shorter in T3-4 group than in T1-2, in all study groups (p=0.014). There was no survival difference when N2-3 groups compared with N0-1 groups. However there was a significant survival difference found between M1a and M1b (p=0.01).

Table 1. *Demographic and clinical characteristics of patients with distant organ metastasis*

	N (%)
Gender	
Female	16 (9.2%)
Male	158 (90.8%)
Cell Type	
SCC	73 (41.9%)
Adenocancer	36 (20.7%)
Adenosquamos cancer	1 (0.6%)
Large cell cancer	1 (0.6%)
Unidentified NSCLC	20 (11.5%)
SCLC	43 (24.7%)
Metastasis locations	
Bone metastasis	72 (41.4%)
Liver metastasis	47 (27%)
Brain metastasis	44 (25.3%)
Adrenal gland metastasis	34 (19.5%)
Contralateral lung metastasis	57 (32.8%)
Pleural metastasis	16 (9.2%)
Other organ metastases*	16 (9.2%)
Organ specific symptoms and findings	
Patients with bone metastasis	62/72 (86.1%)
Patients with brain metastasis	37/44 (84.1%)
Patients with liver metastasis	26/47 (55.3%)

SCC, squamous cell carcinoma; NSCLC, non-small cell carcinoma; SCLC, small cell carcinoma.
*Other organ metastases: pancreas, kidney, thyroid, stomach, intestine, soft tissue.

Discussion

This study showed that NSCLC in bone, brain and contralateral lung; SCLC in liver and adrenal gland

Table 2. *The breakdown in frequency of metastatic disease to specific sites according to histology*

Cell type	n (%)	Brain n (%)	Liver n (%)	Bone n (%)	Adrenal gland n (%)	Contralateral lung n (%)	Pleural metastasis n (%)
SCC	73 (41.9%)	17 (9.8%)	17 (9.8%)	28 (16.1%)	11 (6.3%)	24 (13.8%)	5 (2.9%)
Adeno cancer	36 (20.7%)	12 (6.9%)	3 (1.7%)	17 (9.8%)	5 (2.9%)	16 (9.2%)	5 (2.9%)
Large cell	1 (0.6%)	0 (0%)	0 (0%)	1 (0.6%)	1 (0.6%)	0 (0%)	0 (0%)
Adeno ssquamous	1 (0.6%)	1 (0.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unidentified SCLC	20 (11.5%)	6 (3.4%)	6 (3.4%)	7 (4%)	5 (2.9%)	8 (4.6%)	3 (1.7%)
SCLC	43 (24.7%)	8 (4.6%)	21 (12.1%)	19 (10.9%)	12 (6.9%)	9 (5.3%)	3 (1.7%)
Total	174 (100%)	44 (25.3%)	47 (27%)	72 (%41.4)	34 (19.5%)	57 (32.8%)	16 (9.2%)

SCC, squamous cell carcinoma; SCLC, small cell carcinoma.

Table 3. *Predicting the metastasis with presence of organ-specific symptoms in patients with bone, liver and brain metastases with help of Sensitivity, specificity, PPV, NPV*

Organ specific clinical factors for	sensitivity	specificity	PPV	NPV
Bone metastasis	% 86.1	% 91.7	% 86.1	% 91.7
Liver metastasis	% 59.6	% 93.8	% 75.7	% 87.7
Brain metastasis	% 84.1	% 87.2	% 66.1	% 94.9

PPV, positive predictive value; NPV, negative predictive value.

Table 4. *Survival according to metastasis sites in NSCLC and SCLC*

	NSCLC	SCLC	
Brain metastasis	138 days	81 days	
Bone metastasis	202 days	168 days	
Liver metastasis	157 days	65 days	**p=0.017***
Adrenal gland metastasis	157 days	118 days	
Contralateral lung metastasis	268 days	175 days	

NSCLC, non-small cell carcinoma; SCLC, small cell carcinoma

Table 5. *Relationship between Survival and Organ Specific Symptoms according to Brain-Bone and Liver Metastases in NSCLC and SCLC*

Metastasis sites	Symptom	NSCLC	SCLC	
Brain metastasis	Yes	164 days	257 days	**p=0.0001***
	No	248 days	125 days	
Bone metastasis	Yes	135 days	224 days	**p=0.002***
	No	248 days	118 days	
Liver metastasis	Yes	198 days	65 days	**p=0.005***
	No	219 days	241days	

NSCLC, non-small cell carcinoma; SCLC, small cell carcinoma

were the most frequently seen histologic tumor types. There were organ specific symptoms and signs in patients with bone and brain metastasis, however organ specific signs and symptoms were infrequent in liver and adrenal gland metastasis. The survival was shortened in patients who had symptoms and weight loss. Overall survival was shorter in SCLC than in NSCLC.

Many patients with lung cancer are in advanced stages of the disease at the time of diagnosis. The 5-year survival rate for patients with lung cancer is 10% to 20%, as reported by Stanley[7]. Predicting tumor metastasis sites, understanding metastasis potential of lung cancer subtypes and organ specific symptoms and signs of metastasis may help diagnosing the disease earlier or preventing unnecessary thoracotomy in patients with advanced stage lung cancer.

Although there are some differences in SCLC and NSCLC in the terms of incidence and sites of metastasis; bone, liver, lung, brain and adrenal glands are the most common metastasis sites for both tumor type[8]. In our study, the most common distant metastases sites were bones (41.1%), contralateral-lung (32.8%), liver (27%), brain (25.3%), adrenal (19.5%), pleura (9.2%). While the most common metastases site for NSCLC was bone and it was liver for SCLC.

It is reported that bone metastases from lung cancers occur in 14% to 40% of patients[9]. More than 80% of bone metastases are in the axial skeleton; vertebral column, ribs, pelvis and femur are the most frequently involved bones[10,11]. In a study, multiple bone metastases were seen in more than 84% of patients and the most frequent localization was the vertebrae, which was then the ribs[9], while in another study it was the ribs[12]. In our study, bone metastases tended to be in more than one location in both NSCLC and SCLC. The most common metastasis sites were spine (66.7%) and then ribs (50%). The most frequent clinical symptom in bone metastasis is localized bone pain[11]. In our study, the most common symptom was localized bone pain in 80.6% of cases. There was no pain in 13.9% of patients with bone metastases at all.

Brain metastases are found in about 10–25% of patients at the time of initial diagnosis, and approximately 40–50% of all patients with lung cancer develop brain

metastasis during the course of their disease, with a greater frequency at autopsy (approximately 50%) than predicted from the presence of symptoms[13]. The incidence of brain metastasis is increasing, mainly because of the longer patient survival times resulting from newer treatment modalities. Most patients with brain metastasis have multiple lesions[14]. Metastatic lesions are generally located in supratentorial region, especially in the frontal lobe[14,15]. In our study, brain metastases were detected in 25.3% patients, most often in the frontal lobe (59.1%) and multiple brain metastases were present in 50% of cases. In patients with brain metastases; 70% of patients are asymptomatic and the most common symptom is headache. This is followed by focal sensory or motor loss, speech disorders and epileptic seizures[16]. In a study, there were no symptoms in the half the patients with brain metastases at initial diagnosis[8]. In our study, the most common symptom was headache (45.5%) and 15.9% of patients did not have symptom at all.

Liver is one of the most common metastasis sites of lung cancers. In a study conducted in Japan, 5.8% of lung cancer patients had liver metastases during the initial diagnosis and the most common histologic type was SCLC (45.2%). Number of metastatic nodules in the liver were found to be more than one in 51.6% of patients (47.1% of patients with NSCLC, 92.8% of patients with SCLC)[17]. In our study, 27% of patients had liver metastasis, among them SCLC was the most common histologic type (42.5%). The most of patients had multiple metastases (83%). The disease specific signs and symptoms are infrequent in the early stages of liver metastasis but as the disease progresses, it may occur. Kagogash and colleagues identified the right hypochondriac pain in 8% of patients, irregular nodular liver growth in 3%, jaundice in 3%, the acid in 1.6% and liver enzymes elevation in 22.6%[17]. In our study, hepatomegaly (57.4%), jaundice(4.3%), epigastric pain (2.1%), and acid (2.1%) were detected with descending order. Liver enzymes levels were high in 70.2% of patients with liver metastasis.

Adrenal metastases are often solitary, unilateral localized, small, asymptomatic lesions. Adrenal metastases are seen approximately in 3% of lung cancer patients bilaterally[18]. In our study adrenal metastases were seen in 19.5% of cases and the most common histologic type was SCLC. One-sided settlement was found to be in 67.7% of the cases.

Pleural involvement is seen in 8–15% of cases[18]. There were pleural metastases in 16 (9.2%) of patients in our study. Among them, pleural effusion was seen in 13(7.5%) of cases which was the most commonly due to adenocancers (n=5). There were contralateral lung metastases in 57 (32.8%) patients. It was the most commonly seen in squamous cell carcinoma and then in adenocarcinoma.

Many studies have evaluated the value of organ specific and non-organ specific clinical factors that suggest extrathoracic metastases. The sensitivity, specificity, PPV and NPV have been reported to be 86%, 56%, %31, and 95% respectively for abdomen, 76%, 82%, %52, and 94% for brain and 82%, 62%, 32%, and 90% for liver[19]. In our study, organ-specific symptoms in bone, brain, liver metastases had sensitivity of 86.1%, 59.6%, and 84.1%, specificity of 91.7%, 93.8%, and 87.2%, PPV of 86.1%, 75.7%, and 66.1%, NPV of 91.7%, 87.1%, and 94.9% respectively. Our values were higher than previous studies. We think that organ specific symptoms, physical examination, laboratory findings are important as to show distant organ metastasis. Performing full investigation of extrathoracic metastasis is important so that unnecessary thoracotomy can be prevented.

It was shown that there is a strong correlation between the primary tumor localization, TNM stage and metastases[20]. A study which investigated the brain metastases in NSCLC patients showed the predicted probability of metastatic disease to the brain was positively correlated with size of the primary tumor, cell type and lymph node stage but did not correlate with primary tumor location[21]. In another study showed that, liver metastasis was most frequently seen in centrally localized primary tumors and in T3-T4 and N3[17]. In our study, the primary tumor was the most frequently located in the right upper lobe and the central location (63%) in patients with distant organ metastasis. Also it was revealed that in the brain metastases, the primary tumor was the most frequently settled in the left upper lobe while it was the right upper lobe in bone, liver and adrenal metastasis. Accordingly with other studies, metastases were best correlated with T3-4 and N2-3 in our study.

In a study of 245 patients with advanced NSCLC in which 15.9% of them lived over 2 years showed that long-term survival was closely linked with having a metastases at fewer sites, an absence of bone metastases, a performance status (PS) of 0–1, time to first progression of the tumour of >3 months, normal LDH levels at diagnosis and a haemoglobin concentration >110 g/L at first progression of the tumour[4]. In a study of 84 NSCLC patients presenting a solitary brain metastasis who underwent surgery have had calculated median survival of 9.7 months and survival

was correlated with the tumor stage[22]. In our study the median survival time was 198 days and a significant correlation was observed between weight loss and survival. An increase in TNM stage and the number of metastases were correlated with decreased survival. Survival was shortened in patients with symptoms. Overall survival was shorter in SCLC than in NSCLC.

Limitation of this study; treatment modalities were not evaluated in the survival analysis. Since treatment modalities according to cell type, performance status and site of metastasis may cause differences in survival. However, number of patients was not enough for subgroup analysis according to different treatment modalities. More comprehensive studies on this topic are needed.

As a result patients who have primary tumor T3-4, lymph node metastases N2-3, weight loss, organ-specific symptoms and signs are more likely to have a metastasis. Organ-specific symptoms and signs may help in predicting metastases in patients with lung cancer, however it should not be forgotten that there might be metastases, even in patients who do not have signs and symptoms. In addition, survival in NSCLC and SCLC may vary according to location and number of metastasis and the presence of symptoms. Therefore, evaluation of all these factors by clinicians can help diagnosing the disease earlier and prevent unnecessary surgery.

Financial/Nonfinancial Disclosures

The authors have reported that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

Acknowledgements

The manuscript has been read and approved by all authors and has never been published, or under the consideration for publication elsewhere. All person listed as authors have contributed to preparing the manuscript, and that no persons other than the authors listed have contributed significantly to its preparation. I would like thank you for your time in reviewing this submission. I would also be glad review other authors studies on the behalf your journal.

References

1. Jemal A, Bray F, Center MM, et al. Global cancer statistics. CA Cancer J Clin 2011;61:69–90.
2. Scagliotti GV. Symptoms, signs and staging of lung cancer. European Respiratory Monograph 2001;17:86–119.
3. Jemal A, Murray T, Ward E, et al. Cancer Statistics, 2005. CA Cancer J Clin 2005;55:10–30.
4. Giroux Leprieur E, Lavole A, Ruppert A-M, et al. Factors associated with long-term survival of patients with advanced non-small cell lung cancer. Respirology 2012;17:134–42.
5. Erturan S. The Role of Whole-Body Bone Scanning and Clinical Factors in Detecting Bone Metastases in Patients With Non-small Cell Lung Cancer. Chest 2005;127:449.
6. Detterbeck FC, Boffa DJ, Tanoue LT. The new lung cancer staging system. Chest 2009;136:260–71.
7. Stanley KE. Prognostic factors for survival in patients with inoperable lung cancer. J Natl Cancer Inst 1980;65:25–32.
8. Yamanaka R, Koga H, Yamamoto Y, et al. Characteristics of patients with brain metastases from lung cancer in a palliative care center. Support Care Cancer 2011;19:467–73.
9. Sugiura H, Yamada K, Sugiura T, et al. Predictors of survival in patients with bone metastasis of lung cancer. Clin Orthop Relat Res 2008;466:729–36.
10. Kosteva J, Langer C. The changing landscape of the medical management of skeletal metastases in nonsmall cell lung cancer. Curr Opin Oncol 2008;20:155–61.
11. Tsuya A, Kurata T, Tamura K, et al. Skeletal metastases in non-small cell lung cancer: a retrospective study. Lung Cancer 2007;57:229–32.
12. Mordant P, Arame A, De Dominicis F, et al. Which metastasis management allows long-term survival of synchronous solitary M1b non-small cell lung cancer? Eur J Cardiothorac Surg 2012;41:617–22.
13. Monnet I. Chemotherapy for small cell lung cancer with brain metastases. Bull Cancer 2013;100:89–93.
14. Paralkar VR, Li T, Langer CJ. Population characteristics and prognostic factors in metastatic non-small-cell lung cancer: a Fox Chase Cancer Center retrospective. Clin Lung Cancer 2008;9:116–21.
15. Soffietti R, Cornu P, Delattre JY, et al. EFNS Guidelines on diagnosis and treatment of brain metastases: report of an EFNS Task Force. Eur J Neurol 2006;13:674–81.
16. Hochstenbag MMH, Twijnstra A, Hofman P, et al. MR-imaging of the brain of neurologic asymptomatic patients with large cell or adenocarcinoma of the lung. Does it influence prognosis and treatment? Lung Cancer 2003;42:189–93.
17. Kagohashi K, Satoh H, Ishikawa H, et al. Liver metastasis at the time of initial diagnosis of lung cancer. Med Oncol 2003;20:25–8.
18. Karanikiotis C, Tentes AA, Markakidis S, et al. Large bilateral adrenal metastases in non-small cell lung cancer. World J Surg Oncol 2004;2:37.
19. Silvestri GA, Gould MK, Margolis ML, et al. Noninvasive staging of non-small cell lung cancer: ACCP evidenced-based clinical practice guidelines (2nd edition). Chest 2007;132:178S-201S.
20. Penel N, Brichet A, Prevost B, et al. Pronostic factors of synchronous brain metastases from lung cancer. Lung Cancer 2001;33:143–54.
21. Mujoomdar A, Austin JHM, Malhotra R, et al. Clinical Predictors of Metastatic Disease to the Brain from Non-Small Cell Lung Carcinoma: Primary Tumor Size, Cell Type, and Lymph Node Metastases. Radiology 2007;242:882–8.
22. Hu C, Chang EL, Hassenbusch SJ, et al. Nonsmall cell lung cancer presenting with synchronous solitary brain metastasis. Cancer 2006;106:1998–2004.

KAFKAS TIP BİLİMLERİ DERGİSİ
Kafkas Journal of Medical Sciences
Kafkas J Med Sci 2016; 6(2):121–129 • doi: 10.5505/kjms.2016.60490

DERLEME / *REVIEW*

Kidney Ultrasound Elastography: Review

Böbrek Ultrason Elastografisi: Derleme

Mahmut Duymuş[1], Mehmet Sait Menzilcioğlu[1], Mustafa Gök[2], Serhat Avcu[1]

[1]Gazi University Faculty of Medicine, Department of Radiology, Ankara; [2]Adnan Menderes University Faculty of Medicine, Department of Radiology, Aydın

ABSTRACT

Kidneys are the most important and the functional organs in the body. There are numerous of disorders affecting the kidneys. The most important disorder is chronic kidney disease because of being costly and going to failure. In recent years ultrasound elastography technics showed increasing development line, and more studies were performed about elastography on kidneys. The weighted amount of the elastography studies are about chronic kidney disease, kidney failure and allograft patients, while some of them are about kidney masses or diabetic nephropathy. Various studies presented various results. In this review we want to present the elastography studies about kidney.

Key words: *kidney; elastography; chronic kidney disease*

ÖZET

Böbrekler çok önemli ve fonksiyonel organlardır. Böbreği etkileyen çok sayıda hastalık vardır. Kronik böbrek hastalığı yüksek maliyeti ve yetmezliğe ilerlemesi nedeniyle en önemli hastalıktır. Son yıllarda sonoelastografi tekniği yükselen bir grafik çizmektedir ve böbrekler üzerinde sonoelastografi tekniği kullanılarak yapılmış değişik çalışmalar mevcuttur. Bu çalışmaların çoğunluğu kronik böbrek hastalığı, böbrek yetmezliği ve allograft hastalarını konu alırken, bazıları böbrek kitleleri ve diabetik nefropati hakkındadır. Farklı çalışmalarda farklı sonuçlar sunulmuştur. Bu derlemede böbrekler hakkında yapılan sonoelastografi çalışmalarını sunmayı planladık.

Anahtar kelimeler: *böbrek; elastografi; kronik böbrek hastalığı*

Abbreviations (Listed in Alphabetical Order)

Acoustic Radiation Force Impulse Elastography (ARFI)
Angiomyolipoma (AML)
Chronic Allograft Injury (CAI)
Chronic Allograft Nephropathy (CAN)
Chronic Kidney Disease (CKD)
Dimercaptosuccinic acid (DMSA)
estimated Glomerular Filtration Rate (eGFR)
Glomerular Filtration Rate (GFR)
Intravenous Pyelography (IVP)
kiloPascal (kPa)
Magnetic Resonance Imaging (MRI)
Pulsatility Index (PI)
Renal Cell Carcinoma (RCC)
Resistive Index (RI)
Real-time sonoelastography (RSE)
Region of Interet (ROI)
Real-time elastography (RTE)
Renal Transplant Recipients (RTRs)
Strain Elastography (SE)
Strain Index (SI)
Strain Ratio (SR)
Supersonic Shear Imaging (SSI)
Shear-wave Elastography (SWE)
Shear Wave Speed (SWS)
Shear Wave Velosity (SWV)
Transient Elastography (TE)
Tissue Mean Elasticity (TME)
Ultrasonography (USG, US)
Vesico Ureteral Reflux (VUR)
Zero-Crossing (ZC)

Yard. Doç. Dr. Mahmut Duymuş, Gazi Üniversitesi Tıp Fakültesi, Radyoloji Anabilim Dalı, Ankara, Türkiye, Tel. 0312 212 68 40 Email. mahmutduymush@yahoo.com
Geliş Tarihi: 13.04.2016 • Kabul Tarihi: 21.06.2016

Kidneys

Kidneys are vital and important organs, anatomically and functionally depicted as parenchyma and sinus. Parenchyma consists of cortex and medulla, and sinus consists of fat, tubulary collecting system, pelvis, blood vessels and nerves[1]. There are numerous of disorders affecting the kidneys. Some of them are functional, systemic and diffuse, while some are local and massy, and also vascular, congenital, hereditary and acquired[2,3]. Among all the disorders, chronic kidney disease (CKD) and transplanted kidneys are the subject of elastography in a majority of studies[4–14]. CKD is an important and costly health problem because of not only the increasing incidence and prevalence but also resulting in end-stage renal failure. The progression of CKD shows fibrosis involving first glomeruli or interstitial space[15–19]. Fibrosis can be detected only by the biopsy procedure, which is interventional and non confortable for the patients. To detect the fibrosis, non-invasive and quickly obtained methods are essential for nephrologists not

to waste time and to plan the treatment. The fibrosis changes the microstructure and elasticity of the tissue[20]. Elastography presents the elasticity of the tissue but has not been placed in the routine diagnostic algorithm of the kidney disorders. In this review, we aim to discuss the USG elastography method in kidney disorders with the literature background.

Elastography

Elastography was first described by Ophir et al.[21]. The working principle of elastography is based on the lesion or tissue stiffness. Standard USG device and elastography software are enough to establish the elastography. Basicly two types of elastography can be counted as quasci static and dynamic differentiating each other from data collecting way and the software. Strain elastography (SE) is quasci static method. Shear-wave Elastography (SWE), Acoustic Radiation Force Impulse Elastography (ARFI) and Transient elastography (TE) are the dynamic types[22,23].

Dynamic Methods

(Acoustic Radiation Force Impulse Elastography, Shear-Wave Elastography, and Transient Elastography)

Shear-wave elastography uses shear-waves to collect the data. The propagation speed of the shear wave is measured in this method. The software processes the shear-wave propagation in very very short time and quickly (20.000 frame in second) and presents the quantitable values. The unit of shear wave is m/sec and the tissue elasticity is kiloPascal (kPa) (Fig. 1 and Fig. 2). The elasticity formula is $E=\rho c^2$. The 'E' indicates the tissue elasticity, 'ρ' (kg/cm^3) indicates the tissue density, while 'c' (m/sec) indicates the shear-wave speed. But SWE has some limitations, such as lack of measurement in ascites medium. The operator independency is the superiority of SWE[22,24]. The major handicap of SWE is the anisotropy, which is related with the tissue structure and the beam distribution. The renal cortical structure shows radial distribution from hilus to cortex. The USG beams come in different angles to the poles and equator of the kidney. If the beams come parallel to these structures, shear waves propagate perpendicularly, while beams come perpendicular shear waves propagate parallelly. This anisotropy causes disconcordance in the values of poles and equator[23,25].

