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Effect of neuropathy on pupillary response measured with infrared static pupillography in type 2 diabetes mellitus patients

Tip 2 diyabetes mellitus hastalarında infrared statik pupillografi yardımıyla nöropatinin pupil cevabı üzerine etkisi

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Abstract

Aim: Diabetic autonomic neuropathy is manifested by pupillary dysfunction in the eye; so pupillary assessment can be vital for early detection. We aim to determine the relationship between diabetic polyneuropathy and pupil response for evaluating the presence of neuropathy via static pupillometer that is a non-invasive and quantitative method. This method could be used as an indicator for early diagnosis of neuropathy in diabetic patients.

Methods: This case-control study was planned on 420 patients. All participants have been diagnosed with Type 2 Diabetes Mellitus and were referred to Neurology Department. The first group includes 60 patients who have type 2 diabetes mellitus with distal symmetric polyneuropathy (DPN). Second group includes 212 diabetic patients who don't have polyneuropathy. Besides, age-sex matched 208 non-diabetic controls were included in the study. Mesopic, scotopic and photopic pupil measurements were recorded via infrared static pupillography.

Results: The photopic pupil diameter was 3.72 (0.86) mm, 3.64 (0.78) mm, 3.74 (0.78) mm and mesopic pupil diameter were 4.06 (0.76) mm, 4.22 (0.80), 4.39 (0.83) mm and scotopic pupil diameter was 4.58 (0.76) mm, 4.56 (0.84) mm, 4.77 (0.85) mm respectively in DPN group, non-neuropathic diabetic group, and control group. There was no statistically significant difference in groups (P>0.05) except for mesopic and scotopic pupil diameters between control and non-neuropathic diabetic group (P=0.03 and P=0.01, respectively).

Conclusion: Pupillographic methods are not as reliable as diabetic autonomic neuropathy in the early diagnosis of DPN.

Keywords: Diabetes mellitus, Pupillography, Polyneuropathy, Diabetic complications

Öz

Amaç: Diyabetik otonomik nöropati pupil disfonksiyonu ile karşımıza çıkabildiği için erken tanıda pupil değerlendirmesi önemli olabilir. Bu çalışmada statik pupilometre aracılığıyla diyabetik polinöropatinin pupil cevabına etkisini araştırmayı amaçladık.

Yöntemler: Vaka kontrol çalışmamız 420 katılımcı üzerinde gerçekleştirildi. Tüm hastalar nöroloji departmanına konsülte edilen tip 2 diyabetes mellitus hastalarıydı. Birinci grupta Tip 2 Diyabetes Mellitus u bulunan 60 distal simetrik polinöropatili hasta bulunmaktaydı. İkinci gruba 202 polinöropatisi olmayan diyabetik hasta dahil edildi. Ayrıca diyabetik olmayan 208 hasta da kontrol grubu olarak çalışmaya dahil edildi. İnfrared statik pupillografi cihazı ile mezopik, skotopik ve fotopik şartlarda ölçümler alındı.

Bulgular: Diyabetik Polinöropatili , nöropatisi olmayan diyabetik ve kontrol gruplarındaki cevaplar sırasıyla; fotopik şartlarda 3,72 (0,86) mm, 3,64 (0,78) mm, 3,74 (0,78) mm, mezopik şartlarda 4,06 (0,76) mm, 4,22 (0,80), 4,39 (0,83) ve skotopik şartlarda 4,58 (0,76) mm, 4,56 (0,84) mm, 4,77 (0,85) mm idi. Kontrol grubu ile nöropatisi olmayan diyabetik hastalardaki mezopik ve skotopik pupil çapları dışında (sırasıyla P=0,03 ve P=0,01) gruplar arasında istatiktiksel olarak anlamlı (P>0,05) bir farklılık bulunamadı.

Sonuç: Pupillografik metodlar diyabetik polinöropati nin erken tanısında diyabetik otonomik nöropati kadar güvenilir sonuçlar vermemektedir.

Anahtar kelimeler: Diabetes mellitus, Pupillografi, Polinöropati, Diabet komplikasyonları

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Introduction

Diabetes mellitus is a public health issue that has been increasing rapidly in our country and the world in recent years [1]. It is essential to diagnose diabetes mellitus in the early period and adjust the lifestyle changes with/without medical treatment for prevention of development of possible complications in patients. In ophthalmology department, the majority of patients, especially those who are followed up in the retina, have vision problems related to diabetic retinopathy. Therefore, it is essential to diagnose the disease as soon as possible and apply the appropriate treatment. Another significant complication of diabetes, neuropathy is related to the duration of diabetes, not having proper control of hyperglycemia similar to other complications such as retinopathy, nephropathy, cardiovascular disease.

Diabetic autonomic neuropathy is manifested by pupillary dysfunction in the eye; so early recognition is vital for this [2]. For this reason, sequential autonomic dysfunction screening is necessary. Studying pupillary tests may be a way to diagnose this as early as possible, and abnormalities in pupil function may be detected before cardiovascular autonomic function abnormalities and may be the earliest finding of diabetic autonomic neuropathy [3]. It has been observed, however, that autonomic changes cause an increase in mortality [4]. In this study, we aimed to evaluate the existence of similar relation with diabetic polyneuropathy (DPN) and pupillary dysfunction as if it has been identified in autonomic neuropathy. So, we objected that to determine whether polyneuropathy can be detected at an early stage by pupillography and to investigate whether any changes consist of pupil responses in diabetic patients that no complications have occurred yet. Until this time, all studies have been focused on the relationship between diabetic autonomic dysfunction and pupil responses. Unlike this, we believe that this pupillary response dysfunction may occur in polyneuropathy through different pathophysiological pathways.

Materials and methods

The study was conducted with adherence to the tenets of the Helsinki declaration and under the approval of the institutional ethics committee. Informed consent from each participant was also gathered. Patients that have been just diagnosed with Type 2 Diabetes Mellitus and has been identified previously were referred from the Internal Medicine Department to the Ophthalmology Department for detailed ophthalmological examination and healthy control participants who were admitted for a routine visit to Ophthalmology Department without any retinal complaints between July 2013 and January 2015 were enrolled prospectively in the study. All subjects underwent detailed ophthalmological examination including best-corrected visual acuity (BCVA), intraocular pressure measurement, slit-lamp biomicroscopy. Exclusion criteria were the presence of ametropia more than 3 diopters (D), axial length (AL) less than 22mm or more than 25mm, previous glaucoma diagnosis, age-related macular degeneration, uncontrolled hypertension, previous intraocular surgery or intervention, macular diseases and media opacities that limit to obtain pupillometry measurements. All participants in all groups have been recorded with detailed ophthalmologic examination and in addition to this optical coherence tomography (OCT) (Cirrus HD Spectral domain-OCT Model 4000; Carl Zeiss Meditec, Inc., Dublin, CA, USA) and pupillography measurements. (CSO-Schwind Sirius, SCHWIND eye-tech-solutions GmbH, Kleinostheim, Germany)Pupil diameter size measurements in photopic (40 lux) condition simulating the day-time, in mesopic (4 lux) condition and in scotopic (0.04 lux) condition simulating the level of light encountered at night; recorded via using Scheimpflug/Placido photography-based topography system in the pupillometer mode (Sirius, Italy) by the same technician preoperatively. The integrated pupillometry captures the pupil diameter either dynamically or statically according to the defined lighting conditions. Participants were instructed not to consume caffeine or smoke cigarettes during the measurement day until the measurement time. After pupillographic measurements were completed, the fundus examination was completed by diluting the pupil with 0.5% tropicamide. Patients that have been diagnosed with diabetic retinopathy on dilate fundus examination (except for background diabetic retinopathy), systemic disease that may affect the pupillary function, using medical therapy, previous anterior segment or retinal surgery history and any ocular or systemic disease that able to affect pupillary parameters (pseudoexfoliation syndrome, previous uveitis, active or passive rubeosis iridis) were not included in the study. Age, sex, Hemoglobin A1c (HbA1c) levels, diabetes duration, medications, and concomitant systemic diseases were noted for each participant. Results of blood glucose samples were taken simultaneously with an ophthalmologic examination from all participants that have been identified with Type 2 Diabetes Mellitus and have been studied glycosylated HBA1c values by HPLC (high-performance liquid chromatography) method.

Patients were directed to the Neurology Department for the detection of neuropathy. Diabetic polyneuropathy (DPN) diagnosis was established with the presence of clinical symptoms, Douleur Neuropathique-4 questionnaire (DN-4), neurological examination findings, and electroneurophysiological assessment after other possible causes of peripheral neuropathies were excluded (cancer related, side effect of immunosuppressive drugs, vitamin B12 deficiency, uremic and other metabolic causes, etc.).

Participants in the control group without diabetes mellitus or polyneuropathy has been identified as Group 1 (DM-PNP-); which have Type 2 Diabetes Mellitus without polyneuropathy has been identified as Group 2 (DM+ PNP-) and that have both Type 2 Diabetes Mellitus and polyneuropathy has been identified as Group 3 (DM+ PNP+).

Eventually, 60 eyes of 30 diabetic patients with diabetic polyneuropathy(DPN) (Group 3), 202 eyes of 102 non-neuropathic Type 2 diabetes mellitus patients (Group 2), and 208 eyes of 104 healthy participants (Group 1) those age and sex-matched were included in the study.

Statistical analysis

For the statistical analyses, SPSS (Statistical Package for Social Sciences) FOR Windows 21.0 program was used. One Way ANOVA was used to compare descriptive statistical methods (Mean (Standard deviation)) when study data were

evaluated. The results were evaluated in a 95% confidence interval and a significance level of P <0.05.

Results

The distribution of the gender of the 208 control participants was 109 female (52.40%) and 99 male (47.59%) (Group 1). The mean age of the patients was 57.39 (14.21) (22-85 years) in Group 1. The distribution of the gender of the 202 non-neuropathic diabetic patients was 132 female (65.34%) and 70 male (34.65%) (Group 2). The mean age of the patients was 59.59 (9.60) (32-78 years) in Group 2. The distribution of the gender of the 60 diabetic neuropathic patients was 44 female (73.33%) and 16 male (26.66%) (Group 3). The mean age of the patients was 61.10 (12.30) (29-85 years) in Group 3. Age distributions between groups are shown in Table 1. There was no difference between the mean age and gender distributions of the diabetic group with diabetic neuropathy, diabetic group without diabetic neuropathy, and control group (P=0.06).