ARFI is another method that uses shear-waves as SWE does. But the data acquisition of ARFI is different from the SWE. In ARFI the high energized short term (0.03–0.04 msec) acoustic pulses, make the micrometric (1–20 μm) displacements in the examined tissue. Square shaped Region of Interet (ROI) is used to measure the micrometric displacements. The displacement generates the shear-waves. ARFI uses the displacement of the examined tissue using shear waves, but does not use the speed of shear-wave unlike SWE. The soft tissues are bright, while the hard tissues are dark in ARFI in gray scale screen. The unit of ARFI is m/sec. Operator independency and the quantitative data presentation are the advantages of ARFI, but does not have capability to present data in ascites mediums like in SWE[22,26–28].

TE is one of the methods that use shear-waves. The main usage area and the studies about TE is based on the liver. In this method, the USG probe applies external mechanical impulse to the related tissue, thus shear-wave generates in the related tissue. The speed and the displacement of the shear wave according to the deepness generate an image like in M-mode. So the major handicap of TE is lack of gray scale B-mode USG images. TE can only serve the M-mode USG images. The speed of the shear wave increases with the stiffness of the tissue. TE can not be used in the existence of perihepatic fluid. The evaluated area is 200 times bigger (3 cm^3) than the biopsy. The unit of TE is kPa. In TE, the inter and the intra-observer variability is minimal. But there are also some limitations, such as obesity, does not have capability to present data in ascites mediums and in focal lesion. The main limitation about liver is the non capability of measurement in left lobe[22,23,28–32].

Quasi Static Method (SE)

Strain Elastography is different from shear-wave elastography methods in some ways. In SE the acoustic force is applied by the operator manually. The operator does not only produce the acoustic force, but also produces the dynamic force to the examined tissue, thus this method is semi-static. The operator or transducer applies compression and decompression pulses to the related lesion. The measurements should be collected in the decompression phase, to avoid the pressure effect. SE measures the displacement and the deformation of the lesion. The unit of SE is Strain Index (SI). SI, means the stiffness ratio of the adjacent tissue compared to the examined lesion. The stiffness of the hard lesions is higher, thus the displacement and deformation is lower. So, the strain of hard lesions is lower, but the SI of hard lesions is higher, because of the ratio. In this method, two ROIs

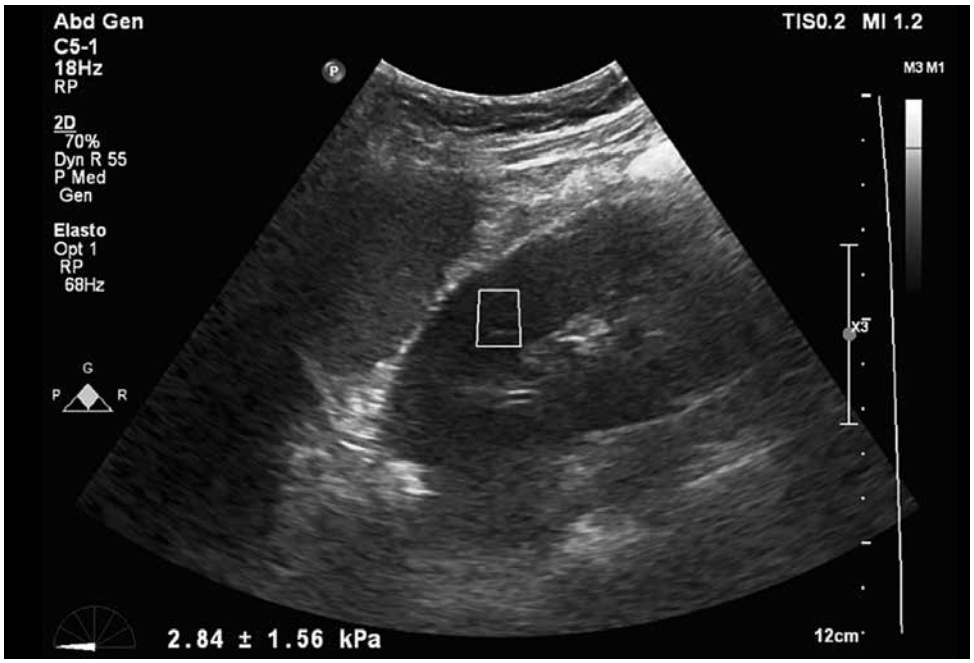

Figure 1. *Shear wave elastography image of kidney parenchyma. The square indicates the measurement localization. The number below the figure indicates stiffness of the tissue in the unit of kPa.*

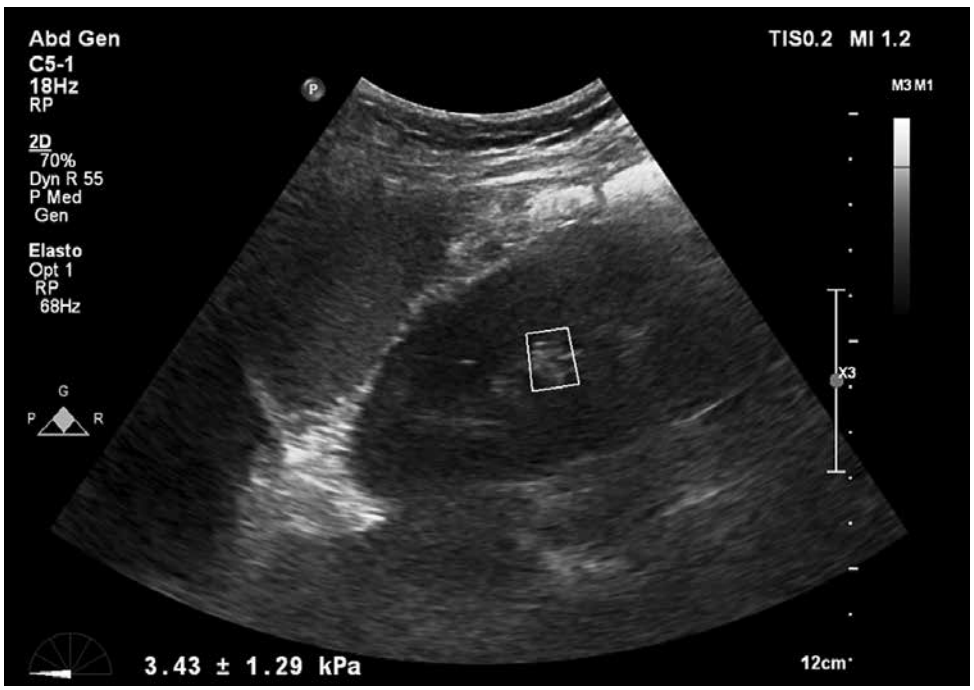

Figure 2. *Shear wave elastography image of kidney sinus. The square indicates the measurement localization. The number below the figure indicates stiffness of the tissue in the unit of kPa.*

are required to measure and compare the stiffness (Fig. 3 and Fig. 4). The major limitation of the SE is operator dependency. The window width and the transducer pressure affects the image quality. The window should be arranged as optimal as the lesion size. The compression and the decompressions should be done slightly and not very slow or not very fast (0.5–2 compressions in a second). The distance between the lesion and the transducer should be less than 3–4 cm to acquire more reliable data. This method has an advantage about providing data in ascites medium, unlike others[20,22,23,33,34].

The major limitation of all elastography methods are small sample size. For example strain ratio needs to rate

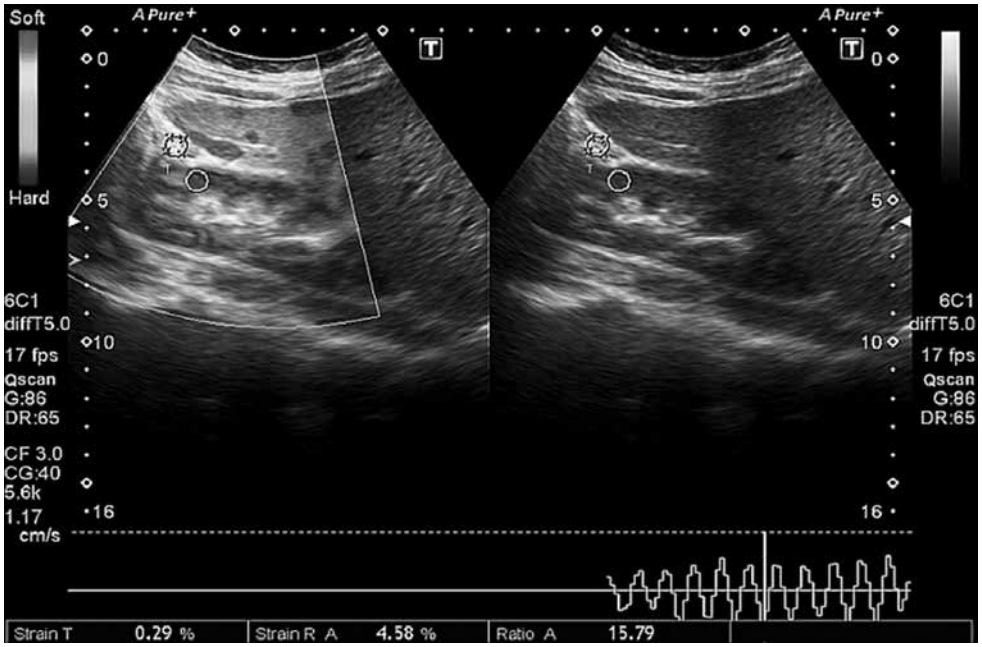

Figure 3. *Strain elastography image of the kidney parenchyma. The image shows active elastography mode of ultrasonography (USG). The screen was divided into three parts as right, left and bottom. The color coded left side indicates elastography mode, while the right side is gray scale B-mode USG image. The bottom indicates the sinusoidal wave, which allows the operator to follow the compression and decompressions. The circles indicates the region of interests (ROI). One ROI was adjusted to the parenchyma while the other was in the perirenal fat tissue. The strain ratio was given below the screen.*

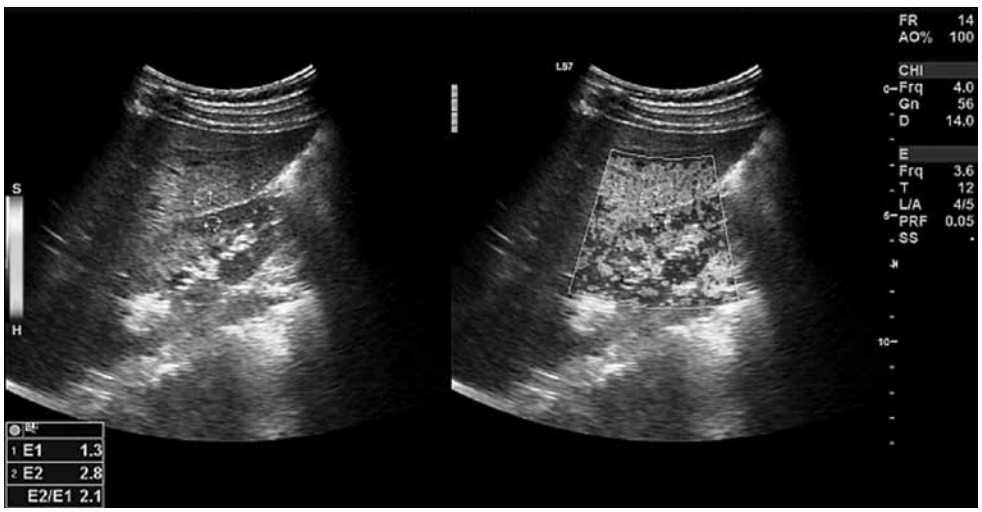

Figure 4. *Strain elastography image of the kidney parenchyma. The right side of the image indicates the elastography mode. Two ROIs seen in the left side image. One of them was udjusted to the liver parenchyma while the other was on the kidney parenchyma. The numbers below the screen indicates the strain ratio of the parenchyma and the adjacent tissue.*

the two adjacent tissue. The operator can only adjust the ROI size according to the parenchyma/sinus and the perisplenic soft tissue. To avoid the tissue wrong sampling, operator should use maximum sampling ROIs. Maximum ROI should present the the more reliable value. But using maximum ROI will take a lot of time. In addition to ROI size, the organs have three dimensions but the US systems allows the operator to measure in two dimension. If operator can measure whole the kidney this measurement will present only two dimentional one slice value[35]. This means that, operator should take more measurements from different aspects of the kidney. This procedure also takes more time.

Literature Review

In the advanced search mode of Pubmed using the words 'kidney elastography', picking the MeSH terms and Title/Abstract, 49 results were listed. Some of them were about animals[36–42], some of them were about MRI or MR elastography[43–52], some of them were about other organ systems[53–65], some of them were about elastography technic[28,66–69] and some of them were about non elastography related kidney studies[70]. We excluded these articles. The rest amount of related articles were 13[4,5,8–11,13,14,25,71–74]. But, pubmed search missed some articles[6,7,12,35,75], that was mentioned in this paper (Table 1).

Table 1. *The articles that we discussed*

Reference	Elastography type	Patient population	Study design	Conclusion
Ardnt 2010 et al. Noninvasive evaluation of renal allograft fibrosis by transient elastography--a pilot study	TE (Fibroscan)	Renal transplanted 55 patients, Biopsies were performed in 20 patients.	Evaluates the feasibility of TE for the assessment of renal allograft fibrosis. Stiffness was significantly correlated to the extent of interstitial fibrosis (Pearson r: 0.67, P: 0.002, R(2): 0.45) and inversely related to eGFR (Pearson r: -0.47, P: 0.0003, R(2): 0.22). The stiffness values of chronic allograft injury Banff grades 0-1 differed significantly from grade 2 (P: 0.008) and grade 3 (P: 0.046).	Parenchymal stiffness measured by TE reflects interstitial fibrosis in kidney allografts.
Asano et al. Acoustic radiation force impulse elastography of the kidneys: is shear wave velocity affected by tissue fibrosis or renal blood flow?	ARFI (Siemens Acoson S2000)	319 CKD, 14 healthy volunteers	Identify the main influencing factor of the SWV. The SWV decreased concurrently with a decline in the eGFR. A low SWV was obtained in patients with a high brachial-ankle pulse wave velocity. Despite progression of renal fibrosis in the advanced stages of CKD, these results were in contrast to findings for chronic liver disease, in which progression of hepatic fibrosis results in an increase in the SWV. Considering that a high brachial-ankle pulse wave velocity represents the progression of arteriosclerosis in the large vessels, the reduction of elasticity succeeding diminution of blood flow was suspected to be the main influencing factor of the SWV in the kidneys.	Diminution of blood flow may affect SWV values in the kidneys more than the progression of tissue fibrosis.
Dillman et al. Can Shear-Wave Elastography be Used to Discriminate Obstructive Hydronephrosis from Nonobstructive Hydronephrosis in Children?	SWE (Siemens)	37 children	Children underwent elastography of the kidneys immediately before and immediately after diuretic renal scintigraphy (reference standard for presence of urinary tract obstruction). Median SWS measurements, as well as change in median SWS (median SWS after diuretic administration minus median SWS before diuretic administration) were correlated with the amount of time required for kidney radiotracer activity to fall by 50% after intravenous administration of the diuretic ($T_{1/2}$). Median SWS measurements were compared with degree of obstruction and degree of hydronephrosis with analysis of variance.	US SWS measurements did not enable discrimination of obstructive hydronephrosis from unobstructive hydronephrosis in children.
Gao 2013 et al. Renal transplant elasticity ultrasound imaging: correlation between normalized strain and renal cortical fibrosis	SE (EchoInsight, Epsilon Imaging)	20 renal transplant	The hardness of the renal cortex in renal transplant allograft patients using a normalized ultrasound strain procedure measuring quasi-static deformation. Normalized strain is defined as the mean developed strain in the renal cortex divided by the overall mean strain measured in the soft tissues from the abdominal wall to pelvic muscles. Banff scoring.	Renal cortex strain is strongly correlated with grade of renal cortical fibrosis. Normalized strain is superior to developed strain in distinguishing moderate from mild renal cortical fibrosis.
Gao 2013 et al. Corticomedullary strain ratio: a quantitative marker for assessment of renal allograft cortical fibrosis	SE (Siemens Acuson Sequoisa 512)	Renal allograft 33 patients	Correlation between the corticomedullary SR and cortical fibrosis in renal transplants. on Banff scoring. We calculated the corticomedullary SR (cortical normalized strain/medullary normalized strain; normalized strain = developed strain/applied strain [deformation from the abdominal wall to the pelvic muscles]).	Strain values vary in different compartments of the kidney. The corticomedullary SR on USG elasticity imaging decreases with increasing renal cortical fibrosis, which makes it potentially useful as a noninvasive quantitative marker for monitoring the progression of fibrosis in renal transplants.
Gao 2014 et al. Ultrasound strain zero-crossing elasticity measurement in assessment of renal allograft cortical hardness: a preliminary observation	SE (quasi-static ultrasound elastography	38 renal transplant patients	USG strain ZC elasticity measurement can be used to discriminate moderate cortical fibrosis or inflammation in renal allografts, we assessed cortical hardness with quasi-static USG elastography in renal transplant patients who underwent kidney biopsy. Banff scoring.	ZC is a new strain marker that could be straightforward to interpret and perform, making it a potentially practical approach for monitoring progression of cortical fibrosis or inflammation in renal allografts.
Goya 2015 et al. The role of quantitative measurement by acoustic radiation force impulse imaging in differentiating benign renal lesions from malignant renal tumours	ARFI (Siemens Acoson S2000)	60 patients with renal lesions; benign, malign and infectious	Evaluate the diagnostic performance of ARFI for differentiating benign lesions from malignant renal tumours. The final diagnoses were determined via pathologic (n = 33), clinical (n = 13) and imaging findings (n = 14). The SWV values of the renal tumours were analysed according to the final diagnoses.	ARFI imaging may be useful for differentiating between benign renal lesions and malignant renal tumours.

Table 1 (continued). *The articles that we discussed*

Reference	Elastography type	Patient population	Study design	Conclusion
Goya 2015 et al. Acoustic radiation force impulse (ARFI) elastography for detection of renal damage in children	ARFI (Siemens Acoson S2000)	88 children, 20 healthy controls	To investigate the contribution of ARFI quantitative USG elastography for the detection of renal damage in kidneys with and without VUR. Patients were assessed according to severity of renal damage on DMSA scintigraphy.	Decreasing SWV of renal units with increasing grades of VUR.
Goya 2015 et al. Acoustic radiation force impulse imaging for evaluation of renal parenchyma elasticity in diabetic nephropathy	ARFI (Siemens Acoson S2000)	114 diabetic nephropathy, 281 healthy	Evaluate the changes in the elasticity of the renal parenchyma in diabetic nephropathy using ARFI acoustic radiation force impulse imaging. The changes in the renal elasticity were compared between the different stages of diabetic nephropathy and the healthy control group.	ARFI imaging could be used for the evaluation of the renal elasticity changes that are due to secondary structural and functional changes in diabetic nephropathy.
Grenier 2011 et al. [Imaging and renal failure: from inflammation to fibrosis]				Article in French
Grenier 2013 et al. Renal ultrasound elastography				Review
Grenier et al., 2012 Quantitative elastography of renal transplants using supersonic shear imaging: a pilot study	SWE	43 kidney transplant recipient, followed by biopsy	The reliability of quantitative ultrasonic measurement of renal allograft elasticity using SSI. Banff score.	Quantitative measurement of renal cortical stiffness using SSI is a promising non-invasive tool to evaluate global histological deterioration.
He WY 2014 Tissue elasticity quantification by acoustic radiation force impulse for the assessment of renal allograft function	ARFI	52 stable renal function, 50 biopsy-proven allograft dysfunction	Renal allograft stiffness using ARFI quantification in patients with stable renal function and those with biopsy-proven allograft dysfunction. ARFI quantification, given as SWV. The RI was calculated by pulsed-wave Doppler ultrasound, and clinical and laboratory data were collected.	Tissue elasticity quantification by ARFI is more accurate than the RI in diagnosing renal allograft function.
Lukenda V 2014 Transient elastography: a new noninvasive diagnostic tool for assessment of chronic allograft nephropathy	TE (Fibroscan Echosense)	52 Renal transplant recipies	CAN is the most common cause of kidney allograft failure. Protocol biopsies remain the “gold standard” in CAN recognition. Usefulness of TE for the assessment of kidney allograft fibrosis in RTRs.	Parenchymal stiffness obtained by TE reflects interstitial fibrosis. Therefore, TE provides the opportunity for noninvasive screening of CAN.
Menzilcioğlu 2015 et al. Strain wave elastography for evaluation of renal parenchyma in chronic kidney disease	SE (Toshiba Aplio 500)	58 patients with CKD, 40 healhty individuals	Determine the difference of SI value of renal parenchyma between patients with CKD and healthy individuals.	SI value can be used to differentiate patients with CKD and healthy individuals. We have not shown that it can reliably differentiate different stages.
Orrlachio 2014 et al. Kidney transplant: usefulness of real-time elastography (RTE) in the diagnosis of graft interstitial fibrosis	SE (real-time elastography-RTE)	50 patients with graft fibrosis	Evaluate the usefulness of RTE in the diagnosis of graft interstitial fibrosis. TME was calculated by two blinded operators. All patients underwent biopsy after RTE. Banff score.	RTE was able to evaluate kidney fibrosis and could be used as complementary imaging during follow-up of renal transplant patients.
Özkan 2013 et al. Interobserver variability of ultrasound elastography in transplant kidneys: correlations with clinical-Doppler parameters	SE (real-time elastography-RTE)	42 adult renal transplant recipients	Evaluate the ability of investigators to use sonoelastography to detect differences in renal cortical stiffness and assess the relationship between stiffness and clinical-Doppler parameters.	SR showed significant positive correlation with RI and PI but sonoelastography has also wide range intra- and low interobserver agreement in renal transplants.
Tan 2013 et al. Real-time elastography for distinguishing angiomyolipoma from renal cell carcinoma: preliminary observations	SE (real-time elastography-RTE) (GE Logiq E9)	47 lesion detected patients 19 RCC, 28 AML	Diagnostic performance of sonoelastography for differentiating AML from RCC. The elasticity patterns and the strain ratio were evaluated independently by two observers. Blue areas in < 50% of lesion, considered type 1 or type 2) by both radiologists, whereas 18 of 19 renal cell carcinomas were classified as having a low-strain elastographic pattern (blue areas in >/= 50% of lesion, considered type 3 or 4) by both radiologists.	Real-time elastography may be useful in differentiating AML from RCC, by use of both elasticity patterns and strain ratios.

TE, transient elastography; eGFR, estimated glomerular filtration rate; ARFI, acoustic radiation force impulse elastography; CKD, chronic kidney disease; SWV, shear-wave velosity; SWE, shear-wave elastography; SWS, shear-wave speed; US, ultrasonography; SR, strain ratio; USG, ultrasonography; ZC, zero-crossing; VUR, Vesico ureteral reflux; DMSA, dimercaptosuccinic acid; SSI, supersonic shear imaging; RI, resistive ındex; CAN, chronic allograft nephropathy; RTRs, renal transplant recipients; RTE, real-time sonoelastography; TME, tissue mean elasticity; AML, angiomyolipoma; RCC, renal cell carcinoma.

Table 2. *Summary of the studies according to patient population, elastography type and study design*

Children	Dillman et al., Goya et al. 2015
Transplanted kidney	Arndt et al., Gao 2013 et al., Gao 2013 et al., Gao 2014 et al., Grenier et al., He WY et al., Lukenda et al., Orlacchio et al., Ozkan et al.
CKD	Asano et al., Menzilcioğlu et al.
SWE (ARFI, SWE and TE)	Arndt et al., Asano et al., Dillman et al., Goya 2014 et al., Goya 2015 et al., Goya 2015 et al., Grenier et al., He WY et al., Lukenda et al.
SE	Gao 2013 et al., Gao 2013 et al., Gao 2014 et al., Menzilcioğlu et al., Orlacchio et al., Özkan et al., Tan et al.
Inter-intraobserver variability	Asano et al., Goya 2015 et al., Grenier et al., Orlacchio et al., Özkan et al.
Mass	Goya 2015 et al., Tan et al.
Diabetic nephropathy	Goya 2015 et al.

CKD, chronic kidney disease; ARFI, acoustic radiation force impulse elastography; SWE, shear-wave elastography; TE, transient elastography; SE, strain elastography.

In the studies about CKD, renal transplant recipient (end-stage CKD) or transplanted patients most of the studies revealed that elastography allows the operator to differentiate the fibrotic cortex from non-fibrotic freely from the elastography method (Table 2). Anyway, there is no adequate and reliable data about differentiating the grades of fibrosis[4–14]. Perhaps in near future these results should assist the clinicians to use elastography instead of biopsy. It is obviously clear that more studies are needed about elastography and kidneys. Althouh there is a consensus about differentiating the fibrosis, inter and intra-observer compatibility is low yet[5,14]. This may be related with the different measurement points (adjusting the ROI different regions) and the lack of number of samples. The more sampling should increase the inter and intra-observer compatibility.

Cortical elasticity has not only the field about CKD but also can be used in the diabetic nephropathy. Goya et al reported a treshold to distinguish the diabetic kidney and apparently normal kidney with the sensitivity of 84.1% and the specificity of 67.3%[72].

There are few studies about children. Goya was reported decrement in SWV with increasing grades of VUR, while Dilman reported as elastography did not allow to disctriminate the obstructive hydronephrosis fron non-obstructive hydronephrosis[35,75].

Goya et al and Tan et al used elastography for characterization of the masses. Goya et al reported that benign and malignant lesions' SWV were higher than those of intact renal parenchyma, while haematomas' SWV values were lower[71]. Tan et al focused on the angiomyolipomas (AML) and renal cell carcinomas (RCC), using two different observers and real time elastography. In conclusion they finished suggesting real-time elastography to differentiate RCC and AML[74].

Conclusion

Sonographic elastography is a new developing technic, and various studies have been made using elastography in kidneys. Most of the studies are made on the transplanted or CKD kidneys to evaluate the effectiveness of elastography in the evaluation of corticomedullary fibrosis to preserve the patient from the invasive method, biopsy. And also most of the studies were performed using SWE elastography. The results showed that, SWV values increase with the degree of fibrosis and perhaps in near future especially SWE would take the place of biopsy.

References

1. Rha SE, Byun JY, Jung SE, et al. The Renal Sinus: Pathologic Spectrum and Multimodality Imaging Approach. RadioGraphics 2004;24:S117-31.
2. Seçil M. Böbrekler. Temel Ultrasonografi ve Doppler. İzmir: Meta Basım Matbaacılık Hizmetleri; 2013;310–60.
3. Tuncel E. Boşaltım ve Üreme Sistemi. Klinik Radyoloji. Bursa: Nobel & Güneş Tıp Kitabevi; 2008:541–670.
4. Arndt R, Schmidt S, Loddenkemper C, et al. Noninvasive evaluation of renal allograft fibrosis by transient elastography –a pilot study. Transpl Int 2010;23:871–7.
5. Asano K, Ogata A, Tanaka K, et al. Acoustic radiation force impulse elastography of the kidneys: is shear wave velocity affected by tissue fibrosis or renal blood flow? J Ultrasound Med 2014;33:793–801.
6. Gao J, Min R, Hamilton J, et al. Corticomedullary strain ratio: a quantitative marker for assessment of renal allograft cortical fibrosis. J Ultrasound Med 2013;32:1769–75.

7. Gao J, Rubin JM. Ultrasound strain zero-crossing elasticity measurement in assessment of renal allograft cortical hardness: a preliminary observation. Ultrasound Med Biol 2014;40:2048–57.
8. Gao J, Weitzel W, Rubin JM, et al. Renal transplant elasticity ultrasound imaging: correlation between normalized strain and renal cortical fibrosis. Ultrasound Med Biol 2013;39:1536–42.
9. Grenier N, Poulain S, Lepreux S, et al. Quantitative elastography of renal transplants using supersonic shear imaging: a pilot study. Eur Radiol 2012;22:2138–46.
10. He WY, Jin YJ, Wang WP, et al. Tissue elasticity quantification by acoustic radiation force impulse for the assessment of renal allograft function. Ultrasound Med Biol 2014;40:322–9.
11. Lukenda V, Mikolasevic I, Racki S, et al. Transient elastography: a new noninvasive diagnostic tool for assessment of chronic allograft nephropathy. Int Urol Nephrol 2014;46:1435–40.
12. Menzilcioglu MS, Duymus M, Citil S, et al. Strain wave elastography for evaluation of renal parenchyma in chronic kidney disease. Br J Radiol 2015;88:20140714.
13. Orlacchio A, Chegai F, Del Giudice C, et al. Kidney transplant: usefulness of real-time elastography (RTE) in the diagnosis of graft interstitial fibrosis. Ultrasound Med Biol 2014;40:2564–72.
14. Ozkan F, Yavuz YC, Inci MF, et al. Interobserver variability of ultrasound elastography in transplant kidneys: correlations with clinical-Doppler parameters. Ultrasound Med Biol 2013;39:4–9.
15. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. Jama 2007;298:2038–47.
16. Guo LH, Xu HX, Fu HJ, et al. Acoustic radiation force impulse imaging for noninvasive evaluation of renal parenchyma elasticity: preliminary findings. PLoS One 2013;8: e68925.
17. Meguid El Nahas A, Bello AK. Chronic kidney disease: the global challenge. Lancet (London, England) 2005;365:331–40.
18. Chatziantoniou C, Boffa JJ, Tharaux PL, et al. Progression and regression in renal vascular and glomerular fibrosis. International journal of experimental pathology 2004;85:1–11.
19. Ricardo SD, van Goor H, Eddy AA. Macrophage diversity in renal injury and repair. The Journal of clinical investigation 2008;118:3522–30.
20. Garra BS. Imaging and estimation of tissue elasticity by ultrasound. Ultrasound Q 2007;23:255–68.
21. Ophir J, Cespedes I, Ponnekanti H, et al. Elastography: a quantitative method for imaging the elasticity of biological tissues. Ultrason Imaging 1991;13:111–34.
22. Onur MR, Göya C. Ultrason Elastografi: Abdominal Uygulamalar. Turkiye Klinikleri Journal of Radiology Special Topics 2013;6:59–69.
23. Bamber J, Cosgrove D, Dietrich CF, et al. EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 1: Basic principles and technology. Ultraschall Med 2013;34:169–84.
24. Ferraioli G, Tinelli C, Zicchetti M, et al. Reproducibility of real-time shear wave elastography in the evaluation of liver elasticity. Eur J Radiol 2012;81:3102–6.
25. Grenier N, Gennisson JL, Cornelis F, et al. Renal ultrasound elastography. Diagn Interv Imaging 2013;94:545–50.
26. Yu H, Wilson SR. Differentiation of benign from malignant liver masses with Acoustic Radiation Force Impulse technique. Ultrasound Q 2011;27:217–23.
27. Nightingale K, McAleavey S, Trahey G. Shear-wave generation using acoustic radiation force: in vivo and ex vivo results. Ultrasound Med Biol 2003;29:1715–23.
28. Davies G, Koenen M. Acoustic radiation force impulse elastography in distinguishing hepatic haemangiomata from metastases: preliminary observations. Br J Radiol 2011;84:939–43.
29. Frulio N, Trillaud H. Ultrasound elastography in liver. Diagn Interv Imaging 2013;94:515–34.
30. Alahdab YÖ, Yılmaz Y. Transient Elastografi (Fibroscan®): Karaciğer Fibrozisinin Değerlendirilmesinde Yeni Ufuk. Güncel Gastroenteroloji 17:59–64.
31. Myers RP, Pomier-Layrargues G, Kirsch R, et al. Feasibility and diagnostic performance of the FibroScan XL probe for liver stiffness measurement in overweight and obese patients. Hepatology 2012;55:199–208.
32. Roulot D, Czernichow S, Le Clesiau H, et al. Liver stiffness values in apparently healthy subjects: influence of gender and metabolic syndrome. J Hepatol 2008;48:606–13.
33. Doyley MM, Bamber JC, Fuechsel F, et al. A freehand elastographic imaging approach for clinical breast imaging: system development and performance evaluation. Ultrasound Med Biol 2001;27:1347–57.
34. Havre RF, Elde E, Gilja OH, et al. Freehand real-time elastography: impact of scanning parameters on image quality and in vitro intra- and interobserver validations. Ultrasound Med Biol 2008;34:1638–50.
35. Goya C, Hamidi C, Ece A, et al. Acoustic radiation force impulse (ARFI) elastography for detection of renal damage in children. Pediatr Radiol 2015;45:55–61.
36. Derieppe M, Delmas Y, Gennisson JL, et al. Detection of intrarenal microstructural changes with supersonic shear wave elastography in rats. Eur Radiol 2012;22:243–50.
37. Gao J, He W, Cheng LG, et al. Ultrasound strain elastography in assessment of cortical mechanical behavior in acute renal vein occlusion: in vivo animal model. Clin Imaging 2014;4:613–18.
38. Gennisson JL, Grenier N, Combe C, et al. Supersonic shear wave elastography of in vivo pig kidney: influence of blood pressure, urinary pressure and tissue anisotropy. Ultrasound Med Biol 2012;38:1559–67.
39. Holdsworth A, Bradley K, Birch S, et al. Elastography of the normal canine liver, spleen and kidneys. Vet Radiol Ultrasound 2014;55:620–7.
40. Ternifi R, Gennisson JL, Tanter M, et al. Effects of storage temperature on the mechanical properties of porcine kidney estimated using shear wave elastography. J Mech Behav Biomed Mater 2013;28:86–93.
41. White J, Gay J, Farnsworth R, et al. Ultrasound elastography of the liver, spleen, and kidneys in clinically normal cats. Vet Radiol Ultrasound 2014;55:428–34.
42. Sommerer C, Scharf M, Seitz C, et al. Assessment of renal allograft fibrosis by transient elastography. Transpl Int 2013;26:545–51.

43. Ehman EC, Rossman PJ, Kruse SA, et al. Vibration safety limits for magnetic resonance elastography. Phys Med Biol 2008;53:925–35.
44. Bensamoun SF, Robert L, Leclerc GE, et al. Stiffness imaging of the kidney and adjacent abdominal tissues measured simultaneously using magnetic resonance elastography. Clin Imaging 2011;35:284–7.
45. Ebrahimi B, Textor SC, Lerman LO. Renal relevant radiology: renal functional magnetic resonance imaging. Clin J Am Soc Nephrol 2014;9:395–405.
46. Herzka DA, Kotys MS, Sinkus R, et al. Magnetic resonance elastography in the liver at 3 Tesla using a second harmonic approach. Magn Reson Med 2009;62:284–91.
47. Korsmo MJ, Ebrahimi B, Eirin A, et al. Magnetic resonance elastography noninvasively detects in vivo renal medullary fibrosis secondary to swine renal artery stenosis. Invest Radiol 2013;48:61–8.
48. Lee CU, Glockner JF, Glaser KJ, et al. MR elastography in renal transplant patients and correlation with renal allograft biopsy: a feasibility study. Acad Radiol 2012;19:834–41.
49. Rouviere O, Souchon R, Pagnoux G, et al. Magnetic resonance elastography of the kidneys: feasibility and reproducibility in young healthy adults. J Magn Reson Imaging 2011;34:880–6.
50. Mannelli L, Valentino M, Laffi G, et al. Functional MRI of the kidney. G Ital Nefrol 2010;27:599–608.
51. Streitberger KJ, Guo J, Tzschatzsch H, et al. High-resolution mechanical imaging of the kidney. J Biomech 2014;47:639–44.
52. Warner L, Yin M, Glaser KJ, et al. Noninvasive In vivo assessment of renal tissue elasticity during graded renal ischemia using MR elastography. Invest Radiol 2011;46:509–14.
53. Al-Dahshan M. Clinical application of transient elastography in prediction of portal hypertension related complication in patients with chronic liver diseases. J Egypt Soc Parasitol 2012;42:79–88.
54. Fahey BJ, Nelson RC, Bradway DP, et al. In vivo visualization of abdominal malignancies with acoustic radiation force elastography. Phys Med Biol 2008;53:279–93.
55. Gara N, Zhao X, Kleiner DE, et al. Discordance among transient elastography, aspartate aminotransferase to platelet ratio index, and histologic assessments of liver fibrosis in patients with chronic hepatitis C. Clin Gastroenterol Hepatol 2013;11:303–8 e1.
56. Goldschmidt I, Stieghorst H, Munteanu M, et al. The use of transient elastography and non-invasive serum markers of fibrosis in pediatric liver transplant recipients. Pediatr Transplant 2013;17:525–34.
57. Koh C, Turner T, Zhao X, et al. Liver stiffness increases acutely during sickle cell vaso-occlusive crisis. Am J Hematol 2013;88:E250–4.
58. Kummer S, Sagir A, Pandey S, et al. Liver fibrosis in recessive multicystic kidney diseases: transient elastography for early detection. Pediatr Nephrol 2011;26:725–31.
59. Liu CH, Liang CC, Huang KW, et al. Transient elastography to assess hepatic fibrosis in hemodialysis chronic hepatitis C patients. Clin J Am Soc Nephrol 2011;6:1057–65.
60. Mikolasevic I, Racki S, Lukenda V, et al. Nonalcoholic Fatty liver disease in renal transplant recipients proven by transient elastography. Transplant Proc 2014;46:1347–52.
61. Mikolasevic I, Racki S, Zaputovic L, et al. Nonalcoholic fatty liver disease (NAFLD) and cardiovascular risk in renal transplant recipients. Kidney Blood Press Res 2014;39:308–14.
62. Wang TY, Hall TL, Xu Z, et al. Imaging feedback of histotripsy treatments using ultrasound shear wave elastography. IEEE Trans Ultrason Ferroelectr Freq Control 2012;59:1167–81.
63. Woo S, Kim SY, Cho JY, et al. Shear wave elastography for detection of prostate cancer: a preliminary study. Korean J Radiol 2014;15:346–55.
64. Mikolasevic I, Racki S, Bubic I, et al. Chronic kidney disease and nonalcoholic Fatty liver disease proven by transient elastography. Kidney Blood Press Res 2013;37:305–10.
65. Son CY, Kim SU, Han WK, et al. Normal liver elasticity values using acoustic radiation force impulse imaging: a prospective study in healthy living liver and kidney donors. J Gastroenterol Hepatol 2012;27:130–6.
66. Arda K, Ciledag N, Aktas E, et al. Quantitative assessment of normal soft-tissue elasticity using shear-wave ultrasound elastography. AJR Am J Roentgenol 2011;197:532–6.
67. Baghani A, Eskandari H, Wang W, et al. Real-time quantitative elasticity imaging of deep tissue using free-hand conventional ultrasound. Med Image Comput Comput Assist Interv 2012;15:617–24.
68. Bharat S, Varghese T. Radiofrequency electrode vibration-induced shear wave imaging for tissue modulus estimation: a simulation study. J Acoust Soc Am 2010;128:1582–5.
69. Song P, Urban MW, Manduca A, et al. Comb-push ultrasound shear elastography (CUSE) with various ultrasound push beams. IEEE Trans Med Imaging 2013;32:1435–47.
70. Tian F, Wang ZB, Meng DM, et al. Preliminary study on the role of virtual touch tissue quantification combined with a urinary beta2-microglobulin test on the early diagnosis of gouty kidney damage. Ultrasound Med Biol 2014;40:1394–9.
71. Goya C, Daggulli M, Hamidi C, et al. The role of quantitative measurement by acoustic radiation force impulse imaging in differentiating benign renal lesions from malignant renal tumours. Radiol Med 2015;120:296–303.
72. Goya C, Kilinc F, Hamidi C, et al. Acoustic radiation force impulse imaging for evaluation of renal parenchyma elasticity in diabetic nephropathy. AJR Am J Roentgenol 2015;204:324–9.
73. Grenier N. Imaging and renal failure: from inflammation to fibrosis. J Radiol 2011;92:323–35.
74. Tan S, Ozcan MF, Tezcan F, et al. Real-time elastography for distinguishing angiomyolipoma from renal cell carcinoma: preliminary observations. AJR Am J Roentgenol 2013;200:W369–75.
75. Dillman JR, Smith EA, Davenport MS, et al. Can Shear-Wave Elastography be Used to Discriminate Obstructive Hydronephrosis from Nonobstructive Hydronephrosis in Children? Radiology 2015;142884.

KAFKAS TIP BİLİMLERİ DERGİSİ
Kafkas Journal of Medical Sciences
Kafkas J Med Sci 2016; 6(2):130–137 • doi: 10.5505/kjms.2016.15010

DERLEME / *REVIEW*

Tekrarlayan Erken Gebelik Kayıplarına Yaklaşım

Approach to Recurrent Early Pregnancy Loss

Rulin Deniz[1], Yakup Baykuş[1], Ebru Çelik Kavak[2]

[1]Kafkas Üniversitesi Tıp Fakültesi, Kadın Hastalıkları ve Doğum Anabilim Dalı, Kars; [2]Fırat Üniversitesi Tıp Fakültesi, Kadın Hastalıkları ve Doğum Anabilim Dalı, Elazığ

ABSTRACT

Abortus is the most common complication of pregnancy. Recurrent pregnancy lost is the termination of the sequential termination of at least two or more pregnancies before the week 20. Early fetal lost consists of abortus before 12th week of gestation. The ones between 12–20 weeks is called late abortus.

It is a threatening state that effects 5% of the woman who wants to give birth and 1% of infertile ones. In half of the cases even after a detailed examination, the etiology can not be found. It is a disappointing situation for both the patient and clinician. Treatment and diagnosis of recurrent pregnancy lost is one of the challenging topics of the obstetric.

Today, it can be prevented to a certain extent by the usage of diagnostic and interventional studies, some biochemical markers and medical, surgical and/or observational approaches. The etiology of recurrent pregnancy lost is parental and fetal chromosomal anomalies, antiphosholipid syndrome, structural uterine anomalies, some thrombophilia, autoimmune diseases and endocrinopathies.

In this study, it is aimed to revise the etiology, current treatment and evaluation of a couple with recurrent pregnancy lost in the light of literature.

Key words: *pregnancy; abortion; recurrent pregnancy loss*

ÖZET

Abortus gebeliğin en sık rastlanan komplikasyonudur. Tekrarlayan gebelik kayıpları (TGK), birbirini izleyen en az iki ya da daha fazla gebeliğin 20. gebelik haftasından önce sonlanmasıdır. Erken gebelik kayıpları 12. gebelik haftasından önce meydana gelen abortusları kapsamaktadır. 12.–20. gebelik haftaları arasında olan abortuslar ise geç abortus olarak adlandırılmaktadır.

Tekrarlayan gebelik kayıpları çocuk sahibi olmak isteyen çiftlerin %5'ini, fertil kadınların ise %1'ini etkileyen endişe verici bir durumdur. Tekrarlayan erken gebelik kayıplarında detaylı bir tarama sonrasında bile olguların yaklaşık yarısında açıklayıcı bir neden bulunamamaktadır. Hem çiftler hem de klinisyen için ümit kırıcı olan bu durumun tanı ve tedavisi üremeyle ilgilenen tıp dallarının en güç konularından birini oluşturmaktadır.

Günümüzde tanısal ve girişimsel işlemlerin kullanımının yaygınlaşması, bazı biyokimyasal belirteçlerin kullanılabilmesi tıbbi, cerrahi tedavi ve veya gözlem uygulanmasıyla tekrarlayan erken gebelik kayıplarında etyolojinin tespit edilmesi ve tedavisi belli bir oranda önlenebilmektedir. Tekrarlayan gebelik kaybı etyolojisi ile ilgili olarak bilinenler parental ve fetal kromozom anomalileri, yapısal uterin anomaliler, antifosfolipid sendrom (APS), bazı trombofililer, otoimmün hastalıklar bazı endokrinopatilerdir.