The demographic features, systemic diseases according to the groups are shown in Tables 2. Group 1 (n=208) was defined as a control group without diabetes mellitus. The mean duration of diabetes was recorded as 4.26 (5.21) years in Group 2 (n=202), and the mean duration of diabetes was recorded as 7.98 (5.30) years in Group 3 (n=60). In group 2, the number of patients that have been just diagnosed with diabetes mellitus was 66 (32.7%); in group 3, this number was 4 (6.7%). Obviously, this result shows that about 6% of patients with diabetes mellitus do not realize the disease even though neurological complications occur during the development of diabetes mellitus.

HBA1c values of the patients was taken simultaneously with ophthalmologic examinations and recorded as 6.23 (1.00) in Group 2 and 8.83 (1.97) in Group 3. The difference between groups 2 and 3 in terms of HbA1c was significant (p<0.01).

The pupil diameter measured by pupillography in the diabetic group with neuropathy (Group 3) was 3.72 (0.86) mm (2.57-6.12 mm) in photopic conditions; 4.26 (0.76) mm (3.02-6.14 mm) in mesopic conditions; 4.58 (0.76) mm (3.28-6.37 mm) in scotopic conditions. The pupil diameter measured by pupillography in the diabetic group without neuropathy (Group 2) was 3.64 (0.78) mm (2.21-6.79 mm) in photopic conditions; 4.22 (0.80) mm (2.49-6.88 mm) in mesopic conditions; 4.56 (0.84) mm (2.52-6.90 mm) in scotopic conditions. The pupil diameter measured by pupillography in control group (Group 1) with neuropathy was 3.74 (0.78) mm (1.85-6.28 mm) in photopic conditions; 4.39 (0.83) mm (2.79-7.22 mm) in mesopic conditions; 4.77 (0.85) mm (3.22-7.81 mm) in scotopic conditions.

There was no difference in pupil diameters between photopic, mesopic and scotopic conditions between all three groups (P=0.38, 0.09, 0.05, respectively); between Group 2 (DM + PNP-) and Group 3 (DM + PNP+). (P=0.48, 0.72 and 0.84, respectively) and between Group 1 (DM-PNP-) and Group 2 (DM + PNP-) (P=0.17, 0.03 and 0.01, respectively) except for mesopic and scotopic pupil diameters. Likewise, there was no statistically significant difference between photopic pupil diameters in these groups (P=0.17). Distribution of pupil diameters and statistical significance values between groups are shown in Table 3.

Table 1: Age-group distributions of participants

	Group 1		Group 2		Group 3		*P*-value
	n	%	n	%	n	%	
Female	109	52.4	132	65.34	44	77.33	0.06
Male	99	47.59	70	34.65	16	26.66	
Age mean (SD)	57.39 (14.21)		59.59 (9.60)		61.10 (12.30)		0.06
Total	208	100	202	100	60	100	

SD: Standard deviation

Table 2: Distribution of systemic diseases of participants

Systemic disease	Group 1 n (%)	Group 2 n (%)	Group 3 n (%)
Hypertension	58 (27.9)	78 (38.6)	23 (38.3)
Chronic Renal Failure	2 (1.0)	6 (3)	2 (3.3)
Coronary Arterial Disease	6 (2.9)	14 (6.9)	3 (5.0)
Cerebrovascular Disease	0 (0)	2 (1.0)	0 (0)
Dyslipidemia	6 (2.9)	12 (5.9)	4 (6.7)
Thyroidopathy	16 (7.7)	18 (8.9)	2 (3.3)
Diabetes inspidus	2 (1.0)	0 (0)	0 (0)
Tuberculosis	0 (0)	2 (1.0)	0 (0)
Gastroesophageal Reflux Disease (GERD)	2 (1.0)	14 (6.9)	0 (0)
Irritable Bowel Disease	0 (0)	2 (1.0)	0 (0)
Osteoporosis	2 (1.0)	0 (0)	0 (0)
Migraine	2 (1.0)	0 (0)	0 (0)
Parkinsonism	10 (4.8)	0 (0)	2 (3.3)
Hemorrhoids	0 (0)	4 (2.0)	0 (0)
Chronic Obstructive Pulmonary Disease (COPD)	0 (0)	4 (2.0)	0 (0)
Asthma	3 (1.4)	2 (1.0)	1 (1.7)
Benign Prostate Hyperplasia (BPH)	2 (1.0)	4 (2.0)	0 (0)
Urinary Incontinence	0 (0)	0 (0)	0 (0)
Essential Tremor	2 (1.0)	0 (0)	0 (0)
Iron Deficiency Anemics	4 (1.9)	16 (7.9)	0 (0)
B12 Vitamin Deficiency	0 (0)	12 (5.9)	6 (10.0)
Total	208 (100)	202 (100)	60 (100)

Table 3: Distribution of pupil diameters according to groups

	Group 1	Group 2	Group 3	*P*-value[1]	*P*-value[2]	*P*-value[3]
Photopic PD	3.74 (0.78)	3.64 (0.78)	3.72 (0.86)	0.17	0.48	0.38
Min-Max	1.85-6.28	2.21-6.79	2.57-6.12			
Mesopic PD	4.39 (0.83)	4.22 (0.80)	4.26 (0.76)	0.03	0.72	0.09
Min-Max	2.79-7.22	2.49-6.88	3.02-6.14			
Scotopic PD	4.77 (0.85)	4.56 (0.84)	4.58 (0.76)	0.01	0.84	0.05
Min-Max	3.22-7.81	2.52-6.90	3.28-6.37			

Values are given as mean (Standard deviation), Min: Minimum, Max: Maximum, [1] Statistical significance value between Group 1 and Group 2, [2] Statistical significance value between Group 2 and Group 3, [3] Statistical significance value among all groups

Discussion

Pupillary responses can be determined quantitatively by the infrared pupillometry method under the constant light stimulus. In photographic methods, reproducibility and reliability indexes are very low due to manual measurements made by photographers. The likelihood of differences due to the operator, who evaluates them by automatization and quantitative measurements, has also ceased to exist. Other advantages include easy measurement and quick results. In the literature, different pupil response measurement methods have been used to investigate the effects of diabetic autonomic neuropathy on pupil response in most studies [23]. In previous studies, there is some evidence that the presence of diabetes leads to damage in the pupil response, even in the absence of neuropathy. In this study, there was no significant difference in the pupillary response between the control group and diabetic patients without neuropathy except for mesopic and scotopic pupil diameters between the control group and diabetic patients without neuropathy.

This result may be caused by the effect of newly diagnosed patients' ratio (n=66, %32.7) on all diabetic groups and an average duration of diabetes was 4.26 (5.21) years in this group. The frequency of diabetic polyneuropathy is closely related to the duration of diabetes. In the meta-analysis, Young et al. have shown that the frequency of diabetic polyneuropathy increases markedly with age. The incidence of diabetic polyneuropathy in the 20-29 age groups is 5% (3.1-6.9%), while it is 44.2% (41.1-47.3%) in the 70-79 age groups. The incidence

of neuropathy is 20.8% (19.1-22.5%) in patients with less than five years of diabetes, and 36.8% (34.9-38.7%) in patients over ten years of age. Diabetic peripheral neuropathy is a common complication associated with diabetes and occurs in patients with Type 2 Diabetes Mellitus over 60 years of age with a 50% excess rate.

The American Diabetes Association recommends that neuropathy screening is performed every five years after diagnosis in Type 1 Diabetes Mellitus patients, and every year after diagnosis in Type 2 Diabetes Mellitus [5]. Therefore, it is not often expected to be affected by pupillary responses even in the absence of polyneuropathy in a population with an average of 4 years of diabetes. In this study, the diabetic patient group was screened for diabetic polyneuropathy, although the change in pupil responses was mostly associated with autonomic neuropathy. This study was designed to show whether changes in pupil responses in the presence of polyneuropathy may be due to autonomic nervous system effects that are predominantly responsible for pupillary response, which is likely to cause deficits in pupillary responses, as well as similar pathophysiological damage pathways. As a matter of fact, the changes in pupil responses in the presence of diabetic polyneuropathy were not statistically significant. Studies in the literature on pupillary reactions of diabetic patients have suggested that pupil changes are often seen in autonomic neuropathic patients, pupillary changes may be present in some polyneuropathic patients, but autonomic neuropathies are also present in these patients simultaneously [6]. It is not likely to declare that pupillary changes are associated with isolated distal somatic polyneuropathy as if autonomic system is not affected. In this study, all participants did not examine for the presence of autonomic neuropathy.

Tentolouris et al. [8] have been conducted another study that investigates the association of diabetic polyneuropathy and autonomic neuropathy; there was a debate on those patients with diabetes were not required to have autonomous and peripheral neuropathy at the same time. Autonomic neuropathy and peripheral neuropathy are found simultaneously in approximately one-third of Type 1 diabetes patients and approximately 45% of Type 2 diabetic patients. Both types of diabetes had a significant group of patients with only autonomic neuropathy or only peripheral neuropathy. polyneuropathy may be presently isolated independently of the presence of autonomic neuropathy in diabetic patients. Pozzessere et al. [9] reported as possible that prediction of fine-fiber neuropathy in diabetic patients. In this study, somatosensory evoked potentials (p-SEP) were recorded after the carbon dioxide laser-mediated painful stimulus were given to participants and values were compared with the monocular pupillometric data (ISCAN, sample rate 50 Hz) taken simultaneously from the participants. Even though the existence of patients with synchronous distal symmetric polyneuropathy and autonomic dysfunction, there was no statistically significant difference between pupillometric values and somatosensory evoked potentials (p-SEP; Pain Induces Somatosensory Evoked Potential). This study revealed that the early, subclinical and selective damage of thin nerve fibers can occur in diabetic patients even with the absence of clinical autonomic dysfunction findings and thick fiber neuropathy proven with electrophysiological methods; also this damage can be evaluated in relation to both autonomic and somatic dysfunction. Another important data reported in the same study shows that the damage appears firstly in the longest nerve pathways of the lower extremity and shows the dysfunction of nerve fibers associated with fiber length. Pupillometry results with changes in pupil response indicate that primarily damage is detected in the longest sympathetic nerve fibers. Therefore, at the beginning of pupillary damage, sympathetic fibers that provide pupillary adaptation in the dark are damaged, and appropriate pupillary response may be encountered after light stimulation. However, if metabolic control is not provided, parasympathetic nerves are also affected by this damage. In this study, any statistically significant difference was found between the pupillometer parameters and somatosensory latencies similar to our study. The main reason for this result could be evaluated as the effects of diabetes on somatic and autonomic nerve fibers occurs in different stages of diabetes. Because of different neural structures of cranial autonomic fibers and peripheral somatic fibers, it is likely that they will be damaged at different stages of the disease. Therefore all studies designed should be designed in such a way as to allow simultaneous assessment of the effects of different nerve fibers [9]. Especially, pupil measurements should be used in clinical practice as a reliable, quantitative method of detecting subclinical diabetic autonomic neuropathy [10].