Bu çalışmada TGK'lı olguların değerlendirmesi, etyolojik faktörlerin ortaya konulması ve etkinliği kanıtlanmış güncel tedavi metodlarınının literatür bilgileri ışığında gözden geçirilmesi amaçlanmıştır.

Anahtar kelimeler: *gebelik; abortus; tekrarlayan gebelik kaybı*

Giriş

Erken gebelik kayıpları kadın hayatının en uzun dönemi olan reprodüktif döneminin sık karşılaşılan problemlerinden biridir. Abortus gebeliğin en sık görülen komplikasyonu olup suprapubik ağrı ve uterin kramplarla ortaya çıkan vajinal kanama ile beraber gebeliğin uterustan atılması, gebeliğe dair bulgu ve semptomların kaybolması olarak tariflenir[1]. Dünya sağlık örgütü ise gebelik ürününün ağırlığı ve gebelik süreci kriter alınarak, 20. gebelik haftasından önce, 500 gramın altındaki embriyo veya fetüs ve eklerinin tamamının ya da bir kısmının uterustan atılması durumunu abortus olarak tariflenmiştir[2]. On ikinci gebelik haftasına kadar olan abortuslar erken abortus, 12.–20. gebelik haftaları arasında olan abortuslar ise geç abortus olarak adlandırılmaktadır.

Geniş bir yelpazeye sahip olan spontan abortus insidansı %15–40 civarındadır. Spontan abortusların %62 si 12. gebelik haftasından önce görülmektedir.

Yard. Doç. Dr. Rulin Deniz, Kafkas Üniversitesi Tıp Fakültesi Hastanesi Kadın Hastalıkları ve Doğum Anabilim Dalı, Kars, Türkiye
Tel. 0533 550 28 46 Email. rulindeniz@hotmail.com
Geliş Tarihi: 22.04.2016 • Kabul Tarihi: 07.05.2016

Konsepsiyonların yaklaşık %30–50'si, klinik olarak tanısı konulmuş gebeliklerin ise yaklaşık %15'i düşük ile sonuçlanmaktadır[3–5].

Abortus insidansı anne, baba yaşları, önceki kötü obstetrik hikaye, genetik faktörler tarafından etkilenebilmektedir[2]. Anne yaşının 18'den küçük veya 35'den büyük olması, önceki gebelik kayıplarının sayısı ve artmış parite ile abortus riski artmaktadır. Otuz beş yaş üstünde oosit yaşlanmasına bağlı olarak anöploidi oranının artışından dolayı gebelik kaybı riskinde keskin bir artış ortaya çıkmaktadır. Yaygın olarak kabul gören görüşe göre, bir sonraki gebeliğin de kaybedilme riski kaybedilen her gebelikle birlikte artar ve 5–6 abortus sonrasında %50'nin üzerine çıkar[6].

Tekrarlayan gebelik kaybı her yıl 500.000'den fazla kadını etkileyen yaygın obstetrik bir problemdir. Tekrarlayan gebelik kayıpları spontan birbirini izleyen en az iki ya da daha fazla gebeliğin sonlanması olarak tanımlanır. Tüm gebeliklerin %0,5–3'ünde görülür[7]. Bazı kaynaklarda TGK arka arkaya 3 veya daha fazla spontan gebelik kaybı olarak tanımlanmaktadır[8]. Tekrarlayan gebelik kayıpları çocuk sahibi olmak isteyen çiftlerin %5'ini etkilemektedir[9]. Fertil kadınların ise yaklaşık %1'inde görülmektedir.

Tekrarlayan gebelik kayıpları etyolojisinde; koagülasyon sistemi bozuklukları, genetik faktörler, anatomik faktörler, immünolojik nedenler, hormonal bozukluklar, enfeksiyonlar, çevresel faktörler suçlanmaktadır. Tam bir değerlendirmeden sonra bile vakaların yaklaşık yarısında açıklayıcı bir neden bulunamamaktadır[10]. Bu çalışmada TGK'lı olguların değerlendirilmesi, etyolojik faktörlerin ortaya konulması ve etkinliği kanıtlanmış güncel tedavi yaklaşımlarına değinilmiştir.

Koagülasyon Sistemi Bozuklukları

Normal gebelikte pıhtılaşma eğilimi bir miktar artmaktadır. Trombofili; trombozlara eğilimi arttıran edinsel ya da kalıtsal olabilen koagülasyon sistemi bozukluklarındandır. Kalıtımsal trombofililer tedavi edilebilir tekrarlayan gebelik kaybı nedenlerindendir. Son yıllarda saptanan kalıtsal trombofili sayısı artmıştır ve TGK ile ilişkileri arasında farklı sonuçları olan raporlar bildirilmektedir.

Kalıtsal trombofili sebepleri içinde Faktör V Leiden mutasyonu en sık görülendir. Faktör V Leiden; genetik bir bozukluk olup, aktive protein C (APC)'ye bozulmuş antikoagülan cevabın olduğu durum olarak tanımlanır. Kısaca APC tarafından aktive faktör V'in inaktivasyonu bozulmuştur. Faktör V genindeki nokta mutasyonu ile APC için klivaj bölgesi hasar görür, böylece oluşan mutant faktör V Leiden proteini normale göre 10 kat daha yavaş inaktive olup dolaşımda fazla süre kalır, trombin oluşumunu arttırarak protrombotik durum yaratır. Hem homozigot (daha fazla) hem de heterozigot mutasyonlar erken ve geç ilk trimester kaybını arttırmaktadır[11]. Faktör V Leiden mutasyonu olmadan olan kazanılmış aktive protein C direnci (APCR); gebelikteki trombotik komplikasyonlar açısından bağımsız risk faktörüdür. Bu durumda APC'nin antikoagülan aktivitesi bozulmuştur. Açıklanamayan TGK olgularının %9–38'inde APCR pozitiftir. Normal gebelikte fizyolojik olarak APCR'de artış olur. Ancak altta yatan faktör V Leiden mutasyonu veya APCR olan olgularda bu fizyolojik değişiklik daha abartılı hale gelip fetal kayıp için daha yüksek risk oluşturur[12]. Faktör V Leiden mutasyonu ve TGK arasında pozitif ilişkiyi gösteren bir çok çalışma vardır[13]. Yapılan çalışmalarda Faktör V Leiden mutasyonu olan kadınlarda canlı doğum oranını arttırmak için heparin tedavisi önerilmektedir. Daha önemlisi yayımlanan randomize kontrollü çalışmalar Faktör V Leiden mutasyonunu rutin taramayı, tekrarlayan düşüğü olan ve bu mutasyonu taşıyan kadınlara tromboprofilaksiyi önermektedir.

Kalıtsal trombofiliye yol açtığı bilinen diğer sebepler Protein C ve Protein S eksikliği, Antitrombin III eksikliği, protrombin gen mutasyonudur[11,14]. Tromboz ve gebelik kaybına neden olan yeni tanımlanmış diğer bir patoloji ise faktör 12 eksikliğidir[15]. Daha az sıklıkta görülen diğer bir mutasyonda da tromboz için bilinen bağımsız bir risk faktörü olan hiperhomosisteinemiye eğilim olmaktadır[16]. Çalışmalarda hiperhomosisteinemiinin tekrarlayan düşüklerde rolü olmadığı belirtilmektedir[17]. Bazı çalışmalarda ise hiperhomosisteinemiinin TGK riskini 3–4 kat arttırdığı belirtilmektedir[18]. Hiperhomosisteineminin defektif koryon villus vaskülarizasyonuna, endotel hasarına ve prokoagülan etkilere neden olup erken fetal kayba neden olduğuna inanılmaktadır[19].

Kalıtsal trombofililer ve gebelik kaybı arasındaki ilişki geniş serili meta-analiz sonuçlarına göre; protein S eksikliğinde TGK riskinde 15 kat, 22 hafta sonrası geç fetal kayıp riskinde ise 7 kat artış saptanırken, protein C ve antitrombin III eksikliği ile fetal kayıp riski arasında anlamlı ilişki gösterilememiştir[11]. Trombofililer ile gebelik kayıpları arası ilişki gebelik kaybı zamanı (erken, geç) ve trombofili tipi ile değişmektedir. Yapılan

bir metaanaliz sonucuna göre trombofililerin hem erken ve hem de geç gebelik kayıplarına neden olduğu halde ikinci trimester ve daha sonraki dönem gebelik kayıplarıyla daha fazla ilişkili olduğu bildirilmiştir[11]. Sekizinci gebelik haftasına kadar maternal intervillöz kan akımının oluşmadığı düşünülecek olursa trombofiliye bağlı tromboz bu yüzden erken gebelik kayıplarını açıklayamayacaktır[20].

Tekrarlayan gebelik kaybı öyküsü olan kadınlarda trombofili tarama endikasyonları net olarak belirtilmemiştir. Açıklanamayan tektarlayan gebelik kaybı olan olgularda ne trombofili taraması ne de genetik polimorfizm bakılması önerilmemektedir[21]. Bununla birlikte tarama, 8 haftanın üzerinde veya tespit edilmiş fetal kalp aktivitesi sonrası nedeni açıklanamayan TGK olanlarda veya tromboz veya plasental yetmezliğe bağlı olabilecek gebelik komplikasyon öyküsü olanlarda (preeklampsi, intrauterin gelişme geriliği, plasental dekolman) uygulanabilmektedir.

Trombofili ile ilgili gebelik kayıpları olan kadınlarda tedavi endikasyonları netlik kazanamamıştır. Kontrolsüz tedavi çalışmalarında, tekrarlayan gebelik kaybı ve bir veya daha fazla trombofilik bozukluğu olan kadınlarda tek başına veya aspirinle birlikte uygulanan heparinin canlı doğum oranını düzelttiği bildirilmiştir[20]. Tekrarlayan erken gebelik kaybı olan kadınlarda uygulanan rutin ampirik aspirin tedavisinin kanıtlanmış bir faydası yoktur[22]. Aspirin ve düşük moleküler ağırlıklı heparin kombine tedavisi sadece geç gebelik kaybı ve antifosfolipid sendromu (edinsel trombofili) birlikteliği olan vakalarda önerilmelidir. Bu kombinasyon tromboembolik hadisesi olmayan tekrarlayan gebelik kaybı ve genetik trombofilili hastalara profilaksi amaçlı önerilmemelidir[21].

Erken ve tekrarlayan gebelik kayıplarına sebep olan, etyolojisinde otoimmün faktörlerin rol oynadığı; Sistemik Lupus Eritomatozus ve Antifosfolipid sendrom (APAS) en sık görülen edinsel trombofili sebepleridir[14]. Antifosfolipid sendromu spesifik klinik ve laboratuar özellikleri olan otoimmun bir hastalıktır. Tekrarlayan gebelik kayıplarının %5–10 kadarından sorumlu olduğu belirtilen APAS tekrarlayan gebelik kayıplarının potansiyel olarak tedavi edilebilen bir nedenidir. Çeşitli antifosfolipid antikorlar tariflenmişse de sadece Antikardiolipin antikor ve Lupus antikoagülanı yaygın kabul görmüştür. Antifosfolipid antikorlar düşük risk popülasyonundaki %2'lik orana karşın TGK'lı olgularda %15 oranında görülmektedir[23]. Antifosfolipid sendromu ve TGK arasında nedensel bir ilişki tanımlanmamış olmasına rağmen düşük doz aspirin, heparin ve steroidler ile çeşitli teröpatik çalışmalar yapılmıştır[24]. Yapılan bir çalışmaya göre aspirin ve düşük molekül ağırlıklı heparin kombinasyonunun antifosfolipid antikoru bulunan kadınlarda gebelik kaybını %54 oranında azalttığı gösterilmiştir[25]. Steroidlerin TGK'lı kadınlarda canlı doğum oranını arttırdığına dair ise bir kanıt bulunamamıştır[24]. Birçok çalışma heparinin aspirinden daha etkili, aspirin ve heparinle kombine tedavinin de ayrı ayrı uygulamalardan daha etkili olduğunu göstermiştir[21,26–29].

Bu bilgiler ışığında trombofililere bağlı gebelik kayıpları erken gebelik dönemi yanında daha çok ikinci-üçüncü trimester kayıplarına neden olmaktadır[30]. Sonuç olarak seçilmiş TGK olgularında faktör V Leiden mutasyonu, protrombin gen mutasyonu için DNA analizi, protein S eksikliği ve Antikardiolipin antikor ve Lupus antikoagulanı taraması yapılmalıdır.

Genetik Faktörler

Kromozom bozuklukları, erken dönem gebelik kayıplarının en sık rastlanan nedenidir. Birçok düşüğün altında yatan neden embriyonun anormal karyotipe sahip olmasıdır. Erken gebelik kayıplarının %50'sinde, ikinci trimester kayıplarının %30'unda kromozomal anomali tespit edilmektedir[31,32]. Abortuslarda tespit edilen kromozom anormalliklerinin %90'ından fazlası sayısaldır (anöploidi, poliploidi), kalanlar yapısal anormallikler (translokasyon, inversiyon) ve mosaizmdir[33]. En sık görülen anormallik otozomal trizomilerdir (kromozom 13, 16, 22, 23). Daha sonra monozomi X (45X) ve poliploidiler gelmektedir[31]. Maternal ve gestasyonel yaşa göre sınıflandırıldığında TGK'lardaki kromozom anormallik dağılımı genel popülasyonda görülenden farklı değildir[34]. Bununla birlikte, TGK olanların %4–8'inde çiftlerden biri veya diğerinde fetüste kromozomal dengesizliğe neden olabilecek parental kromozomal anormallikleri mevcuttur[35]. Tekrarlayan gebelik kayıpları ile ilişkili parental kromozom anomalilerinden en sık görüleni dengeli translokasyonlardır[36].

Tekrarlayan gebelik kayıpları olan çiftlerin %10'undan fazlasında önceki çocuk ve yakınlarında nöral tüp defektleri, diyafragma hernisi, omfalosel, yarık damak ve yarık dudak gibi multifaktöryel patolojiler gözlenmiştir[1]. Bu hastalarda çiftlerin dikkatli bir hikayesi alınmalı, soy ağacı çıkarılmalıdır. Hem çiftlerin hem de abortus materyalinin karyotipik incelemesi yapılmalıdır. Paternal defekt varsa tedavide artifisyel inseminasyon, maternal defektte ise oosit donasyonu gerekebilir[1].

Çiftlerin karyotip analizi ve konsepsiyon ürününün sitogenetik analizi üçüncü erken gebelik kaybında önerilmelidir[21].

Anatomik Nedenler

Anatomik nedenler TGK'ların %15'inden sorumludur. Abortuslara yol açan anatomik nedenler; müllerian kanal defektleri gibi konjenital nedenler, uterin leiomyomlar, küretaj ya da enfeksiyonlar sonrası gelişen intrauterin adezyonlar, endometrial polipler gibi edinsel nedenlerdir. Konjenital nedenlerin edinsel faktörlere göre TGK etyolojisinde daha fazla rol oynadığı düşünülmektedir. Erken gebelik kayıplarından ziyade 2.–3. trimester gebelik kayıplarıyla daha fazla ilişkilidir. Konjenital uterin anomalilerin klasifikasyonunun netleştirilmesi, sadece obstetrik sonuçların, TGK etyolojisi açısından değil, yapılacak cerrahi girişimin seçimi ve sonuçları açısından da son derece önemlidir. Kayıplar genelde ya implantasyon bölgesinin yetersiz kanlanması yüzünden erken dönemde, ya da yapısal defektlere bağlı ikinci trimesterde görülür[37]. Vakaların %70'inde cerrahi tedavi başarılı olmaktadır[17].

Uterin septum en sık görülen konjenital uterin gelişim anomalisi olup TGK'lı olgularda (%3,5 sıklık) ve genel popülasyonda tüm majör malformasyonların %80–90'ını oluşturmaktadır[38]. Bu anomali aynı zamanda kötü gebelik sonuçlarıyla ilişkili olan en sık anomali[39] olup ve en kolay düzeltilebilen bozukluktur. Uterin septum her zaman kötü gebelik sonuçlarıyla birlikte olmayıp özellikle TGK nedeni ise cerrahi onarım olarak histereskopik septoplasti uygulanmasının uygun oldugu kabul görmektedir. Bikornuat veya unikornuat uterusu olan çoğu kadında obstetrik prognoz iyi olduğundan ve bu anomalilerin onarımı daha invaziv, komplikasyon riski yüksek olduğundan bu anomalilerin onarılması önerilmemektedir.

Servikal yetmezlik spontan abortusların %0.2'sinden, 2. ve 3. trimester gebelik kayıplarının %16–20'sinden[40] ve TGK'ların %8–15'inden sorumludur[41]. Preterm doğumların yaklaşık %10'unundan servikal yetmezlik sorumludur[42]. Cerrahi tedavisinde transvajinal veya abdominal serklaj uygulanmaktadır. Cerrahi risklerinden dolayı serklaj daha önceden 2. trimester gebelik kaybı olan seçilmiş kadınlara uygulanması önerilmektedir.

Uterin myomların tekrarlayan gebelik kaybı nedeni olduğunu gösteren kesinleşmiş kanıtlar yoktur. Genel olarak submüköz myomlar tek ve küçük boyutta ise histereskopik myomektominin faydası riskinden çok olması dolayısıyla önerilmemektedir[43].

İntrauterin adezyonlar TGK'lara neden olmakla birlikte, daha sık görülen klinik prezentasyonu menstruel bozukluklar ve infertilitedir[44]. İntrauterin adezyonlarda gebelik sonuçları genellikle kötüdür ancak adezyolizis sonrası düzelme olmaktadır. Prognoz genellikle hastalık derecesiyle ilgilidir.

Hormonal Nedenler

Gebelik kayıplarının yaklaşık %10'u endokrinolojik faktörlerle ilişkilidir. Tiroid disfonksiyonu, luteal faz defekti, diabetes mellitüs (DM), polikistik over sendromu (PKOS), hiperprolaktinemi gibi endokrinolojik problemler abortus etyolojisinde yer alır.

Regüle DM'lerde abortus oranının artmadığı, kontrolsüz DM'lerin ise abortuslara neden olabileceği bildirilmektedir[45]. Kontrolsüz DM varlığında spontan abortus riski 3 kat artmaktadır. Erken gebelik döneminde HbA1c düzeylerinde yükseklik olan olgularda fetal ölüm ve spontan abortus ihtimalinin arttığı bildirilmektedir[37]. Sonuç olarak TGK'lı kadınlarda, kan glukoz ve HbA1C düzeylerinin ölçümü bilinen veya klinik olarak tahmin edilen diyabeti olan kadınlarda yapılmalıdır, fakat bunların dışında tarama rutin olarak önerilmemektedir. Tekrarlayan gebelik kaybı olup yüksek HbA1C konsantrasyonu olan diyabetik kadınlara, düzeyler normal seviyeye gelinceye kadar gebe kalmamaları önerilmelidir.

Luteal faz yetmezliği TGK'ların tartışmalı nedenleri arasındadır[46]. Uterusta implantasyon öncesi hazırlıklar dönemdeki bazı endokrinolojik değişiklikler TGK'ya neden olabilir. Corpus luteumunun özellikle ilk 8 haftadaki yetersiz progesteron üretimi, anormal luteinizan hormon sekresyonu veya mevcut progesterona endometriumun kötü yanıtı durumları luteal faz yetmezliği sebepleri arasındadır. Bu durum TGK'lı olguların %23'ü ile 60'ı arasında değişen oranlarda bildirilmektedir[47]. Serum progesteron seviyesi midluteal fazda 12 ng/ml altında olduğunda gebeliğin kaybedilme riski artar[21].

Tedavide progesteron içeren vajinal suppozituarlar veya korpus luteum fonksiyonunu destekleyen progesteron preparatları, eksojen hCG, gonodotrin ve klomifen sitrat uygulamaları mevcuttur. Ancak etkinliği randomize kontrollü çalışmalarda gösterilememiştir. Literatürde luteal faz yetmezliğinin patolojik bir durum olduğunu destekleyen sınırlı sayıda veri vardır. Bu

nedenle TGK olgularının değerlendirilmesinde luteal faz yetmezliği tanısı ile ilgili testlerin kullanılması önerilmemektedir[48].

Hipotiroidi ve hipertiroidi durumlarının her ikisi de üreme fonksiyonunda bozulmaya neden olabilir. Son çalışmalarda tiroid stimulan hormonu (TSH) düzeylerinin gebelik kayıpları ile ilişkisi üzerinde durulmaktadır. TSH seviyesinin 6 mIU/ml üzerinde olmasının yüksek oranda ölü doğumla ilişkili olduğu bildirilmektedir[49,50]. Klinik hipertiroidi ile ilişkili olarak abortus riskinde bir artış olmadığı gösterilmiştir. Çalışmalarda tiroid fonksiyon testleri normal bulunan tedavi edilmiş hipotiroidi hastalarında gebelik kaybı insidansı çok düşük rapor edilmiştir. Fakat tedavi edilmemiş subklinik hipotiroidi olan ve belirgin hipotiroidi olup da yeterli egzojen tiroid hormon replasmanı almayan kadınların da dahil edildiği yüksek TSH düzeylerinde belirgin olarak artmış risk bildirilmiştir[51–55]. Kolay tedavi edilebilir patolojiler olduğundan, tedavi sonuçları da gebelik prognozunu düzelttiğinden dolayı TGK tetkikleri arasına TSH da dahil edilmelidir. Bazı araştırmalarda antitiroid antikorlarının da gebelik kaybı ile ilişkili olduğu belirtilmektedir. Ancak randomize çalışmaların sonuçlarına göre, antitiroid antikorlarının TGK ile ilişkisi kesin olarak gösterilememiştir ve ayrıca antitiroid antikor pozitifliğinin günümüzde etkin tedavisi de mevcut değildir[53,54]. Bu nedenle tiroid otoantikor taramasının da TGK değerlendirmesi güncel algoritmasında yeri yoktur.