Most studies have reported that the impairment of the pupil response is associated with autonomic dysfunction in diabetic patients. Dütsch et al. [12] reported the first study that distinguishes the presence of pupillary autonomic dysfunction from cardiac autonomic neuropathy and polyneuropathy. As a result, it has been found that pupillary light reflex responses are independent of polyneuropathy and cardiac autonomic neuropathy, consistent with our clinical results. The frequency of pupillary autonomic dysfunction was similar in patients with or without cardiac autonomic neuropathy or polyneuropathy and any correlation detected between cardiovascular and pupillary parameters. We can predict that cardiac parasympathetic neuropathy should be seen earlier than pupillary dysfunction in the presence of diabetic neuropathy by a pathophysiological approach because of the distal part of the vagal nerve, which is quite long, is more easily damaged than the relatively shorter nerve fibers that provide pupil innervation. Dütsch et al. [12] reported that there is no finding of somatic or cardiac neuropathy in patients with pupillary dysfunction contrary to this pathophysiological assumption. In response, they presented an opinion that autonomic innervation could be damaged more easily than peripheral nerves in diabetic conditions and defended by stating that oculomotor and trochlear neuropathy can also be seen without peripheral and cardiac autonomic neuropathy [13-15]. Apart from this, the ciliary and iris muscles are highly selective, and the number of muscle fibers innerved by a single nerve fiber is very few [16]. For this reason, even in the least severe damage of nerve, pupillary dysfunction is evident which can be seen without cardiac or peripheral neuropathy.

The abnormal pupillary response is associated with the pathology of the afferent and efferent pathways [17-19]. Smith & Smith reported that the reduction in pupillary contraction rate and decreased reflex amplitudes would not be related to the small

pupil diameter and that the disturbances in these parameters were due to parasympathetic dysfunction [20]. Hayashi and Ishikawa have been essayed to prove parasympathetic pupillary denervation in diabetic patients by showing super-sensitivity to cholinergic drugs [21]. Smith et al. found that disturbances in pupil diameter at relaxation were due to sympathetic dysfunction and reduction of sympathetic activity in the iris muscle and they evaluated the sympathetic pupillary denervation that has been demonstrated by pharmacological methods in patients with diabetic autonomic neuropathy [22]. It is thought that the sympathetic nerve fibers are more vulnerable due to the longer length of the sympathetic nerve fibers than the parasympathetic nerve fibers.

Therefore, sympathetic nerve dysfunction could be seen than oculomotor parasympathetic nerve dysfunction [2] and this is resulted in that pupillary dysfunction in resting state or as darkness is seen before the defect in the light reflex [12].

The main limitation of this study is its relatively small sample size, which is due to the elimination of a considerable, because of this reason, that is hard to generalize our findings. Besides, all participants did not undergo a specific diagnostic test to rule out autonomic dysfunction because there is not still a gold standard diagnostic test. Autonomic dysfunction is a complication which is thought to be a quite effective factor in pupil response in diabetic patients and only neurological evaluation and questioning of clinical symptoms such as orthostatic hypotension, orthostatic intolerance, postural orthostatic tachycardia syndrome, also known as postural tachycardia syndrome, syncope, neurogenic bowel (gastroparesis, intestinal dysmotility, constipation), erectile dysfunction and neurogenic bladder were excluded in this study. It is obvious that autonomic dysfunction is entirely independent of polyneuropathy. On the other hand, its prospective, randomized and double-masked design fortifies our study results.

In conclusion, pupillography methods exhibit abnormal pupillary function, but this damage can be a direct indicator of autonomic dysfunction. This autonomic dysfunction is entirely independent of polyneuropathy. Pupillography is recommended to diagnose diabetic autonomic dysfunction more frequently in clinical practice because it is a readily applicable, noninvasive and cheap method. On the contrary, this method cannot be applied for the detection of distal symmetric polyneuropathy in diabetic patients. Finally, strict systemic regulation and close follow-up are required to prevent all these complications in diabetic patients.

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Pediatric living donor liver transplantation: A single center experiences

Pediatrik canlı vericili karaciğer nakli: Tek merkez deneyimi

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Abstract

Aim: The only definitive treatment of chronic liver disease (cholestatic, metabolic, autoimmune), acute liver failure and liver tumors are liver transplantation in pediatric patients. The aim of this study was to present the experience of our center on pediatric living donor liver transplantation and review of the literature.

Methods: This is retrospective cohort study. Pediatric patients who receive living donor liver transplantation between December 2014 and December 2017 included in the study. Demographic features, complications after transplantation, and mortality rates were recorded.

Results: A total 29 patients were included in the study. Mean age of cases were 3.1 (1-13) years, 18 (62.1%) of the patients were male. Mean Pediatric End-Stage Liver Disease (PELD) scores were 15.6 (-6-37). Mean follow-up period was 60 months. Complication was detected in 11 patients (37.9%) and 5 patients died (mortality rate: 17.9%). In our study, the causes of death were disseminated intravascular coagulation in three patients and sepsis due to biliary leakage in two patients.

Conclusion: Complications and mortality rates related to pediatric patients with donor liver transplantation in our center are consistent with the literature.

Keywords: Pediatric patient, Living donor liver transplantation

Öz

Amaç: Kronik karaciğer hastalığının (kolestatik, metabolik, otoimmün), akut karaciğer yetmezliği ve karaciğer tümörlerinin pediatrik hastalarda ekin tek tedavisi karaciğer naklidir Bu çalışmanın amacı merkezimizde yapılan pediatrik canlı vericili karaciğer nakillerini değerlendirmek ve literatürü tartışmaktır.

Yöntemler: Bu çalışma retrospektif kohort çalışmadır. Çalışmaya Aralık 2014 ile Aralık 2017 tarihleri arasında canlı vericili karaciğer nakli yapılan pediatrik hastalar alındı. Demografik özellikler, nakil sonrası komplikasyonlar ve mortalite oranları kaydedildi.

Bulgular: Çalışmaya toplam 29 hasta dahil edildi. Hastaların yaş ortalaması 3,1 (1-13) yıl, 18'i (%62,1) erkekti. Hastaların ortalama Pediatrik Son Dönem Karaciğer Hastalığı (PELD) skorları 15,6 (-6-37) idi. Ortalama takip süresi 60 aydı. Komplikasyon oranı %37,9 (11 hasta) ve mortalite oranı %17,9 (5 hasta) olarak saptandı. Çalışmamızda hastalarımızın ölüm nedeni dissemine intravasküler koagülasyon ve safra kaçağına bağlı sepsis idi.

Sonuç: Merkezimizde pediatrik hastalara yapılan canlı vericili karaciğer nakillerinin komplikasyon ve mortalite oranları literatür ile uyumludur.

Anahtar kelimeler: Pediatrik hasta, Canlı vericili karaciğer nakli

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Introduction

The first pediatric liver transplantation was described in 1963 by Starzl et al [1] with congenital biliary atresia. Liver transplantation has become a standard procedure for children with end-stage liver disease [2]. The most common clinical indications for liver transplant in pediatric patients are cholestatic liver disease, which accounts for almost half of the patients; metabolic and genetic disorders; fulminant liver failure; and malignancies [3-5].

Pediatric liver transplant technique can very hard. The care of a pediatric liver transplant patient is optimized through the use of a multidisciplinary team. The aim of our study was to report our experience of pediatric living donor liver transplantation.

Materials and methods

Between December 2014 and December 2017 at Medipol University Medical Faculty Hospital Organ Transplantation Department, Istanbul, Turkey, 29 pediatric patients (0-18 years old) with living donor liver transplantation were studied retrospectively.

Informed consent was obtained from the parents of all pediatric patients.

Twenty-nine pediatric patients with living donor liver transplantation were evaluated demographic features, complication rates and mortality rates.

Post-transplant follow-up

In our center, Immunosuppression regimens were based on calcineurin inhibitor (tacrolimus or cyclosporine), mycophenolate mofetil and corticosteroids in pediatric recipients.

Patients received control once a week for the first month after discharge, and every 15 days for the second month and monthly after that period.

Statistical Analysis

Continuous variables with normal distribution presented as mean (standard deviation). The categorical variables were given as percent and number.

Results

Mean age of pediatric patients were 3.1 (1-13) years, 18 (62.1%) of the 29 pediatric patients were male. Mean PELD scores of pediatric patients were 15.6 (-6-37). Mean body weights pediatric patients were 12.6 (4-42) kilograms. Mean hospitalization time of our patients was 14 days and the mean stay in the intensive care unit was 3 days.

The etiological characteristics of pediatric patients are summarized in table 1. The three most common indications for liver transplantation were; Biliary atresia in 12 (41.4%) patients, acute liver failure in 6 (20.7%) patients, congenital hepatic fibrosis in 3 (10.3%) patients. Another indications in our patients were progressive familial intrahepatic cholestasis in 2 (6.9%) patients, glycogen storage disease in 1 (3.4%) patient, neonatal hepatitis in 1 (3.4%) patient, hepatoblastoma in 1 (3.4%) patient, Alagille syndrome in 1 (3.4%) patient, Crigler Najjar type 1 in 1 (3.4 %) patient, histiocytosis x in 1 (3.4%) patient.

Twenty five (86.2%) patients received left lateral segment living donor liver transplantation, 4 (13.8%) left lobe living donor liver transplantations. Mean graft volume was 293 (140-490) grams; mean graft body weight ratio was 2.8% (1-5).

The complications after liver transplantation are shown in table 2. Complication rate was 37.9% (11 patients) during follow up of 60 months. The observed bleeding at Roux-en-Y jejunojejunal anastomosis was detected in 6 (20.7%) patients, hepatic artery thrombosis in 2 (6.8%) patients, bile leakage in 2 (6.8%) patients and spontaneous intestinal perforation in 1 (3.4%) patients.

Reoperation was performed for bleeding at Roux-en-Y jejunojejunal anastomosis and spontaneous intestinal perforation in 3 patients. Endoscopic sclerotherapy was performed for bleeding at Roux-en-Y jejunojejunal anastomosis in 4 patients, intravascular stent placement was done for hepatic artery thrombosis in 2 patients and percutaneous biliary drainage was made for bile leakage in 1 patient.

Mortality rate was 17.2% (5 of the total 29 patients) during follow up of 60 months. 1-year and 5-year survival rates of our patients were 86.6% and 82.8%, respectively. The cause of death in all cases was disseminated intravascular coagulation in three patients and sepsis due to biliary leakage in two patients.