Polikistik over sendromu olgularının %36–56'sında TGK saptanmaktadır. Polikistik over sendromu olgularında gebelik kaybı lüteinize hormon (LH), hiperandrojenemi ve insülin direncine bağlanmaktadır. Bunun yanında PKOS olmadan insülin rezistansı ve obezitenin birlikte tekrarlayan düşükle ilgili olduğu gösterilmiştir[56]. Çalışmalarda metforminin özellikle anormal glukoz tolerans testi olanlarda gebelik kaybı oranlarını azalttığı bildirilmiştir. Polikistik over sendromu ve insülin direnci olgularına metformin tedavisinin yararlı olduğunu bildiren yayınlar mevcuttur[57,58]. Ancak randomize kontrollü çalışmalarda abortus oranlarında klomifen sitrat ve metformin arasında bir fark olmadığı belirtilmektedir. Obez PKOS'lu kadınlarda kilo verme basit ve başlangıçta önerilmesi gereken yöntemdir. Sonuç olarak seçilmiş TGK olgularında klinik ve laboratuar olarak PKOS açısından değerlendirme yapılması önerilebilir.

Hiperprolaktineminin ovaryan granüloza hücrelerinden progesteron salınımını inhibe ederek (luteal faz defektine neden olarak) endometriyal defektlere sebep olabileceği düşünülse de TGK'larda ki rolü net değildir[49,59]. Bazı çalışmalarda bromokriptin tedavisiyle başarılı gebelik oranları bildirilmektedir. Bunun için hiperprolaktinemili TGK'lı olguda tedavi sonrası gebelik önerilmesi düşünülebilir.

Nedeni açıklanamamış TGK'lı olan kadınlarda nedeni bilinen olgulara göre adetin üçüncü günü foliküler stimülan hormon (FSH) ve estradiol (E2) değerleri daha yüksek bulunmuştur. Bir çalışmada olguların %58'inde TGK nedeni olarak adetin 3. gününde FSH veya E2 yüksekliği gösterilmiştir[60]. Menstürasyonun 3. günü FSH, E2 düzeyi arttıkça oosit kalitesi ve sayısı azalacaktır ve bu kötü kaliteli oositlerden oluşacak embriyolarda kromozom anomalisi ve dolayısıyla düşük insidansı da artmaktadır. Her TGK olgusunda yaşına bakılmadan adetin üçüncü günü FSH düzeyine bakılmalıdır.

İmmünolojik Faktörler

Otoimmün immünolojik faktörlerden APAS'a yukarıda değinilmiştir. İnsanlarda TGK'nın alloimmün nedeni konusunda veriler çelişkilidir. Tekrarlayan gebelik kayıplarının oluşmasında öne sürülen alloimmün mekanizmalar içinde; anne-baba arasındaki HLA uyumu, maternal blokan antikor yokluğu ve maternal lökositotoksik antikorların yokluğu sayılabilir[61]. Ancak öne sürülen alloimmün mekanizmalardan hiçbiri kesin olarak gösterilememiştir. Annenin babaya karşı immün yanıtı için HLA tiplemesi veya lökosit popülasyonunun belirlenmesi gibi immünolojik testler bazı klinisyenler tarafından önerilmektedir. Bu görüş gebelik ürününün semiallojenik graft olarak maternal immünolojik reddinin TGK nedeni olduğu hipotezine dayanmaktadır. Ancak çoğu araştırma bu testleri desteklememektedir. Alloimmünizasyon taraması ve buna bağlı tedavinin klinik prognozu iyileştireceğine ilişkin kanıt yoktur. Birçok ampirik tedavi yöntemi tarif edilmiş olup bunlar arasında en popüler yöntemlerden biri annenin paternal lökösitlerle immünizasyonudur.183 hastanın katıldığı çok merkezli prospektif bir çalışmada lökosit immünoterapisi verilmesinin klinikte katkısı olmadığı belirtilmiştir[62]. Lökosit immünoterapisi günümüzdeki bilgilere göre TGK tedavisinde önerilmemektedir. Lökosit immünoterapisinin yerine önerilen intravenöz immünglobulin (IVIG) tedavisinin etkinliğini gösteren iyi planlanmış geniş serili çalışmalar da bulunmamaktadır. Antifosfolipid sendrom hariç, immünolojik nedenlerin TGK ile ilişkileri çok zayıftır.

Enfeksiyonlar

Herhangi bir bakteriyel veya viral enfeksiyon uterusa yayılarak sporadik abortusa neden olabilir. Ancak ileri sürülen periyodik raporlarda enfeksiyon ajanlarının TGK'ya neden olduğu konusunda kesin kanıtlar yoktur. Sonuç olarak güncel literatür bilgilerine göre TGK'lı olgularda enfeksiyon taramasının rutinde yeri yoktur.

Çevresel Faktörler

Güncel verilere göre çevresel ajanların tekrarlayan gebelik kayıplarına neden olduğu konusunda kesin kanıtlar yoktur.

Diyetteki herhangi bir besin eksikliğinin ya da tüm besinlerin orta derecedeki eksikliğinin abortusta rolü olduğuna dair kesin bir veri yoktur.

Sigara içimi ve düşük riski arasındaki ilişkiyi inceleyen çalışmalarda genel olarak sigara içmenin doza bağımlı bir şekilde spontan düşük riskini attırdığı belirtilmiştir. Sorumlu mekanizmalar net değildir fakat sigara dumanındaki nikotin, karbondioksit, siyanür dahil bazı maddelerin vazokonstrüktif ve antimetabolik etkileri plasental yetmezliğe yol açabilir[63].

Gebeliğin ilk 8 haftasında alkol kullanımı hem spontan abortus hem de fetal anomalilere neden olabilir[64]. Beş yüz kırk altı kişi ile yapılan başka bir prospektif çalışmada gebelik süresince düşük düzeyde alkol tüketiminin anlamlı abortus riski ile ilişkili olmadığı bildirilmiştir[65].

Maternal kafein tüketimi ile düşük riski arasındaki ilişkiyi inceleyen çoğu çalışmada ağır kafein tüketiminin, spontan düşük riskinde 2 kat artışa neden olduğu gösterilmiştir[66].

İsotretinoin yükselmiş spontan düşük insidansı ile ilişkilidir[67].

Son kanıtlar ışığında, 5 Rad'ın altında bir radyasyon dozunda malformasyon, büyüme geriliği veya düşük açısından artmış bir fetal risk yoktur. Brent'e göre 20 Rad değerinin altında radyasyona maruz kalan gebe popülasyonunda büyük konjenital malformasyonlarda artış görülmeyecektir[68].

Sonuç

Tekrarlayan gebelik kayıpları olan olguların değerlendirme sürecine öncelikle ayrıntılı hikaye, fizik muayene ile başlanmalıdır. Tüm gebelik kayıplarının hangi dönemde (preembriyonik, embriyonik) olduğu, düşük öncesi fetal kalp atımının görülüp görülmediği ve abortus şekli ayrıntılı olarak değerlendirilmelidir.

Erken dönem tekrarlayan gebelik kayıplarında; yapılan geniş serili çalışmalarda en sık nedenin genetik anormallikler olduğu ortaya konulmuş olup, bu olguların taranmasında öncelikle hem parental kromozom analizi hem de fetal ürünlerden direkt veya anne periferik kan örneklerinden indirekt kromozom analizi yapılması önerilmektedir.

Geç dönem tekrarlayan gebelik kayıplarında ise özellikle anatomik sebepler, immünolojik nedenler daha olasıdır. Bu olgularda anatomik sebeplerin taramasında detaylı pelvik muayene, ultrasonografi, sonohisterografi, histeroskopi, seçilmiş olgularda ise magnetik resonans yapılmalıdır. İmmünolojik patolojilerin taranmasında tarama endikasyonları net olarak belirtilmemişse de seçilmiş olgularda (özellikle 8 haftanın üzerinde veya tespit edilmiş fetal kalp aktivitesi sonrası nedeni açıklanamayan TGK'lı olgular ve tromboz veya plasental yetmezliğe bağlı olabilecek gebelik komplikasyon öyküsü olanlarda) otoimmünitenin değerlendirilmesi için antikardiyolipin antikor, lupus antikoagülanı, trombofili değerlendirilmesi için faktör V Leiden mutasyonu, aktive protein C rezistansı, protein S düzeyi ve protrombin gen mutasyonu taraması yapılması önerilmektedir.

Kontrolsüz DM'nin ve subklinik hipotiroidi veya aşikar hipotiroidinin TGK ile olan ilişkisi nedeniyle anamnez ve fizik muayenede şüphelenilen bu tip olgularda glukoz, HbA1c, TSH değerleri kontrol edilmelidir. Seçilmiş TGK olgularında klinik laboratuvar olarak PKOS açısından değerlendirme yapılması önerilebilir. Nedeni açıklanamamış TGK'lı olgularda over rezervinin değerlendirilmesi için adetin üçüncü günü FSH ve E2 düzeylerine bakılması önerilmektedir.

Herhangi bir çevresel toksin, radyasyon, ilaç maruziyeti ve bilinen jinekolojik obstetrik enfeksiyon sorgulanmalıdır. Ancak güncel literatür bilgilerine göre tekrarlayan gebelik kayıpları olan hastalarda enfeksiyon taramasının ve çevresel nedenlerin taranmasının rutinde yeri yoktur. Diğer tetkikler ise sadece klinik olarak şüphe duyulan olgularda yapılmalıdır.

Tekrarlayan gebelik kayıpları, çiftler ve bu durumun tanı ve tedavisiyle ilgilenen klinisyenler için yıpratıcı bir durumdur. Aileye danışmanlık hizmeti verilmeli ve gerekirse profesyonel psikolojik destek almaları sağlanmalıdır. Hastaların yarısında belirgin neden bulunamayacağı bilinmesine rağmen yine de bu gruptaki

hastalara tedavi edilmeden bile başarılı gebelik elde edilebileceği bilgisi verilmelidir. Bu olgularda amaç gebelik arzulayan kadınlarda sağlıklı, komplikasyonsuz ya da minimum komplikasyonla gebeliğin devamı ve sonlanmasına katkıda bulunabilmektir.

Gelecekte TGK'lı olgularda etyolojik nedenlerinin belirlenmesi ve üzerinde fikirbirliği sağlanabilmiş standart tedavi protokollerinin oluşturulabilmesi için randomize, kontrollü ve geniş hasta popülasyonlu yeni çalışmalara ihtiyaç duyulmaktadır.

Kaynaklar

1. Atasü T, Şahmay Ş. Abortus. Jinekoloji, Nobel, 2. Baskı, İstanbul, 2001;37:533–45.
2. Beksaç S, Demir N, Koç A, Yüksel A. Erken gebelik problemleri ve düşükler. Obstetrik, Maternal - Fetal Tıp ve Perinatoloji, 1. baskı, Medikal & Nobel, Ankara, 2001;1076–85.
3. Edmonds DK, Lindsay KS, Miller JF, et al. Early embryonic mortality inwomen. Fertil Steril 1982;38:447–53.
4. Wilcox AJ, Weinberg CR, O'Connor JF, et al. Incidence of early loss of pregnancy. N Engl J Med 1988;319:189–94.
5. Jacobs PA, Hassold T. Chromosome abnormalities: origin and etiology in abortions and livebirths. In: Vogel F, Sperling K, eds. Human Genetics. Berlin: Springer-Verlag; 1987;233–44.
6. Clifford K, Rai R, Regan L. Future pregnancy outcome in unexplained recurrent first trimester miscarriage. Hum Reprod 1997;12:387–9.
7. American College of Obstetricans and Gynecologists. Management of recurrent early pregnancy loss. ACOG Practice Bulletin 2001;24:1–8.
8. Alberman E. The epidemiology of repeated abortion. In: Beard RW, Sharp F (eds), Early Pregnancy Loss: Mechanisms and Treatment. London, UK. RCOG Press, 1988;9–17.
9. Roman E. Fetal loss rates and theirrelation to pregnancy order. J Epidemiol Community Health 1984;38:29–35.
10. Stephenson MD. Frequency of factors associated with habituel abortion in 197 couples. Fertil Steril 1996;66:24–9.
11. Rey E, Kahn SR, David M, et al. Thrombophilic disorders and fetal loss: A meta-analysis. Lancet 2003;361:901–8.
12. Rai R, Shlebak A, Cohen H, et al. Factor V Leiden and acquired activated protein C resistance among 1000 women with recurrent miscarriage. Hum Reprod 2001;16:961–5.
13. Grandone E, Margaglione M, Colaizzo D, et al. Factor V Leiden is associated with repeated and recurrent unexplained fetal losses. Thromb Haemost 1997;77:822–4.
14. Yamaç G, Gürsoy R, Çakır N. Gebelik ve Hiperkoagülabilite. Gebelik ve Sistemik Hastalıklar. Medikal&Nobel, 1. Baskı, İstanbul, 2002;20:277–91.
15. Pauner HU, Burfeined P, Kostering H, et al. Factor XII deficiency is strongly associated with primary recurrent abortions. Fertil Steril 2003;80:590–4.
16. Frosst P, Blom HJ, Milos R, et al. A candidate genetic risk factor for vasculer disease: a common mutation in methylenetetrahydrofolate reductase. Nat Genet 1995;10:111–3.
17. Foka ZJ, Lambropoulos AF. Factor V leiden and prothrombin G20210A mutations, but not methylenetetrahydrofolate reductase C677T, are associated with recurrent miscarriages. Hum Reprod, 2000;15:458–62.
18. Nelen WL, Blom HJ, Steegers EA, et al. Hyperhomocysteinemia and recurrent early pregnancy loss: A meta-analysis. Fertil Steril 2000;74:1196–9.
19. Nelen WL, Bulten J, Steegers EA, et al. Maternal homocysteine and chorionic vascularization in recurrent early pregnancy loss. Hum Reprod 2000;15:954–60.
20. Younis JS, Ohel G, Brenner B, et al. The effect of thrombophylaxis on pregnancy outcome in patients with recurrent pregnancy loss associated with factor V Leiden mutation. BJOG 2000;107:415–9.
21. Huchon C, Deffieux X, Beucher G, et al. Pregnancy loss: French clinical practice guidelines. Eur J Obstet Gynecol Reprod Biol 2016;201:18–26.
22. Rai R, Backos M, Baxter N, et al. Recurrent miscarriagean aspirin a day? Hum Reprod 2000;15:2220–3.
23. Rai RS, Regan L, Clifford K, et al. Antiphospholipd antibodies and beta 2-glycoprotein-I in 500 women with recurrent miscarriage: results of a comprehensive screening approach. Hum Reprod 1995;10:2001–5.
24. Cowchock FS, Reece EA, Balaban D, et al. Repeated fetal losses associated with antiphospholipid antibodies: a collaborative randomized trial comparing prednisone with low-dose heparin treatment. Am J Obstet Gynecol 1992;166:1318–23.
25. Empson M, Lassere M, Craig JC, et al. Recurrent pregnancy loss with antiphospholipid antibody: a systematic review of therapeutic trials. Obstet Gynecol 2002;99:135–44.
26. Pattison NS, Chamley LW, McKay EJ, et al. Antiphospholipid antibodies in pregnancy: prevalence and clinical associations, Br J Obstet Gynecol 1993;100:909–13.
27. Lima F, Khamashta MA, Buchanan NM, et al. A study of sixty pregnancies in patients with the antiphospholipid syndrome, Clin Exp Rheumatol 1996;14:131–6.
28. Kutteh WH. Antiphospholipid antibody-associated recurrent pregnancy loss; treatment with heparin and low-dose aspirin is superior to low-dose aspirin alone, Am J Obstet Gynecol 1996;174:1584–9.
29. Tulppala M, Marttlunen M, Söderström-Anttila V, et al. Low-dose aspirin in prevention of miscarriage in women with unexplained or autoimmune related recurrent miscarriage: effect on prostacyclin and thromboxane A2 production, Hum Reprod 1997;12:1567–72.
30. Sarig G, Younis JS, Hoffman R, et al. Thrombophilia is common in women with idiopathic pregnancy loss and is associated with late pregnancy wastage. Fertil Steril 2002;77:342–7.
31. Hassold T, Chiu D. Maternal age-specific rates of numerical chromosome abnormalities with special reference to trisomy, Hum Genet 1985;70:11–7.

32. Warburton D, Kline J, Stein Z, et al. Cytogenetic abnormalities in spontaneous abortions of recognized conceptions, In: Porter IH, ed. Perinatal Genetics: Diagnosis and Treatment, Academic Press, New York 1986, 133.
33. Philipp T, Philipp K, Reiner A, et al. Embryoscopic and cytogenetic analysis of 233 missed abortions: factors involved in the pathogenesis of development defects of early failed pregnancies. Hum Reprod 2003;18:1724–32.
34. Stephenson MD, Awartani KA, Robinson WP. Cytogenetic analysisof miscarriage: a case-control study. Hum Reprod 2002;17:446–51.
35. Tho PT, Byrd JR, McDonough PG. Etiologies and subsequent reproductive performance of 100 couples with recurrent abortion. Fertil Steril 1979;32:389–95.
36. Daniel A, Hook EB, Wulf G. Risks of unbalanced progeny at amniocentesis to carriers of chromosome rearrangements: Data from United States and Canadian laboratories. Am J Med Genet 1989;33:14–53.
37. Arredondo F, Noble LS. Endocrinology of recurrent pregnancy loss. Semin Reprod Med 2006;24:33–9.
38. Homer HA, Li TC, Cooke ID. The septate uterus: a review of management and reproductive outcome. Fertil Steril 2000;73:1–14.
39. Grimbizis GF, Camus M, Tarlatzis BC, et al. Clinical implications of uterin malformations and hysteroscopic treatment results. Hum Reprod Update 2001;7:161–74.
40. Stromme WB, Haywa EW. Intrauterine fetal death in second trimester. Am J Obstet Gynecol 1963;85:223–33.
41. Jewelewicz R. Incompetent cervix. Pathogenesis, diagnosis and treatment. Semin Perinatol 1991;15:156–61.
42. Iams JD, Jhonson FF, Sonek J, et al. Cervical incompetence as a continuum: a study of ultrasonographic cervical length and obstetric performance. Am J Obstet Gynecol 1995;172:1097–106.
43. Fernandez H, Sefrioui O, Virelizier C, et al. Hysteroscopic resection of submucosal myomas in patients with infertility. Hum Reprod 2001;16:1489–92.
44. Al-Inany H. Intrauterin adhesions. An update. Acta Obstet Gynecol Scand 2001;80:986–93.
45. Greene MF, Hare JW, Cloherty JP, et al. First-trimester hemoglobin A1 and risk for major malformation and spontaneous abortion in diabetic pregnancy. Teratology 1989;39:225–31.
46. Noyes RW, Hertiq AT, Rock J. Dating the endometrial biopsy. Fertil Steril 1975;122:262–3.
47. Tulppala M, Björses UM, Stenman UH. Luteal phase defect in habitual abortion: progesterone in saliva, Fertil Steril 1991;56:41–4.
48. Porter TF, Scott JR. Evidence-based care of recurrent miscarriage. Best Pract Res Clin Obstet Gynaecol 2005;19:85–101.
49. Kaur R, Gupta K. Endocrine dysfunction and recurrent spontaneous abortion: An overview. Int J Appl Basic Med Res 2016:6:79–83.
50. Allan WC, Haddow JE, Palomaki GE, et al. Maternal thyroid deficiency and pregnancy complications: implications for population screening. J Med Screen 2000;7:127–30.
51. Abalowich M, Gutierriez S, Alceraz G, et al. Overt and subclinical hypotiroidism complicating pregnancy. Thyroid 2002;12:63–8.
52. Stagnaro- Green A, Roman SH, Cobin RH, et al. Detection of at risk pregnancy by means of highly sensitive assays for thyroid auto-antibodies. JAMA 1990;264:1422–5.
53. Rushworth FH, Backos M, Rai R, et al. Prospective pregnancy outcome in untreated reccurent miscarriers with thyroid antibodies. Hum Reprod 2000;15:1637–9.
54. Esplin MS, Branch DW, Silver R, et al. Thyroid autoantibodies are not associated with reccurrent pregnancy loss. Am J Obstet Gynecol 1998;179:1583–6.
55. Kutteh WH, YetmanDL, Carr AC, et al. Increased prevelance of antitiroid antibodies identified in women undergoing assisted reproduction. Fertil Steril 1999;71:843–8.
56. Wang JX, Davies MJ, Norman RJ. Obesity increases the risk of spontaneous abortion during infertility treatment. Obes Res 2002;10:551–4.
57. Lord JM, Flight IH, Norman RJ. Metformin in polycystic ovary syndrome: Systematic review and meta-analysis. BMJ 2003;327:951–3.
58. McCarthy EA, Walker SP, McLachlan K, et al. Metformin in obstetric and gynecologic practice: A review. Obstet Gynecol Surv 2004;59:118–27.
59. Porter MB, Brumsted JR, Sites CK. Effect of prolactin on follicle-stimulating hormone receptor binding and progesterone production in cultured porcine granulosa cells. Fertil Steril 2000;73:99–105.
60. Trout SW, Seifer DB. Do women with unexplained recurrent pregnancy loss have higher day 3 serum FSH and estradiol values? Fertil Steril 2000;74:335–7.
61. Regan L, Braude PR, Hill DP. Aprospective study of the incidence, time of, appearence of, significance of anti-paternal lymphocytotoxic antibodies in human pregnancy. Hum Reprod 1991;6:294–8.
62. Ober C, Karrison T, Odem RR, et al. Mononuclear cell immunisation in prevention of recurrent miscarriages: a randomized trial. Lancet 1999;354:365–9.
63. Hughes EG, Brennan BG. Does cigarette smoking impair natural or assisted fecundity. Fertil Steril 1996;66:679–89.
64. Floyd RL, Decoufle P, Hungerford DW. Alcohol used prior to pregnancy recognition. Am J Prev Med 1999;17:101–7.
65. Cavallo F, Russo R, Zotti C, et al. Ruggeni AM. moderate alcohol consumption and spontaneous abortion. Alcohol 1995;30:195–201.
66. Rasch V. Cigarette, alcohol, and caffeine consumption: risk factors for spontaneous abortion. Acta Obstet Gynecol Scand 2003;82:182–8.
67. Schnorr TM, Grajewski BA, Hornung RW, et al. Video display terminals and the risk of spontaneous abortion. N Engl J Med 1991;324:727–33.
68. Brent RL. Utilization of developmental basic science principles in the evaulation of reproductive risks from pre and postconception environmental radiation exposures. Teratology 1999; 59:182–204.