Table 1: The etiological characteristics of pediatric liver transplant patients

Etiology	n	%
Biliary atresia	12	41.4
Acute liver failure	6	20.7
Congenital hepatic fibrosis	3	10.3
Progressive familial intrahepatic cholestasis	2	6.9
Glycogen storage disease	1	3.4
Neonatal hepatitis	1	3.4
Hepatoblastoma	1	3.4
Alagille's syndrome	1	3.4
Crigler Najjar type 1	1	3.4
Histiocytosis X	1	3.4
Total	29	100

Table 2: The observed complications after liver transplantation

Complications	n	%
Bleeding at Roux-en-Y jejunojejunal anastomosis	6	20.7
Hepatic artery thrombosis	2	6.8
Bile leakage	2	6.8
Spontaneous intestinal perforation	1	3.4
Total	11	100

Discussion

The most common indications for liver transplant in pediatric patients are cholestatic liver disease, metabolic and genetic disorders, acute liver failure and malignancies. Biliary atresia is the most important diagnosis in approximately 30–50 % of pediatric patients who underwent liver transplantation. The majority of patient with biliary atresia undergo Kasai porto-enterostomy to improve biliary drainage, however 20-40% patients develop end stage liver disease and may need to liver transplantation [6-9]. Acute liver failure is a rare indication in underwent pediatric liver transplant patients. Diagnosis and treatment are very challenging in this disease. Some of the etiologies have been attributed to viral hepatitis, drug toxicity or toxin exposure [10].

Congenital hepatic fibrosis is a very rare indication of pediatric liver transplantation. Kerr et al [11] first reported in 1961 that congenital hepatic fibrosis is a hereditary autosomal recessive fibropolycystic disease of the liver. Congenital hepatic fibrosis is defined pathologically by bands of fibrous tissue within the liver, linking the portal area and containing multiple bile ducts [12].

Alagille's syndrome is cholestatic condition that may result in end-stage liver disease requiring liver transplantation. Alagille's syndrome is an autosomal dominant disorder in which there is a paucity of intrahepatic bile ducts [13].

Progressive familial intrahepatic cholestasis is another inherited cholestatic disorder in which bile salt, phospholipid or cholesterol transport genes are mutated such that protein function is either abnormal or absent [14]. Patients with inherited metabolic disorders comprise a large subcategory of pediatric living donor liver transplantation. These disorders are typically a result of mutations that affect amino acid, metal, lipid metabolism or mitochondrial function. Some metabolic diseases such as Wilson's disease, tyrosinemia, α1-antitrypsin deficiency, urea cycle defects and Maple syrupurine disease [15]. Hepatoblastoma is the most common pediatric primary liver tumor and is the most prevalent indication for liver transplantation for malignant disease [16]. In our study, the three most common indications for liver transplantation were; Biliary atresia in 12 (41.4%) patients, acute liver failure in 6 (20.7%) patients, congenital hepatic fibrosis in 3 (10.3%) patients. Other indications in our patients were progressive familial intrahepatic cholestasis in 2 (6.9%) patients, glycogen storage disease in 1 (3.4%) patient, neonatal hepatitis in 1 (3.4%) patient, hepatoblastoma in 1 (3.4%) patient, Alagille's syndrome in 1 (3.4%) patient, Crigler Najjar type 1 in 1 (3.4%) patient, histiocytosis x in 1 (3.4%) patient.

The most common complications after pediatric liver transplant are vascular, biliary and infectious [17]. Hepatic artery thrombosis is most serious technical complication in the pediatric liver transplantation and incidence is 4-8%. The most important predisposing factor is very small caliber of the arterial anastomosis. Portal vein thrombosis is formed in 2-6% of cases. Usually occur in children with hypoplastic portal veins such as those with biliary atresia. Acute hepatic vein outflow obstruction is a very serious complication which can result in Budd-Chiari syndrome, complete graft thrombosis and graft loss [17-19]. The incidence of complications at the biliary system (leakage and stricture) in pediatric liver transplant patients is approximately 10% [20]. The incidence of bleeding at Roux-en-Y jejunojejunal anastomosis is very rare. Only around 3-5% of after liver transplantation gastrointestinal system bleeds are attributed to jejunojejunal anastomotic bleed [21].

In our patients, complication rate was 37.9% (11 patients) during follow up of 60 months. The observed bleeding at Roux-en-Y jejunojejunal anastomosis in 6 (20.7%) patients, hepatic artery thrombosis in 2 (6.8%) patients, bile leakage in 2 (6.8%) patients and spontaneous intestinal perforation in 1 (3.4%) patients respectively.

In the literature the post-transplant mortality rate of pediatric liver transplantation patients was 10-20% [22]. In our patients, mortality rate was 17.2% (5 of the total 29 patients) during follow up of 60 months. 1-year and 5-year survival rates of our patients were 86.6% and 82.8%, respectively. The cause of death in all cases was disseminated intravascular coagulation in three patients and sepsis due to biliary leakage in two patients.

Our study has several limitations. First, this study was retrospective. Second, the number of cases was small.

Conclusion

Despite the limitations described, our morbidity and mortality results concerning pediatric living donor liver transplantations are proper with the results in the literature. It appears that with the development of surgical technique more liver transplantations will be carried out in the future.

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Investigation of inflammation with neutrophil/lymphocyte ratio in restless legs syndrome

İdiyipatik huzursuz bacaklar sendromunda enflamasyonun nötrofil/lenfosit oranları ile incelenmesi

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Abstract

Aim: Restless Legs Syndrome (RLS) is a chronic, progressive, sensorimotor disorder characterized by the urge to move legs and abnormal sensations in the limbs. The pathophysiology of RLS is not clear. In recent years, many studies have used different serum biomarkers to discuss pathophysiology or to follow up the diagnosis and treatment. There are not enough studies that entirely investigating the relationship between RLS and serum neutrophil/lymphocytes (N/L). Therefore, in this study it was aimed to examine the relationship between idiopathic RLS and serum N/L.

Methods: A case control study was planned. After sample size analysis, 93 patients with diagnosed RLS (study group) and age- and gender matching 50 healthy volunteers (control group) were included in the study. N/L ratio was compared between two groups.

Results: The median of N/L ratio was 2.58 in the RLS group and 2.72 in the control group. There was no statistically significant difference between the groups (P=0.89). The mean duration of disease was 3.2 (1.37) years in patients' group. Sleep disorders were found in 81.7% (n=76) of the patients, and similar complaints were observed on the upper extremities in 34.4% (n=32) of the patients. Severity scale of disease was determined according to the International Restless Legs Syndrome Study Group (IRLSSG). It was observed to be low severity of the symptom in 6.3%, middle severity of the symptom in 15.2%, severe severity of the symptom in 64.8%, high severity of the symptom in 13.7% of the patients. There was no correlation neither between duration of disease and N/L ratio (r:-0.117, P=0.28) nor between severity of the symptoms and N/L (r:0.68, P=0.41).

Conclusion: In this study, it was investigated the role of inflammation in the pathophysiology of RLS was evaluated with N/L ratio and it was not observed statistically significance on behalf of patients group.

Keywords: Restless legs syndrome, Neutrophil/lymphocyte ratio, Inflammation

Öz

Amaç: Huzursuz bacaklar sendromu (HBS); ekstremitelerde öncelikle bacaklarda hareket ettirme dürtüsü ve anormal duyularla karakterize, kronik, ilerleyici sensorimotor bir bozukluktur. HBS' nin patofizyolojisi net değildir. Son yıllarda birçok çalışmada patofizyoloji hakkında yorum yapabilmek ya da tanı ve tedavi takibi için farklı serum biyomarkerları kullanılmaktadır. HBS ve Nötrofil/Lenfosit (N/L) ilişkisini detaylı araştıran yeterli sayıda çalışma bulunmamaktadır. Bu nedenle çalışmamızda idiopatik HBS ile serum N/L arasında ilişkinin incelenmesi amaçlandı.

Yöntemler: Olgu kontrol çalışması planlandı. 93 HBS tanılı hasta (çalışma grubu) ile yaş ve cinsiyet açısından eşleştirilen 50 sağlıklı gönüllü (kontrol grubu) çalışmaya dahil edildi. İki grubun N/L oranları restrospektif olarak incelendi.

Bulgular: N/L'nin ortanca değeri hasta grubunda 2.58 ve kontrol grubunda 2.72 idi. Hasta ve kontrol grubu arasında istatistiksel olarak anlamlı bir farklılık yoktu (P=0.89). Çalışmamızda hasta grubunda hastalık süresinin ortalama 3,2 (1,37) yıl olduğu tespit edildi. Olguların %81,7'sinde (n=76) uyku bozukluğu, %34,4'ünde (n=32) üst ekstremitelerde benzer yakınmaların olduğu görüldü. Hastalığın şiddet skalası Uluslarası Huzursuz Bacaklar Sendromu Çalışma Grubu (IRLSSG)'na göre belirlendi. Semptomların şiddetinin dağılımı %6,3'ünde hafif, %15,2'sinde orta, %64,8'inde ciddi, %13,7' sinde ağır şiddette olduğu izlendi. Hastalık süresi ile N/L arasında anlamlı korelasyon yoktu (r:-0.117, P=0,28). Semptomların şiddeti ile N/L arasında istatistiksel olarak anlamlı korelasyon görülmedi (r:0.68, P=0,41).

Sonuç: Bu çalışmada, HBS patofizyolojisinde enflamasyonun rolü N/L oranı ile birlikte değerlendirilmiş ve hasta grubunda enflamasyon lehine istatistiksel olarak anlamlı bir ilişki gözlenmemiştir.

Anahtar kelimeler: Huzursuz bacaklar sendromu, Nötrofil/lenfosit oranı, Enflamasyon

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Introduction

RLS is a chronic neurologic disorder of sensorimotor system with circadian features manifested by the need or urges to move the extremities to stop unpleasant sensations in the evenings or rest. [1,2]. RLS, also known Wills-Ekbom Disease, was defined the first time by Dr. Ekbom in 1945 [3].

Diagnosis criteria of RLS have been developed by the International Restless Legs Syndrome Study Group (IRLSSG) and still these diagnosis criteria have been used [4]. Although, incidence of RLS has been found as between 0.25% and 15.3% in studies, it is more common in women [5,6]. RLS is divided into two forms as of primary and secondary. Family history in primary RLS, also known as idiopathic form, is remarkable. Allen et al. [7] reported that the first-degree relatives of patients with primary RLS were in a much higher risk group for RLS than their second-degree relatives, and that this form of familial features had an earlier onset. Although secondary or symptomatic RLS tends to late-onset and faster progression than idiopathic RLS, there is no clear difference between seconder and idiopathic RLS with regards to characteristics of symptoms [8]. Studies on the pathogenesis of the disease have focused on iron metabolism, changes in dopaminergic system, hypoxic / inflammatory response and genetics [9,10]. It has been reported that RLS is more common in cases where peripheral oxygen saturation decreases, such as chronic obstructive pulmonary disease and obstructive sleep apnea [11,12] and improvement of RLS symptoms with correction of peripheral hypoxia [13]. Hypoxia in pathophysiology of RLS was supported with post-mortem studies [14].

The serum neutrophil/lymphocytes (N/L) ratio has been used as a marker of systemic inflammation recently. N/L measurements cost less than other inflammatory markers, and it is practical and easy to perform [15].

Zahorec [16] was the first, reporting the relationship between neutrophils and lymphocytes during the inflammatory response. Neutrophils, lymphocytes, and other white blood cells are essential proinflammatory and anti-inflammatory cells [16,17]. Neutrophils are the paramount cells in causing inflammatory response during acute phase reactions. Lymphocytes constitute the main components of both the humoral and cellular responses [18,19]. Stress response of circulating lymphocytes results in a rise in the neutrophil count and reduction in the lymphocyte count. Therefore, the ratio of these two subgroups of white blood cells (N/L ratio) is used as an inflammatory marker [16]. It was examined the relationship between N/L ratios and some diseases [20-22].

Although different results were indicated in many studies which investigated the relationship between RLS and N/L ratios, it was not examined the relationship between severity of disease symptoms and N/L ratios [22]. Therefore, in this study we aimed to investigate the relationship between idiopathic RLS, severity of its symptoms and serum N/L.

Materials and methods

N/L ratios of 93 patients with diagnosed idiopathic RLS (42 male + 51 female) in neurology polyclinic according to the IRLSSG, and 50 healthy volunteers (24 male + 26 female) aged between 18 and 65 years were evaluated retrospectively from January 2018 to November 2018. Additionally, disease duration of patients with RLS, upper limb involvement, and presence of sleep disorder and severity of symptoms were compared to the N/L ratios. Severity scale of disease was determined according to the IRLSSG. When falling asleep latency (prolonged sleep latency) is longer than 30 minutes and/or waking up 3 or more than 3 in staying sleep were considered as a sleep disorder [23]. Participants with polyneuropathy, lumbosacral radiculopathy, amyotrophic lateral sclerosis, multiple myeloma, multiple sclerosis, Parkinson disease, poliomyelitis, diabetes mellitus, uremia, amyloidosis, cancer, peripheric vascular disorders, pneumopathy, congestive heart failure, Cushing syndrome, hyper or hypothyroidism, pregnancy, lactation, chronic kidney failure, use of neuroleptic or antidepressant, smoking, steroid treatment (by any means), systematic inflammatory disorders and hematologic disorders were excluded. N/L ratios were obtained by dividing the absolute number of neutrophils by the number of lymphocytes. Local ethics committee approval was taken from Ataturk University Faculty of Medicine (Protocol No: B.30.2.ATA.0.01.00/60).

Statistical analysis

All statistical analyses were performed using Medcalc statistical software (version. 12, Ostend, Belgium). D'Agostino Pearson Test was used to determine whether the variables were normal distribution or not. Since D'Agostino-Pearson test is based on the fact that when the data is normally distributed the test statistic has a chi-square distribution with two degrees of freedom, it is recommended [24]. While data with normal distribution were expressed as mean, standard deviation, as for non-normal distribution data were expressed as median and interval. The independent samples t-test was used in comparisons of normal distribution variables. Non-normal distribution of the data was compared using the Mann Whitney U test. Nominal variables were compared with chi-square test. Pearson Correlation was used to analyze the correlation between the numerical parameters. P <0.05 value was considered statistically significant.

Results

One hundred forty-three participants including 93 patients with idiopathic RLS and 50 controls were included in the study. Both groups had similar sociodemographic features. Sociodemographic features such as age, sex, marital status, etc. of both groups and biochemical and hemogram examinations of the routine examinations were compared (Table 1).

The median of N/L ratio was 2.58 in the RLS group and 2.72 in the control group. There was no statistically significant difference between the groups (P=0.89). The mean duration of disease was 3.2 (1.37) years in patients' group. Sleep disorders were found in 81.7% (n=76) of the cases and similar complaints were observed in 34.4% (n=32) of the upper extremities. It was observed to be low severity of the symptom in 6.3%, middle severity of the symptom in 15.2%, severe severity of the symptom in 64.8%, high severity of the symptom in 13.7% of the cases. There is no significant correlation neither between duration of disease and N/L ratio (r:-0.117, P=0.28) nor between severity of the symptoms and N/L (r:0.281, P=0.41).

Table 1: A comparison between sociodemographic features and laboratory database in RLS patients and healthy subjects

	RLS (n=93)	Control (n=50)	*P*-value
Age, mean (SD)	38.5 (12.4)	36.38 (11.8)	0.28
Sex			
male	42 (45.2)	24 (48)	0.89
female	51 (54.8)	26 (52)	
Marital status			
Married	65 (69.9)	33 (66)	0.81
Single	28 (30.1)	17 (34)	
Occupation			
House wife	32 (34.4)	15 (30)	0.91
Civil Servant	13 (14)	8 (16)	
other	19 (20.4)	11 (22)	
Health-care professional	16 (17.2)	9 (18)	
student	13 (14)	7 (14)	
Education level			
Non-educated	9 (20.0)	7 (15.6)	0.75
≤8 years educated	7 (15.6)	11 (24.4)	
8-12 years educated	9 (20.0)	8 (17.8)	
>12 years educated	20 (44.4)	19 (42.2)	
Economic situation			
Low	40 (43)	17 (34)	0.67
Middle	21 (25.6)	18 (36)	
High	32 (34.4)	15 (30)	
Hemoglobin, mean (SD)	14.6 (2.7)	14.1 (2.1)	0.64
B12 vitamin, mean (SD)	283.7 (119.7)	278.1 (113.4)	0.87
Folic acid, mean (SD)	9.5 (5.3)	7.9 (4.1)	0.06
Serum iron, mean (SD)	64.2 (47.1)	81.9 (39.7)	0.03
UIBC, mean (SD)	293.1 (87.4)	248.4 (74.2)	0.04
Ferritin, mean (SD)	54.7 (89.7)	50.8 (67.1)	0.79
N/L ratio median (reference range)	2.058 (1.4-3)	2.072 (1.4-2.9)	0.89

RLS: Restless legs syndrome, SD: Standard deviation

Discussion

Although various assumptions such as dopaminergic hyperstimulation, iron deficiency, insensitivity of dopaminergic receptors in the tubero-infundibular area have been suggested, still the pathophysiology of RLS is not clear enough [25]. Nevertheless, in recent years, the role of systemic inflammation in the pathogenesis of RLS has been discussed in some studies. The coexistence of RLS with some diseases associated with systemic inflammation such as systemic lupus erythematosus, rheumatoid arthritis, human immunodeficiency virus infection, and inflammatory bowel disease was shown, and it has been pointed out the association of RLS with immunologic and inflammatory mechanisms [26,27].

N/L is drawn attention as a new, cost-effective, and simple to perform method that providing the assessment of inflammation. High levels of N/L were determined in acute or chronic inflammatory situations such as acute pancreatitis, chronic tonsillitis, acute mesenteric ischemia, coronary artery disease, diabetes mellitus, heart failure and malignancies [22]. Also, N/L was assessed in some central or systemic neurologic diseases such as ischemic and hemorrhagic cerebrovascular diseases, myasthenia gravis and multiple sclerosis and was demonstrated the relation with prognosis [28]. On the other hand, in some studies have been demonstrated that the RLS was more common in neurologic conditions where the N/L was observed increment [29]. The only one study in the literature was evaluated the inflammation with N/L in patients with RLS demonstrated higher N/L values in the RLS group, and it was discussed the effect of inflammation in the etiology [30]. In this study we evaluated the N/L to investigate the role of inflammation in etiology of RLS and found no significant increment in the RLS group fort this parameter.

It is known that there is an improvement in symptoms with dopaminergic agonists in RLS as well as exacerbations with anti-dopaminergic agents. While this exacerbation is explicitness in dopamine antagonists that can cross the blood brain barrier such as metoclopramide, no exacerbation is seen with dopamine antagonists that cannot cross the blood brain barrier. This shows that RLS is not a peripheral, but it is central nervous system (CNS) dysfunction [31]. In one study carried out by Patton et al. [14] demonstrated higher levels of HIF1α, which acts as a regulator in inflammation in the substantia nigra of patients with RLS, indicating the effect of inflammation at cellular level. Contrary to this study, Varım et al. [30] indicated the high-level N/L ratios in RLS in their study. With the difference of Varım et al. [30], in this study, N/L ratios were found lower in patients and no statistically significant difference compared to healthy controls. Low N/L values in patients with RLS may suggest that systemic inflammation does not have a role in etiology, rather than inflammatory changes in RLS. In addition, hematologic parameters such as neutrophil and lymphocyte counts can easily be affected by various conditions such as ethnicity, age, sex, eating habits, and environmental factors or our small sample group may be influence to our results.

Vitamin B12, folate, and ferritin levels were found normal in the study which was carried out by Varım et al. [30], but in their study these values were significantly different between the patient and control groups. We did not find such a difference in our study. Although ferritin levels were lower in the RLS group compared with the control group, the difference was not statistically significant. This result may be related with the replacement treatments that patients might have taken before.

Conclusion

We investigated the role of inflammation in the pathophysiology of RLS was evaluated with N/L ratio and it was not observed statistically significance on behalf of patients group. This result may be related with non-evaluation of other biomarkers such as C-reactive protein, sedimentation and interleukin 6 and also small sample group. It is thought that multicenter and longitudinal studies on the larger sample groups can be beneficial for the literature.

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Is there any association between childhood trauma and chronic dermatological diseases? A case-control study

Çocukluk çağı travması ile kronik dermatolojik hastalıklar arasında ilişki varmı? Bir vaka kontrol çalışması

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Abstract

Aim: It is known that traumatic experiences in childhood cause many psychosomatic and psychodermatological diseases. Common dermatological diseases bring about not only dermatological but also psychosocial problems. In our study, we aimed to investigate association of depression, anxiety and childhood trauma with chronic dermatological diseases.

Methods: After power analysis, 76 patients with chronic dermatological diseases (study group) and 75 healthy volunteers (control group) were included in this study. Beck Anxiety Inventory, Beck Depression Inventory and Childhood Trauma Scale (CTQ 28) were administered to these individuals.