KAFKAS TIP BİLİMLERİ DERGİSİ
Kafkas Journal of Medical Sciences
Kafkas J Med Sci 2016; 6(2):138–141 • doi: 10.5505/kjms.2016.34603

OLGU SUNUMU / *CASE REPORT*

An Unusual Cause of Sleep Apnea: Laryngeal Schwannoma

Nadir Bir Uyku Apnesi Nedeni: Larenks Schwannoması

Hande Senem Deveci[1], Tülay Erden Habesoğlu[1], Cem Karataş[1], Ali Okan Gürsel[1], Adnan Somay[2], Nurver Özbay[2]

[1]Fatih Sultan Mehmet Education and Research Hospital, Department of Otorhinolaryngology, İstanbul; [2]Fatih Sultan Mehmet Education and Research Hospital, Department of Pathology, İstanbul

ABSTRACT

Laryngeal schwannomas are slow growing, quite rare benign tumors. Although they are slow growing and histologically benign, they have the potential to cause significant morbidity with laryngeal involvement. In this case report we presented a 28-year-old man with a huge laryngeal schwannoma which causes intensive snoring and obstructive sleep apnea. The tumor was totally excised by transhyoid pharyngotomy approach without any complication. There was no other documented laryngeal schwannoma case has presented with obstructive sleep apnea before.

Key words: *laryngeal schwannoma; sleep apnea; transhyoid pharyngotomy*

ÖZET

Larenks schwannoması oldukça nadir görülen, yavaş büyüyen benin karakterde bir tümördür ancak larengeal tutuluma bağlı olarak yüksek morbiditeye yol açma potansiyelleri vardır. Genellikle ariepiglotik plikayı veya band ventrikülü tutar. Biz bu bildiride horlama ve uyku apnesi şikayetleri ile polikliniğimize başvuran 28 yaşındaki erkek hastayı sunmaktayız. Hastanın larenks kitlesi transhiyoid faringotomi yaklaşımıyla total olarak çıkarılmış ve herhangi bir komplikasyon görülmemiştir. Literatürde uyku apnesi şikayeti ile başvuran başka bir vakaya rastlanmamıştır.

Anahtar kelimeler: *larenks schwannoması; uyku apnesi; transhiyoid faringotomi*

Introduction

The schwannomas are benign, slow growing, encapsulated neoplasms arising from Schwann cells that comprise the myelin sheaths surrounding peripheral nerves. They occur at any age frequently in women than in men[1]. Approximately 45% of these tumors present in the head and neck region but laryngeal schwannomas are quite rare, accounting of approximately 0.1% of all benign laryngeal tumors[2]. Laryngeal schwannomas arise from the internal branch of the superior laryngeal nerve[3]. Therefore they usually originated from aryepiglottic folds or false vocal cords[3].

Symptoms of this lesion are related to the mass effect; they include hoarseness, globus sensation, sore throat, odynophagia, dysphagia, dyspnea, stridor, and dysphonia. Symptoms progress over months to years. Stridor and dyspnea are the late findings[4]. As a result of acute respiratory failure, death was reported only once in the literature[5].

Obstructive sleep apnea (OSA) occurs due to enlarged tissues such as tonsils, base of tongue or soft palate, pharyngeal space narrowing, decreased muscle tone of the pharyngeal dilator muscles, or head and neck neoplasms[6].

In this case report we presented a 28-year-old man with a laryngeal schwannoma which causes snoring and sleep apnea, and treated with transhyoid pharyngotomy approach. We described the clinical picture, diagnosis and treatment management of this patient with the aid of his histopathological and radiological images.

Case

A 28-year-old male who was newly-wed admitted to our Ear-Nose-Throat Polyclinic of Fatih Sultan Mehmet Education and Research Hospital (Istanbul, Turkey) with his wife. They complained about the husband's severe snoring and sleep apneas. He did not have any significant medical history. When the history of the patient was detailed, as well dysphagia and exercise related dyspnea have been occurred. During physical examination a submucosal, well-demarcated laryngeal

Uzm. Dr. Hande Senem Deveci, Fatih Sultan Mehmet Eğitim ve Araştırma Hastanesi, E-5 Üzeri, Üst Bostancı, Ataşehir, İstanbul, Türkiye
Tel. 0216 372 17 57 Email. senemesen@yahoo.com
Geliş Tarihi: 25.01.2015 • Kabul Tarihi: 06.05.2015

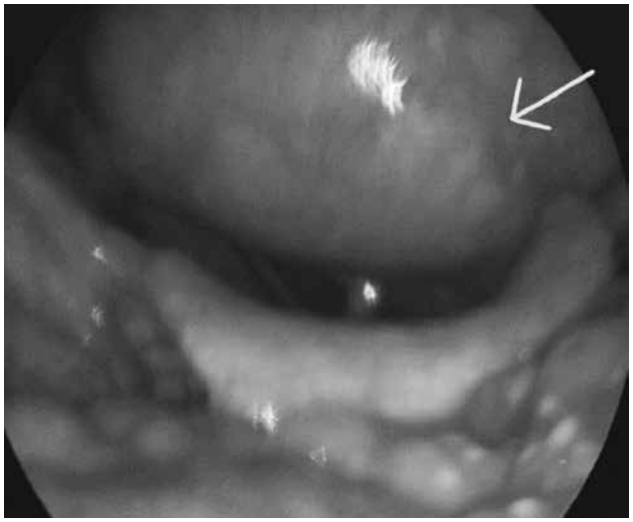

Figure 1. *Preoperative laryngoscopic image of the patient. Blue arrow indicates the mass.*

mass posterior to the epiglottis was noted (Fig. 1). The left vocal cord was fixed but the right vocal cord was mobile.

Magnetic Resonance Imaging (MRI) of the lesion revealed hyperintense and inhomogeneous image in contrast-enhanced scans. The lesion was expanded to the left parapharyngeal space. Both pyriform sinuses were obliterated. On the left side the lesion invaded the aryepiglottic fold and expanded to the proximal esophagus (Fig. 2).

After the imaging procedure and preoperative preparations, the patient was ready for the surgery. First of all, under the local anesthesia tracheotomy was performed and then the patient went under general anesthesia. After suspension microlaryngoscopic evaluation, at the hyoid level a 3 cm midline incision was performed. Through transhyoid approach we entered the pharynx. After lateralization of the epiglottis to the right side, the mass was visualized. The mass dissected from surrounding tissues and totally excised. The mass size was larger than the size of the incision, so the tumor was pushed towards pharynx with the help of a finger and removed through mouth.

Macroscopically the surgical specimen consisted of a well encapsulated white-colored tumor mass, measuring 5×4×2.5 cm. At microscopic examination, the tumor was encapsulated with a fibrous capsule. In the tumor, there were densely cellular and less cellular areas with sheets of spindle cell palisading around amorphous matrix and spindle cells in myxoid stroma respectively. There was no atypia or mitosis (Fig. 3).

At the end of 6-month follow-up the patient was symptom free and we have not encountered any recurrence.

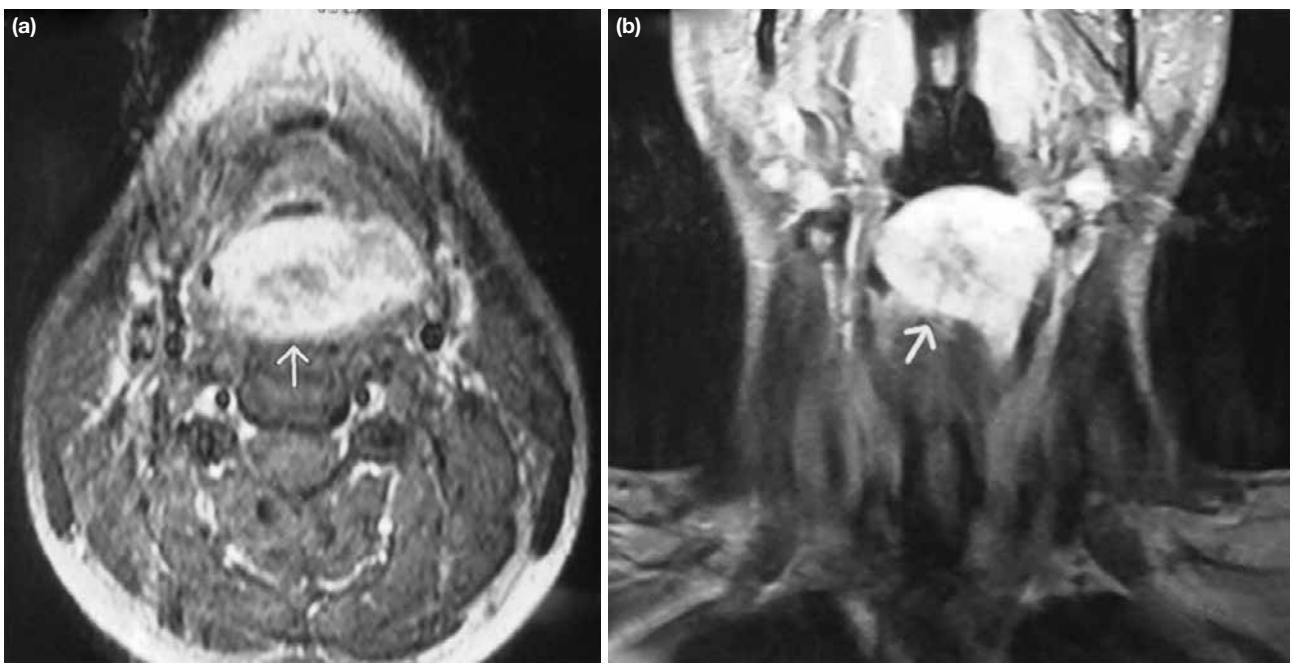

Figure 2. a, b. *Coronal (**a**) and axial (**b**) MR images. Red arrow indicates the mass.*

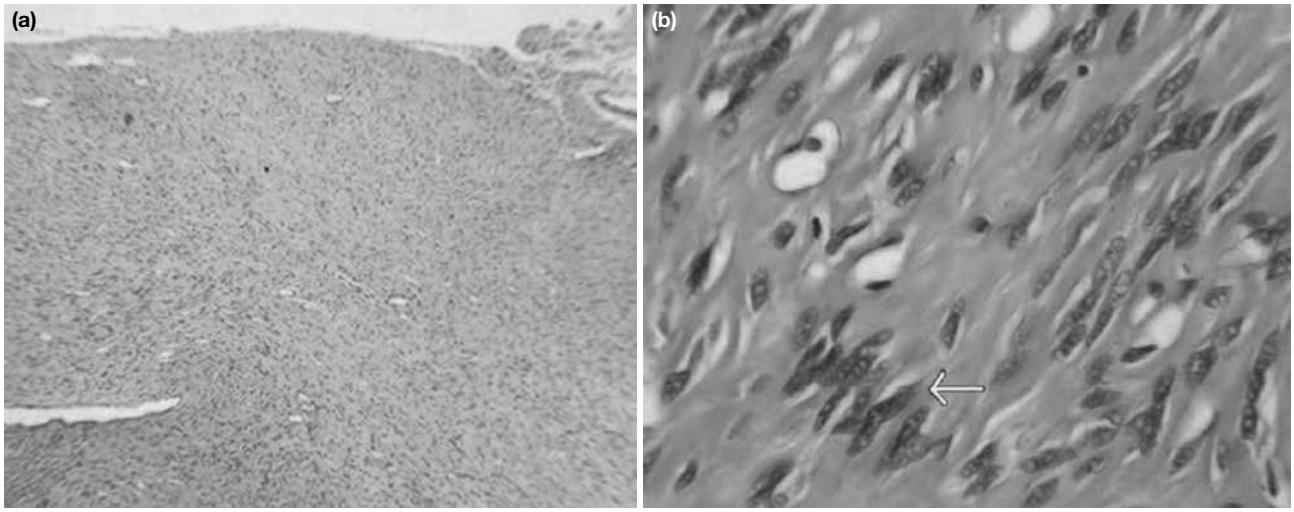

Figure 3. a, b. *Stromal tumor with fibrous capsule H&Ex40 (**a**). Palisading spindle cell in the stroma. Arrow indicates a palisading spindle cell H&Ex400 (**b**).*

Discussion

Verocay was the first to describe the tumors deriving from Schwann cells in 1908[5]. Since then only a few cases of laryngeal schwannomas have been reported in the literature[2].

Symptoms are those associated with any slow-growing tumor of larynx, such as hoarseness and foreign body sensation during swallowing. As the tumor expands, it may cause dyspnea and stridor[2]. The most serious consequence of a large schwannoma reported in the literature was asphyxiation because of a "ball and valve effect"[5]. In our report, the patient presented with snoring and sleep apneas. However, he also had dysphagia and exercise related dyspnea complaints. There was no other documented laryngeal schwannoma case which has presented with obstructive sleep apnea before.

Computed tomography (CT) scans revealed a well-defined, hypodense submucosal mass without any sign of infiltration. Small schwannomas are seen as homogeneously enhancing masses but tumors bigger than 3 cm in size are recognized as masses with slightly heterogeneous contrast enhancement[7].

At magnetic resonance imaging (MRI), T1-weighted imaging of the mass shows variable intensity with high inhomogenenous enhancement after gadolinium injection, whereas T2-weighted images reveal a hyperintense image[8]. However, CT and MRI scans are not effectively diagnostic. In different being tumor also similar findings are recognized. In our case, MRI of the patient showed hyperintense and inhomogeneous image in contrast-enhanced scans and gave information about the expansion of the tumor.

A definitive diagnosis of schwannoma can only be done histologically although it may be difficult to distinguish schwannoma and neurofibroma on small samples obtained with biopsy[4]. Schwannomas are made up almost entirely of Schwann cells. Histologically, they appear as two types of different areas: Antoni A and Antoni B. Antoni A areas contain spindle-shaped cells with their nuclei aligned in a parallel-rows palisade pattern. The Antoni B type is less cellular and loosely organized, with vacuoles and spindle-shaped nuclei. Also in our case pathologically we recognized these densely cellular palisading areas (Antoni A regions), and less cellular regions with myxoid matrix (Antoni B regions)[3].

When we reviewed the literature, the tumor size of this case was the second biggest laryngeal schwannoma[8]. Although the size of the tumor was very big, the patient admitted to our clinic only with snoring and sleep apnea.

Obstructive sleep apnea is caused by obstruction of the upper airways such as due to tonsillary and adenoid hypertrophy, pharyngeal space narrowing, decreased muscle tone of pharyngeal dilator muscles, or head and neck neoplasms[6]. The patient with OSA is rarely aware of having difficulty in breathing. It is recognized as a problem by others. Also in our case, the snoring and apnea of the patient were realized by his wife and the patient was presented to hospital because of these

symptoms. If the OSA is not treated, cardiovascular complications, such as heart failure, myocardial infarction, arryhtmias, systemic and pulmonary hypertensions, and clinical depression risk increase[7]. Therefore the cause of the apnea should be eliminated. In our case to eliminate the disease, we removed the schwannoma through a transhyoid pharyngotomy approach.

Complete surgical removal is the treatment of choice. According to the size or the localization of the tumor endoscopic or external approaches could be chosen[4]. If the tumor size is too big for endotracheal intubation, tracheotomy followed by an external approach with median thyrotomy, lateral pharyngotomy, lateral thyrotomy or transhyoid pharyngotomy[3]. Furthermore, in a selected case, transrobotic approach without any tracheotomy was done in a patient[9]. However, this technique requires advanced experience and it is not available in each center. Wide excision of laryngeal schwannoma is necessary to prevent recurrence. Incomplete excision of the tumor may result in rapid regrowth and airway compromise[10].

In our case the tumor size exceeded the resectability limits of direct laryngoscopy, so open approach was chosen. As an open approach we preferred transhyoid pharyngotomy. This mid-line approach provided a good view for complete excision of tumor safely.

Conclusion

Laryngeal schwannomas are rare, slow growing, benign neurogenic tumors usually located in the supraglottic larynx. These tumors cause globus sensation, dysphagia, dysphonia and upper airway obstruction symptoms. A definite diagnosis can only be made histologically. The only curative treatment option is complete surgical excision.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

References

1. Martin PA, Church CA, Chonkich G. Schwannoma of the epiglottis: first report of a case. Ear, Nose and Throat Journal 2002;81(9):662–3.
2. Taylor J, Stiefel M, Park SY. Schwannoma of the true vocal fold: a rare diagnosis. Ear, Nose and Throat Journal 2006;85(1):52–3.
3. Cadoni G, Bucci G, Corina L, et al. Schwannoma of the larynx presenting with difficult swallowing. Otolaryngol Head Neck Surg 2000;122:773–4.
4. Mannarini L, Morbini P, Bertino G, Gatti O, Benazzo M. Acute respiratory distress in patient with laryngeal schwannoma. Case Report Med 2012;2012.
5. Gardner PM, Jentzen JM, Komorowski RA, et al. Asphyxial death caused by a laryngeal schwannoma: a case report. Journal of Laryngology and Otology 1997;111(12):1171–3.
6. Farboud A, Pratap R, Helquist H, et al. An unusual cause of obstructive sleep apnoea. J Laryngol Otol 2009;123(11):e22.
7. Plantet MM, Hagay C, De Maulmont C, et al. Laryngeal schwannomas. Eur J Radiol 1995;21:61–6.
8. Sabat S, Chapman P. Radiology Quiz Case 2. Arch Otolaryngol Head Neck Surg 2010;136(6):631.
9. Kayhan FT, Kaya KH, Yilmazbayhan ED. Transoral robotic approach for schwannoma of the larynx. J Craniofac Surg 2011;22(3):1000–2.
10. Rosen FS, Pou AM, Quinn FB Jr. Obstructive supraglottic schwannoma: a case report and review of the literature. Laryngoscope 2002;112(6):997–1002.

KAFKAS TIP BİLİMLERİ DERGİSİ
Kafkas Journal of Medical Sciences
Kafkas J Med Sci 2016; 6(2):142–144 • doi: 10.5505/kjms.2016.26349

OLGU SUNUMU / *CASE REPORT*

Bilateral Breast Abscess in a Newborn Baby

Yenidoğan Bir Bebekte Bilateral Meme Apsesi

Sara Erol[1], Hasibe Gökçe Çınar[2], Ayşegül Zenciroğlu[1], Nurullah Okumuş[1]

[1]Neonatal Intensive Care Unit, Dr. Sami Ulus Maternity and Children Training and Research Hospital, Ankara, Turkey;
[2]Pediatric Radiology Unit, Dr. Sami Ulus Maternity and Children Training and Research Hospital, Ankara, Turkey

ABSTRACT

Mastitis and breast abscess are rarely seen in neonatal period. Neonatal mastitis is generally localized to the breast. A seven-day-old male infant was admitted to the neonatal intensive care unit because of fever and swelling in the bilateral mammary areas. In ultrasound examination, hypoechoic area was monitored in the bilateral retroareolar region. Bilateral breast abscess responded to surgical and medical treatment.

Key words: *infant; abscess; mastitis*

ÖZET

Mastit ve meme apsesi yenidoğan döneminde nadiren görülür. Yenidoğan döneminde mastit genellikle memede lokalizedir. Yedi günlük erkek hasta, yenidoğan yoğun bakı ünitesine ateş ve her iki memesinde şişlik nedeniyle başvurdu. Ultrasonografik incelemede bilateral retroareolar bölgede hipoekoik alan izlendi. Bilateral meme apsesi, cerrahi ve medikal tedavi ile düzeldi.

Anahtar kelimeler: *infant; apse; mastit*

Introduction

Mastitis and breast abscess are rarely seen in neonatal period. Neonatal mastitis is defined as evidence of breast inflammation with or without abscess in the first two months of life; with a female: male ratio of approximately 2:1 after two weeks of life[1]. The majority of cases of neonatal mastitis are caused by Staphylococcus aureus; less common causes include gram-negative enteric organisms, anaerobes, and Group B Streptococcus[2]. Although, neonatal mastitis is generally localized to the breast, it can be complicated by extensive cellulitis, necrotizing fasciitis, and osteomyelitis[3-4]. Neonatal mastitis and breast abscess must be treated promptly to prevent complications. Herein, we report a newborn case of bilateral breast abscess recovered with medical treatment.

Case Report

A seven-day-old male infant was admitted to the neonatal intensive care unit because of fever and swelling in the bilateral mammary areas. The mother had no previous history of infection. His mother said that there has been superficial pustules on diaper and axillar region of the baby for two days before fever. On admission, body temperature was 38.4°C, respiratory rate 64 per minute, and hearth rate 158 per minute. He had approximately 2×2 cm size swelling lesions in the bilateral retroareolar regions. These lesions were hard on palpation, with increased local temperature, redness of skin and tenderness. Superficial pustule was not observed. Laboratory investigation revealed a hemoglobin of 15.2 g/dl, a hematocrit of 47.2%, a leukocyte count of 22,000/mm^3. Serum C-reactive protein (CRP) level was high (46 mg/L, normal value: <10 mg/L). Peripheral smear revealed; 64% neutrophil, 30% lymphocyte, 6% monocyte, rare toxic granulation was seen. In ultrasound examination, hypoechoic area was monitored in the bilateral retroareolar region. And dimension of the lesions were 19×15 mm on the right and 19×12 mm on the left side. Drainage was performed and ampicillin and cefotaxime treatments were initiated promptly. Lumbar puncture was performed, and examination of the cerebrospinal fluid (CSF) was normal. CSF, blood and abscess cultures were negative but *"E.coli"* was isolated from urine culture.

At follow-up, patient's fever and inflammatory signs in the breast areas gradually improved with the medical treatment. Antibiotic treatment was given for 2 weeks. The patient was discharged home after full recovery.