Results: The anxiety (P=0.001) and depression (P<0.001) levels were higher in the study group than control group. However, there was no difference with CTQ 28 total (P=0.22) and subscales scores (P=0.16, P=0.98, P=0.90, P=0.23 and P=0.27, respectively) between groups. Physical neglect scores differed significantly according to educational status in the patient group (F=3.643, P=0.03). Emotional neglect and total CTQ 28 scores were higher in patients with lichen simplex chronicus (P=0.23).

Conclusion: In our study, unlike previous studies, dermatological diseases such as lichen planus, Behçet's disease, chronic urticaria and vitiligo were included in the study. This group of diseases should be considered because they adversely affect every aspect of patients' lives in almost. Patients should be carefully evaluated for psychiatric support. We think that the detailed investigation of traumatic experiences from both dermatologists and psychiatrists can lead to better results in the treatment of chronic patients by using psychotherapeutic interventions.

Keywords: Depression, Anxiety, Childhood trauma, Psychodermatology

Öz

Amaç: Çocukluk döneminde meydana gelen travmatik yaşantıların birçok psikosomatik ve psikodermatolojik hastalığın oluşmasına neden olduğu bilinmektedir. Sık görülen kronik dermatolojik hastalıklar sadece dermatolojik değil çeşitli psikososyal sorunları da beraberinde getirmektedir. Çalışmamızda kronik dermatolojik hastalıklar ile depresyon, anksiyete ve çocukluk çağı travması ilişkisini incelemeyi amaçladık.

Yöntemler: Güç analizinden sonra, kronik dermatolojik hastalıkları olan 76 hasta (çalışma grubu) ve 75 sağlıklı gönüllü (kontrol grubu) çalışmaya dahil edildi. Bu kişilere Beck Anksiyete Ölçeği, Beck Depresyon Ölçeği ve Çocukluk Çağı Travmaları Ölçeği (CTQ 28) uygulanmıştır.

Bulgular: Anksiyete (P=0,001) ve depresyon (P<0,001) düzeyleri çalışma grubunda kontrol grubuna göre anlamlı derecede yüksekti. Ancak, CTQ 28 total (P=0,22) ve alt ölçek puanlarında (P=0,16, P=0,98, P=0,90, P=0,23, P=0,27) gruplar arasında fark yoktu. Fiziksel ihmal skorları hasta grubundaki eğitim durumuna göre anlamlı farklılık gösterdi (F=3.643, P=0,03). Duygusal ihmal ve toplam CTQ 28 skorları liken simpleks kronikusu olan hastalarda anlamlı olarak yüksekti (P=0,23).

Sonuç: Çalışmamızda daha önceki çalışmalardan farklı olarak liken planus, behçet hastalığı, ürtiker, vitiligo gibi dermatolojik hastalıklar da dahil edilmiştir. Bu hastalık grupları hastaların yaşamlarını hemen her açıdan olumsuz yönde etkilediği için önemsenmesi gereken bir gruptur. Psikiyatrik destek gerekliliği açısından hastalar dikkatle değerlendirilmelidir. Hem dermatologların hem de psikiyatristlerin hastaların travmatik yaşantılarını detaylı araştırmasının, psikoterapötik girişimler kullanarak kronik hastaların tedavisinde daha iyi sonuçlara yol açabileceğini düşünüyoruz.

Anahtar kelimeler: Depresyon, Anksiyete, Çocukluk çağı travmaları, Psikodermatoloji

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Introduction

Many factors are effective in the formation of diseases and their consequences. As a result of physical illnesses, psychological problems can be experienced, and as well as psychological problems may also appear as physical illnesses [1]. Psychodermatology is a common field of psychiatry and dermatology examines the relationship between the most visibly visible skin and mental disorders [2]. The development of psychodermatology as a working discipline based on the interaction and relationship between the brain, nerves and the skin that develops from the same germ leaf as the embryology has reached its present form through the stages of maturation very similar to the development of a child and has gone in parallel with the development of psychosomatic medicine [3,4].

Skin is the most important communication tool between the outer world and the inner universe of the person and is the source of the most important sensory tactile perception [5]. Every disease that disrupts the functioning of the skin can lead to serious psychiatric problems and may impair quality of life [1]. Psychodermatologic diseases are classified into three groups: (1) Psychophysiologic disorders: A skin condition is exacerbated by emotional stress, (2) Primary psychiatric disorders; there is no primary skin disease, (3) Secondary psychiatric disorders: As a result of having a skin disorder the patient develops psychiatric disorder [6]. The pathogenetic mechanisms that play a role in the relationship of these diseases with psychological stress have been clarified in recent years with the contributions of psychoneuroendocrinology and psychoimmunology study disciplines. Especially in the field of psychodermatology studies, psychophysiological skin diseases, dermatological treatment alone cannot be sufficient and emphasizes the importance of approaches in the axis of psychological treatment [7].

Dermatological diseases at least 25-30% have a psychiatric disease or psychosocial factors [8]. The most common diagnoses were depression with 44% and anxiety disorder with 55% [9]. Epidemiological and clinical studies have also consistently focused on the impact of stress-related environmental risk factors, including childhood trauma (CT) or childhood adversity (including physical abuse, physical neglect, emotional abuse, emotional neglect and sexual abuse) in the development of psychosis [10]. It is thought that there is a bidirectional relationship between psychodermatologic diseases, psychological problems and psychiatric comorbidity [11]. There are a small number of studies demonstrating the relationship between CT and dermatological disease. The aim of this study was to determine the association between childhood trauma with anxiety and depression in chronic dermatologic diseases and sociodemographic data.

Materials and methods

This study was approved by the Institutional Review Board (No: 2018/17), and informed consent was obtained from all participants. After power analysis, 76 patients with consecutive manner in outpatient clinic examination diagnosed with chronic dermatologic diseases and 75 healthy controls were included in the study. Patients diagnosed with psychiatric and neurological disorders or receiving any psychiatric treatment at the time of the study, abnormal intelligence level were excluded from the study. Healthy volunteers included subjects with no other dermatological or additional diseases, between 20-65 years of age and similar sociodemographic characteristics like patients. The interviews were held in the private interview room, with the patient not taking care of someone else. The purpose of the study and the absolute confidentiality of personal information were explained to the patients, and they were asked whether they wanted to participate in the study. The demographic features of all subjects like age, gender, education, marital status were recorded. The diagnosis of chronic dermatological disease was made by the dermatologist.

Data were collected on each of the participants, including the Childhood Trauma Questionnaire (CTQ 28), Beck Depression Inventory and Beck Anxiety Inventory.

Childhood Trauma Questionnaire (CTQ-28): Childhood trauma was examined using the Turkish short version of the CTQ [12]. CTQ is a self-administered questionnaire for screening retrospective Childhood Sexual Abuse, Physical Abuse, Emotional Abuse, Emotional Neglect and Physical Neglect. It measures several dimensions of maltreatment experiences, including the severity, frequency, and duration, consisting of 28 items. The severity of each childhood trauma subscales includes “mild”, “moderate”, “severe” and “extreme”. These five sub points and their combined weighted total average score are obtained.

Beck Depression Inventory (BDI): It was developed by Beck et al. [13] and was conducted with adaptation, validity and reliability for Turkish society by Hisli [14]. This scale includes 21 questions, measures physical, emotional, cognitive and motivational symptoms seen in depression.

Beck Anxiety Inventory (BAI): It was used to assess anxiety symptom severity and features 21 items with 4-point scales (0–3). Responses are summed to arrive at a single score ranging from 0 to 63, with scores ≥8 indicating clinically significant levels of anxiety [15].

Statistical Analysis

The data were analyzed using SPSS (Statistical Package for The Social Sciences) version 22 for Windows. Number, percentage and mean (standard deviation) were used as descriptive statistical methods for evaluating the data. The power of the test was calculated with the G * Power 3.1 program. In order to determine the power of the study to exceed 80%; 5% significance level and 0.8 effect size, a total of 42 people, 21 of them are required to be reached (df=40; t=1.684). The t test was used to compare the quantitative continuous data between the two independent groups and the one way (One way) Anova test was used to compare quantitative continuous data between more than two independent groups. Scheffe test was used as complementary post-hoc analysis to determine the differences after the Anova test. Pearson correlation analysis was applied to the continuous variables of the study.

Results

The study evaluated 76 patients with chronic dermatological diseases and 75 healthy controls. The groups are distributed homogeneously according to the gender (P=0.23) and the marital status (P=0.08). Gender, marital status, education and

type of dermatological disease are presented in Table 1. There was no significance between the groups and age (P=0.45). The mean age of the study group was 36.4 (10.9) years; the mean age of the control group was 35.1 (10.3) years.

When CTQ 28 scores were evaluated; emotional abuse, physical abuse, physical neglect, emotional neglect, sexual abuse and total average score did not differ significantly according to the group variable (P>0.05). According to the Beck Anxiety Inventory, the patient's anxiety scores (14.2 (10)) were higher than the anxiety scores of the control group (9.4 (7.6)) (P=0.001). BDI scores also showed significant differences with respect to groups ($t_{(149)}$=4.174; P<0.001). The depression scores of the patients (14.9 (9.5)) were higher than those of the control group (9 (7.8)) (P<0.001) (Table 2).

The correlation analysis of CTQ 28 subscales, total score and BDI and BAI scores in patient group can be seen in Table 3.

Table 1: Distribution of descriptive properties by groups

		Study group		Control group		*P*-value
		n	%	n	%	
Gender	Female	49	64.5	43	57.3	X^2=0.808
	Male	27	35.5	32	42.7	P=0.23
Marital status	Married	51	67.1	41	54.7	X^2=2.453
	Single	25	32.9	34	45.3	P=0.08
Education	Basic training	33	43.4	8	10.7	X^2=26.548
	High school	21	27.6	17	22.7	P<0.001
	University	22	28.9	50	66.7	
Type of dermatological disease	Vitiligo	8	10.5			
	Chronic urticaria	17	22.4			
	Psoriasis	14	18.4			
	Lichen simplex chronicus	13	17.1			
	Lichen planus	8	10.5			
	Behçet's disease	4	5.3			
	Alopecia areata	12	15.8			

Table 2: Independent Groups T-Test. CTQ 28 subscales, total scores, BAI scores and BDI scores differentiation status by groups.