Uzm. Dr. Sara Erol, Babür Caddesi No: 44, Altındağ, Ankara, Türkiye
Tel. 0312 305 62 84 Email. sarasurmeli@gmail.com
Geliş Tarihi: 28.01.2014 • Kabul Tarihi: 12.05.2015

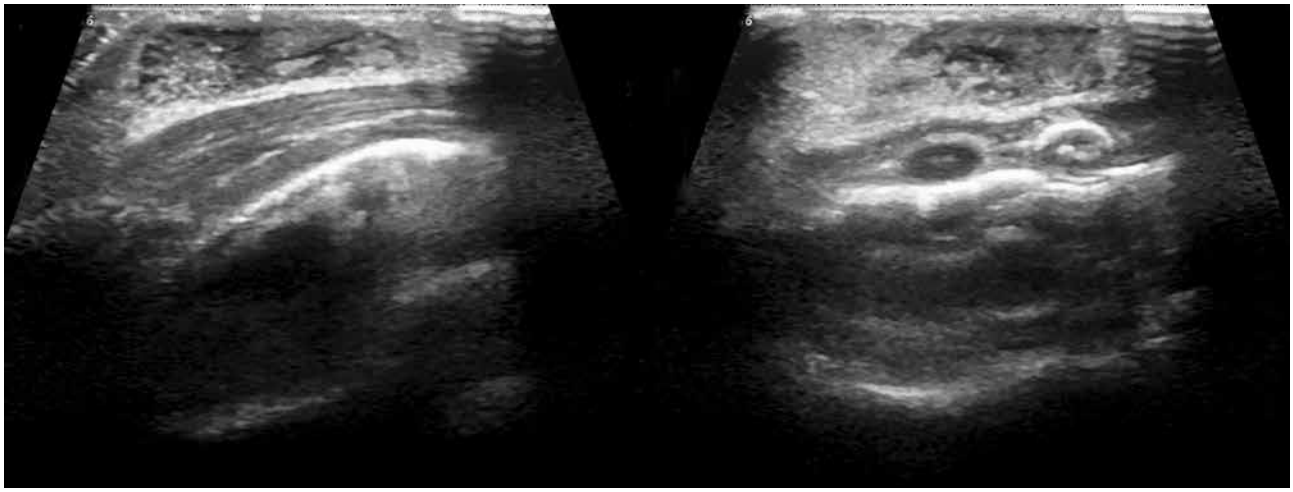

Figure 1. *Breast USG showing bilateral abscess.*

Figure 2. *Appearance of the patient before and after treatment.*

Discussion

The pathogenesis of neonatal mastitis is related to the physiologic breast hypertrophy in the term infant, which is induced by maternal hormones, and to the presence of potentially pathogenic bacteria on the skin and/or mucous membranes that spread to the breast parenchyma through the nipple[5]. Manipulation of the neonatal breast to express a nipple discharge ("witch's milk") is a risk factor for breast abscess[6]. In our patient there was no history of maternal infection and manipulation of the infant's breasts.

Neonatal mastitis is usually unilateral and local in nature[6]. Our case had bilateral breast abscess but purulent nipple discharge and enlargement of axillary lymph nodes were not seen either. One-quarter of patients may also have fever (>101°F (38.3°C) such as our patient. Approximately one-half have evidence of skin infection such as superficial pustules or bullae at other parts of the body[1]. Our patient had superficial pustules on the inguinal and axillary region prior to admission.

If the lesion is fluctuant, aspiration (with or without ultrasonographic guidance) should be performed and drainage material also should be sent for Gram stain and culture[7]. However during this procedure, it is important not to injure the underlying breast.

In neonates, it is important to distinguish mastitis from physiologic breast hypertrophy. In contrast to mastitis, in physiologic hypertrophy, the breast bud is neither red nor tender and resolves spontaneously[8].

No randomized controlled studies have evaluated antibiotic regimens for neonatal mastitis. Recommendations for treatment are based upon the causative pathogens and the response to therapy described in observational studies[9]. The empiric antibiotic choice should be guided by local susceptibility

patterns and the Gram stain, if one is available. The duration of therapy is 7–14 days, depends on the clinical response of the patient[9]. In conclusion breast abscess is a rare disorder in neonatal period and to the best of our knowledge this is the first case of bilateral breast abscess responded to surgical and medical treatment.

Declaration of Interest

The authors report no conflict of interest. The authors alone are responsible for the content and writing of the article.

References

1. Walsh M, McIntosh K. Neonatal mastitis. Clin Pediatr 1986;25:395–9.
2. Efrat M, Mogilner JG, Lujtman M, Eldemberg D, Kunin J, Eldar S. Neonatal mastitis –diagnosis and treatment. Isr J Med Sci 1995;31:558–60.
3. Hsieh WS, Yang PH, Chao HC, Lai JY. Neonatal necrotizing fasciitis: a report of three cases and review of the literature. Pediatrics 1999;103:53.
4. Michael IK, Howard FH. Osteomyelitis due to penicillin-resistant staphylococci in infancy following suppurative mastitis. (Report of a case). J Trop Pediatr 1960;6:19.
5. Sloan B, Evans R. Clinical pearls: neonatal breast mass. Acad Emerg Med 2003;10:269–70.
6. Rudoy RC, Nelson JD. Breast abscess during the neonatal period. A review. Am J Dis Child 1975;129:1031–4.
7. DiVasta AD, Weldon C, Labow BI. The breast: Examination and lesions. In: Emans SJ, Laufer MR, editors. Goldstein's Pediatric & Adolescent Gynecology, 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2012. p.405.
8. Fleisher, GR. Infectious disease emergencies. In: Fleisher GR, Ludwig S, Henretig FM, editors. Textbook of Pediatric Emergency Medicine, 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006. p.783.
9. Fortunov RM, Hulten KG, Hammerman WA, Mason EO Jr, Kaplan SL. Evaluation and treatment of community-acquired Staphylococcus aureus infections in term and late-preterm previously healthy neonates. Pediatrics 2007;120:937–45.

KAFKAS JOURNAL OF MEDICAL SCIENCES
Kafkas J Med Sci 2016; 6(2):145–148 • doi: 10.5505/kjms.2016.85866

OLGU SUNUMU / *CASE REPORT*

Two Cases of Nasal Glioma Treated by Endoscopic Transnasal Surgery

Endoskopik Transnazal Cerrahi ile Tedavi Edilen İki Nazal Gliom Olgusu

Abdulkadir Özgür[1], Engin Dursun[1], İbrahim Şehitoğlu[2], Zerrin Özergin Coşkun[1], Özlem Çelebi Erdivanlı[1], Suat Terzi[1]

[1]Recep Tayyip Erdoğan University Faculty of Medicine, Department of Otorhinolaryngology, Rize, Turkey; [2]Recep Tayyip Erdoğan University Faculty of Medicine, Department of Pathology, Rize, Turkey

ABSTRACT

Nasal glioma is a rare congenital benign midline tumor consisting of heterotropic glial tissue. Similarly, to the other intranasal tumors it causes symptoms like nasal obstruction, rhinorrhea, and bleeding. The only treatment option is surgical excision. Since the tumor recurrence is a very common condition the surgery should be performed very carefully. In addition, in cases with intracranial extension fatal postoperative meningitis may occur. In this report, we aimed to present clinical and therapeutic features of the two cases of nasal glioma patient which were both treated by transnasal surgery at the age of nine months and thirteen months old.

Key words: *endoscopic transnasal surgery; congenital midline tumors; nasal glioma*

ÖZET

Nazal gliomlar heterotropik glial dokudan oluşan, nadir görülen, kongenital benign orta hat tümörleridir. Diğer intranazal tümörlere benzer şekilde burun tıkanıklığı, burun akıntısı ve burun kanaması gibi semptomları vardır. Tek tedavi seçeneği cerrahi eksizyondur. Fakat cerrahisi çok dikkatli yapılmalıdır. Çünkü tümör nüksü çok sık karşılaşılan bir durumdur. Ayrıca intrakraniyal uzanımı olan vakalarda ölümcül seyredebilen postoperatif menenjit ortaya çıkabilir. Bu yazıda biri dokuz aylık, diğeri ise on üç aylıkken transnazal cerrahi tedavi uygulanan iki nazal gliom vakasının klinik ve tedavi özelliklerinin sunulması amaçlanmıştır.

Anahtar kelimeler: *endoskopik transnazal cerrahi; konjenital orta hat tümörleri; nazal gliom*

Yard. Doç. Dr. Abdulkadir Özgür, İslampaşa Mah. Şehitler Sok., Rize, Türkiye
Tel. 0464 213 04 91 Email. akozgur53@gmail.com
Geliş Tarihi: 29.10.2014 • Kabul Tarihi: 12.05.2015

Introduction

Nasal gliomas are very rare benign tumors formed by presence of heterotopic glial tissue on the nasal dorsum and/or nasal cavity congenitally. There are intranasal, extranasal and mixed types. Although most commonly seen in the nasal area; can also occur in other areas such as skin, palate, orbit, scalp and lungs[1,2]. It is frequently diagnosed in newborn and pre-school ages, however, can be also observed in adults in very rare amount[3]. Similarly to other intranasal masses, patients with intranasal localization have symptoms like nasal obstruction, rhinorrhea, and bleeding. Those located extranasally can cause cosmetic deformities. Clinically, these tumors are often seen as hard, non-pulsatile and gray or pink colored masses[1,4]. Treatment choice is surgical excision. Although rarely seen, they are nevertheless clinically important tumors because of the possibility of connection with central nervous system. After excision or biopsy cerebrospinal fluid (CSF) leakage or meningitis may occur[5].

Case 1

Thirteen month old baby boy was admitted with complaint of a mass protruding from the left nasal vestibule existing since birth. The physcical examination of the patient showed a mass filling the left nasal cavity with stiff elastic consistency. A magnetic resonance imaging (MRI) was performed to determine the localization and possibility of intracranial extension of the mass. It showed a 9×16×20 mm cystic mass filling the the left nasal cavity and pushing the middle turbinates. There was no intracranial connection (Fig. 1).

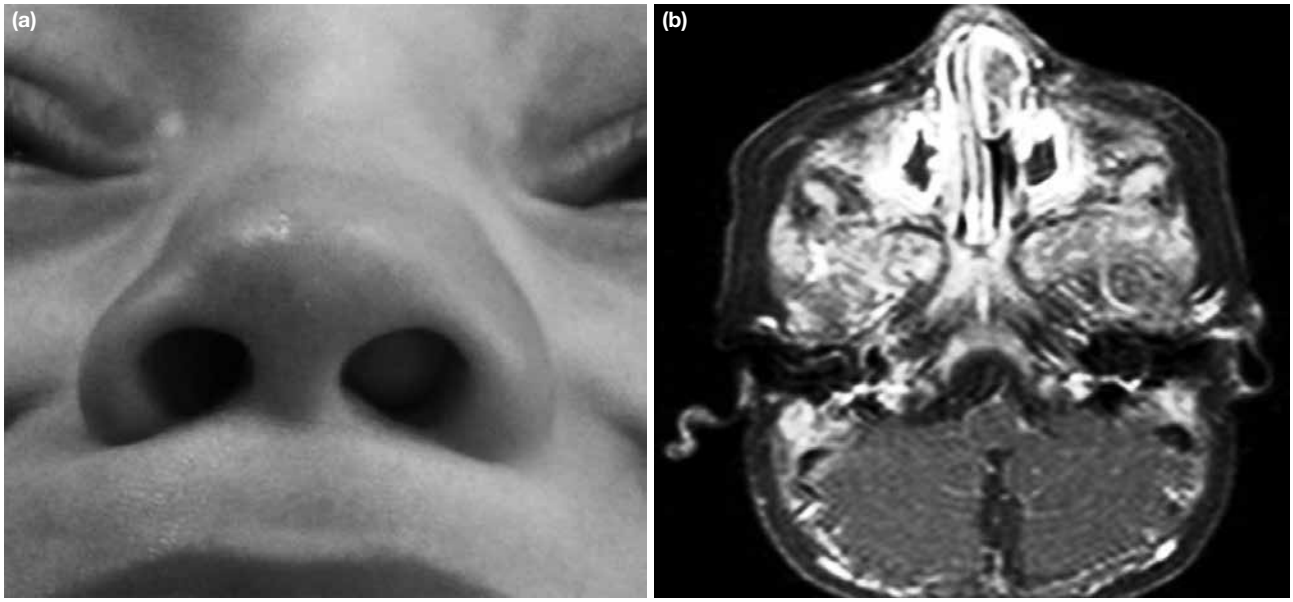

Figure 1. a, b. *The mass filling the left nasal cavity (**a**). MRI of the tumor in axial plan (**b**).*

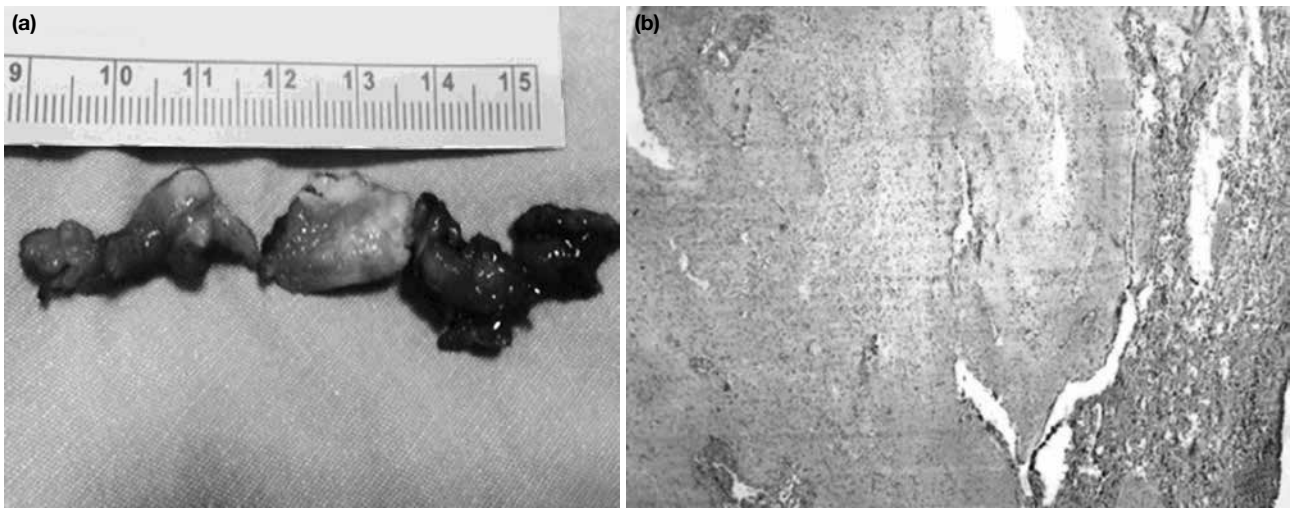

Figure 2. a, b. *The macroscopic appearance of the excised mass (**a**). The microscopic appearance of the mass (the eosinophilic glial tissue located just under the pseudo-stratified epithelium [H&E×40]) (**b**).*

Total tumor excision with endoscopic transnasal surgery was performed under general anesthesia with a preliminary diagnosis of nasal glioma. During the operation, the tumor was seen partially adhered to the mucosa of the nasal septum and so the adjacent septal mucosa was excised with the mass. The postoperative pathologic examination of the excised specimen confirmed the diagnose of nasal glioma (Fig. 2). There was no major complication or recurrence during the postoperative two years follow up.

Case 2

Nine month old baby boy was admitted to the to our clinic with the complaint of a mass in the right nasal cavity that led to progressive respiratory distress after birth. The physical examination of the patient showed a mass filling the right nasal cavity with hard elastic consistency. MRI of the patient revealed a cystic mass in the right nasal cavity which was approximately 7×15×22 mm in size without significant enhancement. There was no intracranial extension (Fig. 3).

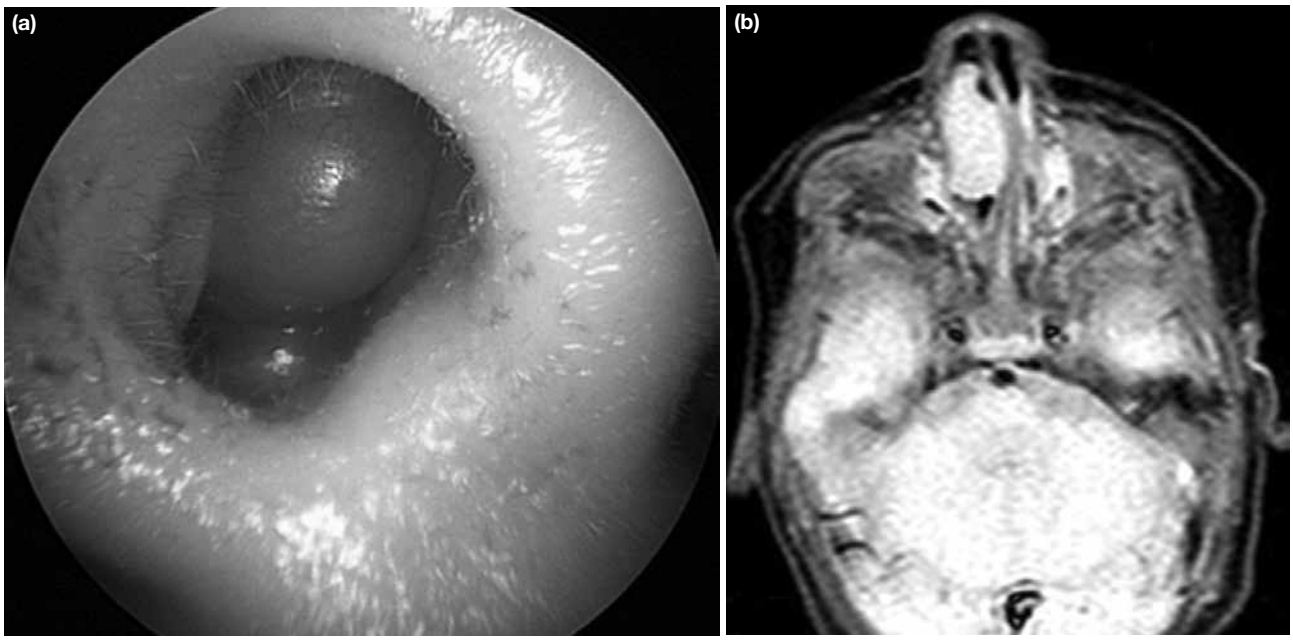

Figure 3. a, b. *The mass filling the right nasal cavity (**a**). Preoperative MRI of the patient in axial plan (**b**).*

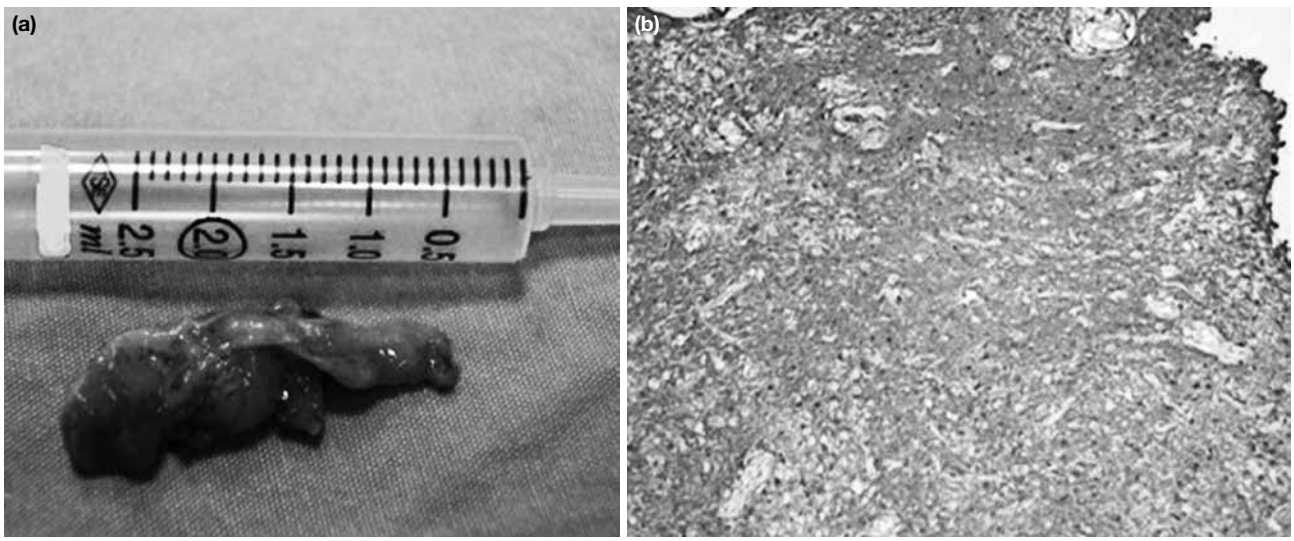

Figure 4. *Postoperative macroscopic appearance of the excised tumor and microscopic appearance of it (diffuse and strong glial fibrillary asidic protein involvement in glial tissue, ×100).*

Total tumor excision with endoscopic transnasal surgery was performed under general anesthesia with a preliminary diagnosis of nasal glioma. The postoperative pathologic examination comfirmed the diagnose (Fig. 4). There was no recurrence or major complication during the postoperative eighteen months follow-up.

Discussion

Congenital midline nasal masses are very rare anomalies. The most common forms are dermoid cysts, nasal gliomas, encephaloceles and hemangiomas[6]. Nasal glioma is not a real tumor. During embryonic development, as a result of the abnormal closure of the nasal and frontal bones it occurs as extracranial settlement of ectopic glial tissue. Histologically, it is composed of

glial cells and neuroglial elements in the matrix within the connective tissue. Therefore, it is also called as glial heterotropia by some authors. Nasal gliomas may be associated with subarachnoid space or dura[4,5]. İt is frequently seen in infants and preschool-age but very rarely can be also observed in adults. Clinically,it can be seen in the form of extranasal (60%), intranasal (30%) or mixed type (10%)[3]. The cases presented were thirteen and nine months male patients and the masses were located intranasally and presented just after the birth.

Similar to other intranasal tumors, intranasal glial heterotopia can cause symptoms like nasal obstruction, rhinorrhea, and bleeding. Clinically, these tumors are often seen as hard, non-pulsatile and gray or pink colored mass[1,4]. Clinical findings and preoperative imaging methods, such as computed tomography and MRI can not distinguish nasal gliomas from the other midline masses (dermoid cyst, teratoma, hemangioma, lipoma etc.). Histopathological and immunohistochemical examination is needed for the differential diagnosis. Preoperative imaging techniques are used for evaluation of the boundaries of the mass and relationship of it with the surrounding tissues[2]. To support the diagnosis of nasal glioma neuron-specific antigens such as neuron specific enolase (NSE), glial fibrillary asidic protein (GFAP) and S-100 protein examination can be performed immunohistochemically[1]. In the cases presented MRI was used as preoperative imaging technique and it did not show any intracranial connection or invasion into surrounding tissues. Immunohistochemical examination of the excised specimens showed NSE, GFAP and S-100 protein positivity.

Treatment choice is surgical excision. Lateral rhinotomy approach or endoscopic surgical methods can be applied in intranasal masses. After excision or biopsy complications such as CSF leak and recurrent meningitis may occur. Nowadays transnasal endoscopic surgery is more preferred since the use of it is minimally invasive[1,5]. In both of the cases presented here, masses were excised completely with transnasal endoscopic surgery. In the follow-up of our cases there was no recurrence or complication observed.

As a result; nasal glioma should be kept in mind in the differential diagnosis of patients presenting with nasal mass especially in the newborn and infancy period. Treatment choice is total excision of the tumor and we believe that endoscopic transnasal surgery could be performed as a minimally invasive method in the management of the disease.

References

1. Yokoi H, Wada R, Ichikawa G. Endoscopic treatment of so-called intranasal glioma. Rhinology 2002;40:217–9.
2. Ramadass T, Narayanan N, Rao P, et al. Glial Heterotopia in ENT-Two Case Reports and Review of Literature. Indian J Otolaryngol Head Neck Surg 2011;63:407–10.
3. Penner CR, Thompson L. Nasal glial heterotopia: a clinicopathologic and immunophenotypic analysis of 10 cases with a review of the literature. Ann Diagn Pathol 2003;7:354–9.
4. Sürmelioğlu Ö, Tarkan Ö, Tuncer Ü, et al. Nasal Glioma: Case report. Cukurova Med J 2011;36:34–6.
5. Talwar OP, Pradhan S, Swami R. Nasal glioma: a case report. Kathmandu Univ Med J 2007;5:114–5.
6. Ma KH, Cheung KL. Nasal glioma. Hong Kong Med J 2006;12:477–9.

AMAÇ VE KAPSAM

Kafkas Tıp Bilimleri Dergisi (Dergi) Türkçe ve İngilizce yazılmış makaleleri kabul eden, hakemli bir genel tıp dergisidir. Dergi tıbbi bilimleri geliştiren ve aydınlatan ya da okuyucularını eğiten orijinal biyomedikal makaleleri (Tıp bilimleri ile ilgili araştırma, kısa bildiri, derleme, editöryal, editöre mektup, çeviri, tıbbi yayın tanıtma vb türlerden yazılar) yayımlar. Yılda 3 sayı halinde (Nisan, Ağustos, Aralık) tek cilt olarak, matbu ve elektronik ortamlarda basılır. Dünyanın her yerinden makaleler kabul edilir.

MAKALE GÖNDERME

Makale toplama ve değerlendirme işlemleri http://meddergi.kafkas.edu.tr web adresinden online yapılır. Web adresinden giriş yapılmasını takiben "online makale gönder, takip et, değerlendir" butonunun tıklanması ile çıkacak direktiflerin takip edilmesi gereklidir.

ETİK

Dergi, Yayın Etikleri Komitesi'nin (COPE) rehberlerindeki iyi yayın uygulamaları ilkelerine sıkı bir şekilde bağlıdır (http://publicationethics.org/resources/guidelines). Makale başvurusunda bulunan yazarlar; çalışmalarının etik, hukuki ve bilimsel kurallara uygun olduğunu, daha önce yayınlanmamış ve başvuru sırasında başka bir yerde yayınlanmak için değerlendirme aşamasında olmadığını kabul ederler. Daha önce yayınlanmış tablo, şekil ve yazı makalede açıkça belirtilmeli ve yayın haklarını elinde tutanlardan izin alınmalıdır. Dergi, uygun etik kurul başvurularının yapılmış olmasını, bilgilendirilmiş onamların alınmasını ve bunların makalede bildirilmesini zorunlu tutar. İnsan öğesini içeren tıbbi çalışmalarda, Helsinki Deklarasyonu ilkelerine sıkıca bağlıdır (http://www.wma.net/e/policy/pdf/17c.pdf). Yazarlar, laboratuvar hayvanlarının kullanımında ve bakımında kurumsal ya da ulusal rehberlere uygun davrandıklarını bildirmek zorundadır.

BAŞVURU SIRASINDA İSTENEN MAKALE NİTELİKLERİ

Dergi, Uluslararası Tıp Dergileri Editörleri Komitesi'nin (ICMJE) rehberlerine sıkıca bağlıdır (http://www.icmje.org/index.html). Türkçe makaleler için, Türkçe özete ek olarak İngilizce özet; İngilizce makaleler için, İngilizce özete ek olarak Türkçe özet istenmektedir.

MAKALE HAZIRLANMASI

Tercihen Times New Romans yazı karakteri, 12 punto ve çift aralıklı yazılması önerilir. Makaleler açık, kısa ve akıcı bir Türkçe veya İngilizce ile yazılmalı, imla kurallarına uyulmalıdır. Dergi, özellikle giriş ve tartışma kısmı olmak üzere, makale uzunluğunu içerdikleri bilgiyle orantılı ölçüde kısa tutulmasını önerir. Bütün yazarlara bir istatistik uzmanı ile görüşmeleri önerilir.

Başlangıç Sayfası: Makale başlığı kısa ve devamlı nitelikte olmalıdır. Başlık indeksleme ve bilgi toplama açısından yararlı olacak biçimde tanımlayıcı ve bilgi verici olmalıdır. Bütün yazarların ad ve soyadları yazılmalıdır. Her yazar için çalıştığı bölüm, kurum belirtilmeli, iletişim yazarının şehir, ülke ve posta kodunu da içeren tam yazışma adresi, fax, telefon ve Email adresi sunulmalıdır.

Özet: Özetler anlaşılır olmalı ve yazının amaç ve belirgin sonuçlarını gösterebilmelidir. Yalnızca temel bulgu ve sonuçları belirterek, uyarlanmaya gerek duymadan özetleme servislerince kullanılabilmelidir. Araştırma makalelerinde özet bölümü yazısını şu alt başlıklara (Giriş, yöntem, bulgular, sonuç) göre sıralamak gerekir. Derlemeler,olgu sunumlarında alt başlık gerekmez. Editöryal, editöre mektup gibi türlerde özetleme yapılmaz. Özetlemede yalnızca standart kısaltmalar kullanılmalıdır.

Anahtar Kelimeler: Yazıyla ilgili "Index Medicus: Medical Subject Headings ve Türkiye Bilim Terimleri" standartlarına uygun üç ile altı arası anahtar kelime özet altına yazılmalıdır.

Giriş: Anlaşılır ve kısa olmalı, son paragrafında çalışmanın amacı açıkça belirtilmelidir. Literatürün gözden geçirilmesi çalışmanın nedenselliğine yönelik olmalı ve önemli bilgileri içermelidir.

Yöntem: Gözlemsel ya da deneysel çalışma katılımcılarının neye göre seçildiği (hastalar, kontroller ya da laboratuvar hayvanları) açıkça tanımlanmalıdır. Katılımcıların yaş, cinsiyet ve diğer önemli özellikleri belirlenmelidir. İnsan ve hayvanlar üzerinde yapılan çalışmalarda etik standartlar açıkça tanımlanmalıdır. Yazarlar, diğer araştırmacılar tarafından da bulguların tekrarlanabilmesi için yöntem, cihaz ve işlemleri yeterli açıklıkta tanımlamalıdırlar. İstatistiksel yöntemler de dahil, daha önceden kabul görmüş yöntemler için referanslar sağlanmalıdır. Yeni ya da uyarlanmış eski yöntemler tanımlanmalı, neden kullanıldıkları ve sınırları açıklanmalıdır. Bütün ilaç ve kimyasallar jenerik isimleri, dozları ve uygulanma yolları sunulmalıdırlar. Randomize kontrollü klinik çalışmalarda, çalışmanın ana öğeleriyle ilgili, çalışma protokolü (çalışma populasyonu, müdahaleler ya da maruziyetler, beklenen sonuçlar ve istatistik analizin nedenselliği), müdahalelerin belirlenmesi (randomizasyon yöntemi, gruplara ayırmada gizlilik) ve grupların maskelenmesini (körleme) içeren özellikler sunulmalıdır. Yapılan istatistiksel analiz yöntemi belirtilmelidir. Makalenin anlaşılması için özellikle gerekli değilse, istatistiksel testlerin ayrıntılarla anlatılması gerekmez. Ancak, özellik arz eden yöntemler kullanıldığında ve makale istatistik ağırlıklı olduğunda ayrıntılı tanımlar gereklidir.

Bulgular: Tablo, şekil ve yazıda sunulan bilgilerin gereksiz tekrarlanmasından kaçınılmalıdır. Yalnızca tartışma ve ana sonucun anlaşılması için gerekli olan önemli bilgiler sunulmalıdır. Veriler bütünlük içinde ve tutarlı olarak sunulmalı, raporun açık ve mantıksal ilerlemesi sağlanmalıdır. Tablo ve şekillerdeki veriler yazıda tekrarlanmamalıdır. Yalnızca önemli gözlemler vurgulanmalı ya da özetlenmelidir. Aynı veriler hem tablo hem de grafiklerde sunulmamalıdır. Verilerin yorumlanması tartışma bölümüne saklanmalıdır.

Tartışma ve Sonuç: Tartışma asıl bulguları anlatan kısa ve özlü bir cümle ile başlamalı, çalışmanın güçlü ve zayıf yönlerini tanımlamalı, bulguları diğer çalışmalarla ilişkilendirerek tartışmalı, olası açıklamalar sağlamalı ve gelecekte yanıtlanabilecek sorulara işaret etmelidir. Tartışma, bulgular bölümünde zaten sunulmuş bulguların tekrarıyla değil, bunların yorumlanmasını ile ilgilenmelidir. Yeni bulgularla, zaten bilinenlerin ilişkisini kurmalı ve mantıksal çıkarsamalar yapmalıdır. Sonuç çalışmanın amacıyla ilişkilendirilebilir ama niteliksiz önermelerden ve verilerle desteklenmeyen sonuçlardan kaçınmak gerekir. Çalışmanın üstünlüğü konusunda iddialarda bulunmaktan kaçınmak gerekir. Öneriler kesinlikle gerekli ve konuyla ilintiliyse tartışma bölümünde belirtilmelidir.

Teşekkürler: Teşekkürler kısa ve net olmalı, yalnızca bilimsel/teknik destek ve finansal kaynak için yapılmalıdır. Rutin kurum olanaklarının kullanılması, makale hazırlanmasındaki destek ya da yardımlar (yazma işi ya da sekreterlik işleri) gibi durumları içermemelidir.

Kaynaklar: Normalde toplam kaynak 30 adet ile sınırlandırılmalıdır. Literatüre atıfta bulunan kaynaklar ardışık olarak sıralanmalı ve makalenin sonunda yer almalıdır. Yazının bütününde atıflar üst karakterle cümle bitiminde yer almalıdır. Olabildiğince yazı içinde yazar isimleri kullanmaktan kaçınmak gerekir. Kafkas Tıp Bilimleri Dergisi aynı zamanda ulusal dergilerin kaynak gösterilmesini teşvik eder. Kaynaklar; Index Medicus stiline uygun yapılmalıdır. *Üç yazarlıya kadar makale:* Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med 2002; 347:284-7. *Üçten fazla yazarlı makale:* Rose ME, Huerbin MB, Melick J, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res 2002; 935:40-6. *Kitap:* Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002:93-113.

Tablolar: Tablolar ayrı olarak yazılmalı ve verilen rakamlar ile sıralanmalıdır. Her tablo kendisi ile ilgili tanımları içermeli ve kısa tanımlayıcı başlık içermelidir. Tablo içindeki kısaltmalar, tablo altında açıklanmalıdır. Tablo (ilgili başlık, tanımlayıcı ve açıklayıcı bilgiler) ayrı bir sayfada sunulmalıdır.

Şekiller: Şekiller (ilgili başlık, tanımlayıcı ve açıklayıcı bilgiler) ayrı bir sayfada sunulmalıdır.

MAKALE DEĞERLENDİRME SÜRECİ

Dergiye sunulan bütün yazılar en az iki hakem tarafından değerlendirme işlemine alınır. Karar hakem değerlendirme raporlarına göre verilir. Bütün kabul görmüş makaleler dergi kural ve formatına uygun olarak redaksiyon işlemine tabi tutulur.

SON KONTROL

Yazının kabulünü takiben yapılacak editöryal işlemlerden sonra, yazının mizanpajlı şekli yazarların onayına sunulacak ve üç gün içinde telif hakkı devir formu ile birlikte geri istenecektir.

TELİF HAKKI DEVİR FORMU

Kafkas Tıp Bilimleri Dergisi'ne yazı teslimi, çalışmanın daha önce hiçbir yerde yayımlanmadığı (özet şeklinde ya da bir sunu, inceleme ya da tezin bir parçası şeklinde yayımlanması dışında), başka bir yerde yayımlanmasının düşünülmediği ve Kafkas Tıp Bilimleri Dergisi'nde yayımlanmasının tüm yazarlar tarafından uygun bulunduğu anlamına gelmektedir. Yazar(lar), çalışma ret edilmedikçe, yazıya ait tüm hakları Kafkas Üniversitesi ve Kafkas Tıp Bilimleri Dergisi'ne devretmektedir(ler). Yazar(lar), Kafkas Üniversitesi ve Kafkas Tıp Bilimleri Dergisi'nden izin almaksızın çalışmayı başka bir dilde ya da yerde yayımlamayacaklarını kabul eder(ler).

DOI NUMARASI

Yayımlanan her bir makaleye dijital nesne tanımlayıcı numarası (doi) atanır.

KAFKAS TIP BİLİMLERİ DERGİSİ
Journal of Medical Sciences

Guideline for Authors

SCOPE

The Journal of Kafkas Medical Sciences (KJMS) is a peer-reviewed general medical journal and welcomes manuscripts in Turkish and English. The KJMS publishes original communications of biomedical research that advances or illuminates medical science or that educates the journal readers. It is issued three times per year, and distributed in written form and in electronic format. All manuscripts are accepted throughout the globe.

MANUSCRIPT SUBMISSION

Manuscripts are submitted online from http://meddergi.kafkas.edu.tr. After registration, authors can send their manuscripts by clicking "online manuscripts submission, follw-up and review" buton placed in web site and following directives written in site.

ETHICS

KJMS adheres strictly to the Committee of Publication Ethics (COPE) guidelines (http://publicationethics.org/resources/guidelines) on good publication practice. Authors submitting a manuscript accept that their work contains unpublished work and that it is not under consideration for publication elsewhere. Previously published tables, illustrations or text should be clearly indicated in the manuscript and the copyright holder's permission must be obtained. Copies of permission letters should be enclosed with the paper. Failure to comply with these guidelines will be considered as a double publishing and treated appropriately. KJMS anticipates appropriate ethical approval and, where relevant, the patients' written informed consent in studies involving humans and animals or human or animal material. KJMS respects to the Declaration of Helsinki for Medical Research involving Human Subjects (http://www.wma.net/e/policy/pdf/17c.pdf). The authors should indicate whether the institutional and national guidelines for the care and use of laboratory animals were followed, when reporting experiments on animals.

MANUSCRIPT REQUIREMENTS AT SUBMISSION

KJMS adheres strictly to the International Committee of Medical Journal Editors (ICMJE) guidelines (see http://www.icmje.org/index.html). For manuscripts in Turkish, in addition to the Turkish version, an English version of the abstract is recommended.

MANUSCRIPT PREPARATION

Double spacing on one side of the paper only, use preferably Times New Roman, 12 point font size. Manuscripts should be written using clear and concise English or Turkish, with English standard spelling and conventions. KJMS advices the authors to restrict the length of manuscripts, especially Introduction and Discussion sections, to the appropriate amounts in relation to the information they contain. It is advisable for authors to refer a statistics expert before final submission.

Title Page: Title of the article should be short (less than 25 words), continuous (broken or hyphenated titles are not acceptable). It should be sufficiently descriptive and informative so as to be useful in indexing and information retrieval. Give initials and family name of all authors. The department, institution and e mail should be supplied for each author. The full postal address, city and country should be given with postal code for the corresponding author, who should be clearly identified. The corresponding phone and fax numbers should be provided.

Abstract: Abstract should be brief (of about 250 words) and indicate the scope and significant results of the paper. It should only highlight the principal findings and conclusions so that it can be used by abstracting services without modification. For original research articles, abstracts should be subdivided into four headings (Introduction, Materials and Methods, Results, Conclusion). No subheadings are required for reviews and case reports. No abstracts are required for editorials and letters to the editor. Only standart abbrevations could be used in abstract section.

Keywords: Between three and six keywords that are suitable with "Index Medicus: Medical Subject Headings and Turkish Scientific Terms" standards should be written under abstract section.

Introduction: Introduction should be brief and state precisely the scope of the paper. Review of the literature should be restricted to reasons for undertaking the present study and provide only the most essential background.

Materials and Methods: The selection of the observational or experimental subjects (patients, controls or laboratory animals) should be described clearly. Identify the age, sex, and other important characteristics of the subjects. For experiments on human subjects and animals, the followed ethical standards regulated down by the national bodies or organizations of the particular country should be clearly mentioned. The authors should identify the methods, apparatus (list the manufacturer's name and original country in parentheses), and procedures in sufficient detail to allow other workers to reproduce the results. References should be supplied for established methods, including statistical methods. New or substantially modified methods should be described and reasons for using them with their limitations should be provided. All drugs and chemicals should be identified with their generic name (s), dose (s), and route (s) of administration. Reports of randomized clinical trials should include the information on all major study elements including the protocol (study population, interventions or exposures, outcomes, and the rationale for statistical analysis), assignment of interventions (methods of randomization, concealment of allocation to treatment groups), and the method of masking (blinding). The statistical analysis done and statistical significance of the findings when appropriate, should be mentioned. Unless absolutely necessary for a clear understanding of the article, detailed description of statistical treatment may be avoided. Articles based heavily on statistical considerations, however, need to give details particularly when new or uncommon methods are employed.

Results: Unnecessary overlap between tables, figures and text should be avoided. Only such data as are essential for understanding the discussion and main conclusions emerging from the study should be included. The data should be arranged in unified and coherent sequence so that the report develops clearly and logically. Data presented in tables and figures should not be repeated in the text. Only important observations need to be emphasized or summarised. The same data should not be presented both in tabular and graphic forms. Interpretation of the data should be taken up only under the Discussion and not under Results.

Discussion and Conclusion: The discussion should begin with a succinct statement of the principal findings, outline the strengths and weaknesses of the study, discuss the findings in relation to other studies, provide possible explanations and indicate questions which remain to be answered in future research. The discussion should deal with the interpretation of results without repeating information already presented under Results. It should relate new findings to the known ones and include logical deductions. It should also mention any weaknesses of the study. The conclusions can be linked with the goals of the study but unqualified statements and conclusions not completely supported by the data should be avoided. Claiming of priority on work that is ongoing should also be avoided. All hypotheses should, if warranted, clearly be identified as such; recommendations may be included as part of the Discussion, only when considered absolutely necessary and relevant.

Acknowledgements: Acknowledgment should be brief and made for specific scientific/technical assistance and financial support only and not for providing routine departmental facilities and encouragement or for help in the preparation of the manuscripts (including typing or secretarial assistance).

References: The total number of References should normally be restricted to a maximum of 30. References to literature cited should be numbered consecutively and placed at the end of the manuscript. In the text they should be indicated above the line (superior). As far as possible mentioning names of author(s) under references should be avoided in text. Citations should be made accoridng to Index Medicus Style. *Articles with up to three authors:* Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002; 347:284-7. *Articles with more than three authors:* Rose ME, Huerbin MB, Melick J, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res. 2002; 935(1-2):40-6. *Book Chapters:* Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93-113.

Tables: Tables should be typed separately and numbered consecutively with Roman numerals (I, II, III, etc). They should bear brief title and column headings should also be short. Abbrevations should be explained under associated table. Tables (short title and descriptive information) should be presented in seperate pages.

Figures: Figures Tables (short title and descriptive information) should be presented in seperate pages. Please note that only file formats with .jpeg extensions could be uploaded to system

REVIEW PROCESS

All papers submitted to KJMS are subject to peer review process by at least two reviewers. Final decision is given by editor according to review results. All accepted articles are subject to redaction according to journal rules and format.

PROOFS

Authors are sent page proofs for checking by the production editor after acceptance of the article. Proofs are sent by e mail as PDF files and should be checked and returned within 3 working days of receipt.

COPYRIGHT TRANSFER AGREEMENT FORM

Submission of a manuscript to Kafkas Journal of Medical Sciences means that the manuscript has not been published anywhere (except as an abstract, summary of a presentation or part of an assessment or thesis), has not been submitted to anywhere to be considered for publication, and all contributors agreed publication in Kafkas Journal of Medical Sciences. Author(s) give all copyright transfer permissions to Kafkas University and Kafkas Journal of Medical Sciences until the manuscript is rejected by the journal. Without permission of Kafkas University and Kafkas Journal of Medical Sciences, all author(s) accept(s) that they will not publish the article in anywhere in any language.

DOI NUMBER

A DOI *(digital object identifier)* number will be allocated to all accepted manuscripts.

KAFKAS TIP BİLİMLERİ DERGİSİ
Journal of Medical Sciences