Groups	Patients (n=76)		Controls (n=75)		t	SD	*P*-value
	Mean	SD	Mean	SD			
Emotional abuse	6.340	1.957	5.950	1.442	1.412	149	0.16
Physical abuse	5.390	0.981	5.400	1.197	-0.030	149	0.98
Physical neglect	7.210	2.473	7.160	2.579	0.123	149	0.90
Emotional neglect	10.530	4.765	9.600	4.753	1.196	149	0.23
Sexual abuse	5.280	1.001	5.590	2.194	-1.121	149	0.27
CTQ 28 total scores	35.890	7.418	34.320	8.164	1.241	149	0.22
BAI scores	14.180	9.906	9.360	7.587	3.357	149	0.001
BDI scores	14.880	9.504	8.960	7.839	4.174	149	<0.001

SD: Standard deviation

CTQ 28 subscales, total score, BDI and BAI scores according to descriptive properties in patient group are as follows: 1-Emotional abuse, physical abuse, physical neglect, emotional neglect, sexual abuse, CTQ 28 total, anxiety, depression scores did not differ significantly from gender and marital status variable (P>0.05). 2-Physical neglect scores differed significantly according to educational status (F=3.643; P=0.03); when education increased, physical neglect scores were decreased (P<0.05). Also total CTQ-28 scores showed a similar decrease. Emotional abuse, physical abuse, emotional neglect, sexual abuse, anxiety and depression scores of patients did not differ significantly according to educational status (P>0.05). 3-Emotional neglect scores of the patients (F=3.088; P=0.01) and total CTQ 28 scores (F=2.465; P=0.03) differed significantly according to the type of disease (F=3.088; P=0.01); the emotional neglect scores (15.6 (5)) and total CTQ 28 scores (40.9 (7)) of the patients with lichen simplex chronicus were higher than the other disease groups (P=0.01), total CTQ 28 scores of the patients with lichen planus (40.3 (8.4)) were higher than vitiligo and alopecia areata (P=0.03). 4- The other parameters like emotional abuse, physical abuse, physical neglect, sexual abuse, anxiety and depression scores of the patients did not differ significantly according to the type of disease (P=0.28, P=0.31, P=0.26, P=0.49, P=0.14 and P=0.15, respectively) (Table 4).

Discussion

The purpose of this study was to reach and discuss findings on relationships between chronic dermatological diseases and CT, anxiety and depression. Significantly reduced anxiety and depression scores was observed in patients with dermatological diseases as well as controls. But there was no significantly relationship between CT and study group other than controls. Physical neglect and total scores of CTQ 28 was associated with educational status in study group. Emotional neglect and CT was observed significantly higher in patients with lichen simplex chronicus.

Table 3: The correlation analysis between age, CTQ 28 subscales and total scores, anxiety and depression points in the study group

		Age	Emotional abuse	Physical abuse	Physical neglect	Emotional neglect	Sexual abuse	CTQ 28 total	BAI	BDI
Age	r	1.000								
	p	0.000								
Emotional abuse	r	0.060	1.000							
	p	0.608	0.000							
Physical abuse	r	0.084	0.255*	1.000						
	p	0.473	0.026	0.000						
Physical neglect	r	0.206	0.183	0.108	1.000					
	p	0.075	0.113	0.352	0.000					
Emotional neglect	r	0.235*	0.314**	0.175	0.483**	1.000				
	p	0.041	0.006	0.131	0.000	0.000				
Sexual abuse	r	-0.052	0.155	0.105	-0.002	-0.101	1.000			
	p	0.654	0.180	0.368	0.984	0.387	0.000			
CTQ 28 total	r	0.228*	0.555**	0.414**	0.689**	0.857**	0.146	1.000		
	p	0.047	0.000	0.000	0.000	0.000	0.209	0.000		
BAI	r	0.060	0.420**	0.157	0.279*	0.349**	0.280*	0.481**	1.000	
	p	0.608	0.000	0.175	0.015	0.002	0.014	0.000	0.000	
BDI	r	-0.077	0.397**	0.220	0.313**	0.420**	0.173	0.525**	0.635**	1.000
	p	0.506	0.000	0.057	0.006	0.000	0.135	0.000	0.000	0.000

*<0.05; **<0.01

Table 4: The differentiation of CTQ 28 subscales, total scores, BAI, BDI scores by descriptive characteristics in the study group.

Demographic features	n	Emotional abuse	Physical abuse	Physical neglect	Emotional neglect	Sexual abuse	CTQ 28 total	BAI	BDI
Gender		Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)
Females	49	6.530(2.199)	5.240(0.693)	7.100(2.510)	10.630(5.302)	5.160(0.624)	35.760(8.102)	15.310(9.115)	16.040(9.635)
Males	27	6.000(1.387)	5.670(1.330)	7.410(2.438)	10.330(3.679)	5.480(1.451)	36.150(6.119)	12.150(11.090)	12.780(9.057)
t=		1.134	-1.822	-0.513	0.260	-1.333	-0.220	1.337	1.443
P=		0.261	0.134	0.610	0.795	0.286	0.827	0.185	0.153
Marital status		Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)
Married	51	6.270(1.919)	5.350(0.976)	7.350(2.536)	10.370(4.745)	5.250(1.017)	35.800(7.563)	14.710(10.456)	15.160(9.569)
Single	25	6.480(2.064)	5.480(1.005)	6.920(2.361)	10.840(4.888	5.320(0.988)	36.080(7.262	13.120(8.781)	14.320(9.538)
t=		-0.428	-0.528	0.715	-0.400	-0.265	-0.151	0.653	0.359
P=		0.670	0.599	0.477	0.691	0.792	0.880	0.516	0.721
Education		Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)
Basic training	33	6.520(2.252)	5.330(0.854)	7.480(2.612)	11.610(5.651)	5.090(0.522)	37.090(8.338)	13.000(7.886)	14.640(9.003)
High school	21	6.480(1.940)	5.570(1.207)	7.950(2.872)	10.620(4.141)	5.520(1.436)	37.570(7.500)	17.950(11.690)	18.000(10.090)
University	22	5.950(1.463)	5.320(0.945)	6.090(1.269)	8.820(3.347)	5.320(1.041)	32.500(4.459)	12.360(10.280)	12.270(9.228)
F=		0.604	0.466	3.643	2.346	1.234	3.486	2.194	2.024
P=		0.550	0.630	0.031	0.103	0.297	0.036	0.119	0.139
Post-Hoc=				1 > 3.2 > 3 (*P*<0.05)			1 > 3.2 > 3 (*P*<0.05)		
Type of disease		Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)
Vitiligo	8	5.500(1.069)	5.500(1.414)	6.120(1.458)	9.120(3.044)	5.000(0.000)	32.380(3.583)	8.880(8.790)	11.500(8.586)
Chronic urticaria	17	6.060(1.600)	5.000(0.000)	7.060(2.410)	10.000(4.330)	5.350(0.996)	34.470(6.226)	12.940(8.181)	11.760(7.005)
Psoriasis	14	6.430(1.869)	5.790(1.424)	6.790(2.326)	8.790(4.353)	5.570(1.284)	35.210(8.903)	12.860(9.478)	14.930(9.872)
Lichen simplex chronicus	13	6.770(2.242)	5.540(0.967)	8.150(2.154)	14.620(4.925)	5.080(0.277)	40.920(7.017)	17.540(9.726)	17.380(8.827)
Lichen planus	8	7.380(2.669)	5.000(0.000)	8.620(3.662)	12.620(6.093)	5.750(2.121)	40.250(8.396)	19.880(11.789)	21.250(13.339)
Behçet's disease	4	7.500(3.317)	5.750(1.500)	7.750(3.202)	8.000(4.761)	5.000(0.000)	35.250(10.720)	20.750(14.930)	20.500(12.477)
Alopecia areata	12	5.670(1.371)	5.420(0.793)	6.500(2.195)	9.250(3.194)	5.000(0.000)	32.920(4.562)	11.420(8.826)	12.670(8.038)
F=		1.286	1.217	1.317	3.088	0.901	2.465	1.697	1.645
P=		0.275	0.308	0.261	0.010	0.499	0.032	0.135	0.148
Post-Hoc=					4 > 1.4 > 2.4 > 3.4 > 6.4 > 7 (*P*<0.05)		4 > 1. 5 > 1, 4 > 2.4 > 3.4 > 7.5 > 7 (*P*<0.05)		

Consistent with the literature the prevalence rates of anxiety and depression were higher in study group than in the control group. Woodruff et al. [16] reported that the most common psychiatric diagnoses were depression with 44% and anxiety with 35% in patients who shipped psychiatry after referring to the dermatology clinic. Yalçın et al. [11] found depression with %39.5 and anxiety with %21 in patients with neurotic excoriation and significantly higher BDI and BAI scores in study group. In another studies, Snorrason et al. [17] and Misery et al. [18] observed closely related to depression and anxiety disorders in patients with neurotic excoriation.

Childhood maltreatment and traumatic events in the first years of life pose a risk for all types of psychopathology [19]. Severe stress experienced in early life affects the stress-induced glucocorticoid, noradrenergic and other response systems; adverse childhood experiences can be associated with many psychosomatic diseases such as irritable bowel disease, chronic fatigue syndrome and fibromyalgia [20-21]. In dermatology; Yalçın et al. [11] reported higher CTQ 28 scores in both groups emotional abuse, physical abuse, emotional neglect and the CTQ 28 scale total score in patients with neurotic excoriation. On the other hand, they did not observe a statistically significant difference in sexual abuse and physical neglect scores.

In our study, we found higher emotional neglect and total CTQ scores in patients with lichen simplex chronicus other than diseases, too. Misery et al reported in their study of 10 patients with neurotic excoriation that the majority of patients had personal problems before the onset and 4 patients described abuse during childhood and adolescence [18]. Again, Sesliokuyucu et al. [22] observed higher CTQ 28 scores in patients with psoriasis (74.07 (10.58)) than controls (66.9 (8.13)) in their study. Willemsen et al. [21] found life-long and childhood trauma in adult alopecia areata patients significantly higher than the control group. However, there are limited numbers of studies related to dermatological diseases. In our study, CT was investigated by including many dermatological diseases, not just 1 disease group.

We did not find significance with CTQ total scores and subscales between the study and control groups. But we found a positive correlation between CTQ scores and BAI and BDI scores in study group. This situation implies that traumatic childhood experiences may also play an important role in the etiology of both dermatological disease and accompanying psychiatric problems. An important relationship was reported with sexual abuse and self-harm behavior in the childhood. It is known that history of sexual abuse in childhood is frequently seen in psychodermatology patients, but this history is usually obtained at the end of a psychiatric consultation or long term psychotherapy period [23,24]. Therefore, we believe that some of the patients who participated in the study may not have experienced sexual trauma in their childhood due to the nature of the study and the CTQ 28 was a self-report scale.

In our study, there was a significant relationship between education status and childhood trauma and physical neglect. As the education level increased, these scores decreased. In previous studies, we have not found any studies showing this relationship with the educational status and so we couldn't find the possibility comparing the results.

Our findings had shown that dermatologists and psychiatrists should always query traumatic experiences in patients with chronic dermatological diseases like psoriasis, lichen simplex chronicus, alopecia areata, vitiligo, lichen planus and Behçet's disease. Thus, patients may be given the opportunity to start talking about psychotherapy and to start psychotherapy with known psychodermatologic diseases [18-23].

The present study has some limitations. First, the small sample size of patients at a single clinic and controls does not reflect the general population. A second limitation is the possibility that some patients did not report their experience with sexual abuse due to the cross-sectional nature of the study, current psychiatric comorbidity, anxiety and depression levels, and the effect of childhood traumatic experiences on the course of the disease, and the fact that a single evaluation interview could be conducted with patients. Finally, to our best knowledge, this is the first study of investigate the relationship of CT in

chronic dermatological diseases and for this reason, the results cannot be compared with another research.

Conclusion

Dermatological diseases are a group of disease which should be considered because of their effect on patients' lives in almost every way. For these reasons, only skin lesions of patients should not be considered; depression, anxiety, mental traumatic life and life quality should be carefully evaluated and determined the need for psychiatric support. These measures can reduce the severity of the disease as well as patient compliance and it is thought to make them more at peace with life.

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Assessment of the white blood cell subtypes ratio in patients with supraventricular tachycardia: Retrospective cohort study

Beyaz küre alt tipleri oranının supraventriküler taşikardili hastalarda değerlendirilmesi: Retrospektif kohort çalışma

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Abstract

Aim: Neutrophil/lymphocyte ratio (NLR), monocyte/lymphocyte ratio (MLR) and lymphocyte/monocyte ratio (LMR) have been considered to be the new cardiovascular risk predictors. Inflammation has been shown to be associated with various types of arrhythmia. This study aimed to investigate the relationship between NLR, LMR and MLR in patients with supraventricular tachycardia (SVT).

Methods: Our study included 59 patients aged 18 years or older who visited our clinic between December 2017 and December 2018. Thirty-three patients were diagnosed with definitive diagnosis of tachycardia using electrocardiographic (ECG) method, and hospitalized for ablation. The other 26 patients were the ones who underwent electrophysiological study (EPS) as it was not possible to make a diagnosis of arrhythmia using non-invasive methods despite ongoing complaints of palpitation. Blood samples were taken from all patients for pre-operative complete blood count analysis. NLR was calculated as the ratio of neutrophil count to lymphocyte count. MLR was calculated as the ratio of monocyte count to lymphocyte count. LMR was calculated as the ratio of lymphocyte count to monocyte count. In addition, electrophysiological study (EPS) was performed for treatment purposes in patients diagnosed with SVT; and for diagnosis and treatment purposes in patients who have the complaint of palpitation, however, could not be diagnosed using non-invasive methods.

Results: This study included 33 patients with SVT and 26 healthy controls who underwent EPS. When hematological parameters were compared, there was no statistically significant difference in NLR values (1.96 (0.69) 103/μL vs. 2.17 (1.29) 103/μL, *P*=0.42). Moreover, both MLR (0.25 (0.09) 103/μL vs. 0.22 (0.08)) 103/μL, *P*=0.19) and LMR (4.64 (1.37) 103/μL vs. 4.64 (1.45)) 103/μL, *P*=0.49) were not statistically significant between the two groups.

Conclusion: This study showed that NLR, LMR and MLR values cannot be used as predictors for the presence of SVT.

Keywords: White blood cell subtypes, Supraventricular tachycardia, Inflammation

Öz

Amaç: Nötrofil/lenfosit oranı (NLO), monosit/lenfosit oranı (MLO) ve lenfosif/monosit oranı (LMO) yeni kardiyovasküler risk belirleyicileri olarak değerlendirilmiştir. Inflammation has been demonstrated to be associated with various types of arrhythmia. Bu çalışmadaki amacımız geriye dönük olarak supraventriküler taşikardi (SVT) tanılı hastalarda NLO, LMO ve MLO ile ilişkisini araştırmayı amaçladık.

Yöntemler: Çalışmamız 18 yaş ve üzerinde, Aralık 2017- Aralık 2018 tarihleri arasında kliniğimizde takip edilen 59 hastayı içermektedir. Hastaların 33 tanesi çarpıntı tanısı konmuş ablasyon için yatış verdiğimiz hastalar olup, diğer 26 tanesi noninvaziv yöntemlerle ritm bozukluğu tanısı konulamayan fakat çarpıntı şikayetleri devam eden kesin tanısını koyabilmek için elektrofizyolojik çalışma (EPS) yaptığımız hastalardan oluşmaktadır. Tüm hastalardan işlem öncesi hemogram ölçümü için kan örneği alındı. NLO değeri nötrofil sayısının lenfosit sayısına oranı, MLO değeri monosit sayısının lenfosit sayısına oranı ve LMO değeri lenfosit sayısının monosit sayısına oranı olarak hesaplandı. Ayrıca SVT tanısı mevcut hastalarımıza tedavi amaçlı; hem de noninvaziv yöntemlerle tanısı konulamayan çarpıntı hastalarına tanı ve tedavi amaçlı EPS yapıldı.

Bulgular: Çalışmaya SVT'li 33 hasta ve EPS sonucu normal olan 26 tane sağlıklı kontrol grubu dahil edildi. Hematolojik parametreler karşılaştırıldığında NLO (1,96 (0,69) 103/μL karşı 2,17 (1,28) 103/μL, *P*=0,42) istatiksel olarak anlamlı değildi. Bir diğer parametrelerde hem MLO iki grup arasında (0,25 (0,09) 103/μL karşı 0,22 (0,08) 103/μL, *P*=0,19) hem de LMO iki grup arasında istatiksel olarak anlamlı değildi. (4,38 (1,37) 103/μL karşı 4,64 (1,45) 103/μL, *P*=0,49).

Sonuç: Yaptığımız çalışmada NLO, LMO ve MLO değerlerinin SVT'nin varlığı için kullanılabilir gösterge olmadıklarını göstermiş olduk.

Anahtar kelimeler: Beyaz kan hücresi alt tipleri, Supraventriküler taşikardi, İnflamasyon

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Introduction

Supraventricular tachycardia (SVT), also called paroxysmal supraventricular tachycardia, is defined as an abnormally rapid heartbeat. It is a broad term that includes many heart rhythm disorders that originates from the region above the atrium or AV node. The normal heart rate is 60 to 100 beats per minute. Having a heart rate above 100 beats per minute is called tachycardia. There are three main types of SVT; AV nodal re-entrant tachycardia (AVNRT), atrioventricular re-entrant tachycardia (AVRT) and atrial Tachycardia (AT). Recently, neutrophil / lymphocyte ratio (NLR), monocyte/lymphocyte ratio (MLR) and lymphocyte/monocyte ratio (LMR) values which can be calculated rapidly were considered as new predictors for cardiovascular diseases [1-3].

Previous studies in the field of arrhythmia have shown that inflammation plays a predisposing role for SVT [4,5]. However, data about the relationship between SVT, and NLR, LMR and MLR is not sufficient. Therefore, we aimed to investigate the relationship between NLR, LMR and MLR levels in patients with definite diagnosis of SVT.

Materials and methods

This retrospective study consisted of 59 patients who were followed-up at our clinic between December 2017 and December 2018. Electrophysiological study (EPS) was performed in all patients. Ethics committee approval was not received as the study design was retrospective and written informed consent was obtained from all patients before the procedure. All participants underwent diagnostic EPS procedure. Successful RF catheter ablation procedure was performed in patients with diagnosed SVT. EP Tracer electrophysiology system, Medtronic stimulator and Atakr RF generator were used in the study. Patients with a history of past ablation, renal dysfunction (serum creatinine level being >1.5 mg/dL), cancer, cerebral vascular disease, hematological disorders, patients with a history of infection in the past two weeks, acute or chronic infection, hepatic dysfunction, immunosuppressant, anti-inflammatory or patients receiving steroids were excluded from the study.

Sampling and laboratory analysis

The blood samples were taken through antecubital vein into dry tubes and into tubes containing ethylenediaminetetraacetic acid (EDTA). Dry tubes were used for the biochemical analysis and EDTA tubes were used for the hematological analysis. MLR was calculated as the ratio of monocyte count to lymphocyte count. NLR was calculated as the ratio of neutrophil count to lymphocyte count. LMR was calculated as the ratio of lymphocyte count to monocyte count.

Statistical analysis

Statistical analysis was performed using SPSS 21.0 (IBM 1989, 2012) package software. Continuous data were expressed as mean (standard deviation), and categorical data were expressed as number and percentage. Categorical data were compared by chi-square test; continuous data were analyzed by Student's t-test after testing for normal distribution. A *P* value of <0.05 was considered to be statistically significant.

Results

Table 1 summarizes the baseline demographic and clinical characteristics, and laboratory findings of the patients included in this study. The study population consisted of 59 patients.

The mean age was 44.85 years, and 47 patients (79%) were female. There were no statistically significant differences between the groups in terms of age, sex, smoking status, and hemoglobin, monocyte and lymphocyte levels. RF ablation treatment was performed in 33 patients. In EPS, the neutrophil count was 4.77 (1.76) x 10^3/μL. In SVT, the neutrophil count was 4.32 (1.40) x 10^3/μL. In the control group the monocyte count was 0.54 (0.25) x 10^3/μL. In the study group the monocyte count was 0.55 (0.18) x 10^3/μL.

Consequently, NLR, LMR and MLR values were analyzed in the control and the study groups, and there was no significant difference found between the groups (figure 1-3).

Table 1: Baseline demographic, biochemical and hematological characteristics of the study population (n=59)

	Study group mean (SD)	Control group mean (SD)	*P*-value
Age	45.94 (14.96)	43.77 (8.97)	0.49
*Female, n(%)	24 (72.7)	23 (88.5)	0.14
*Tobacco use, n(%)	9 (27.3)	6 (23.1)	0.71
Glucose (mg/dL)	102.09 (23.15)	122.82 (61.04)	0.11
Creatinine, mg/dL,	0.78 (0.16)	0.74 (0.13)	0.31
Hemoglobin, g/L	13.87 (1.93)	13.40 (1.67)	0.33
Neutrophil count, x10^3/μL	4.32 (1.40)	4.77 (1.76)	0.28
Lymphocyte count, x10^3/μL	2.32 (0.68)	2.48 (1.04)	0.48
Monocyte count, x10^3/μL	0.55 (0.18)	0.54 (0.25)	0.82
Neutrophil/lymphocyte ratio	1.96 (0.69)	2.17 (1.28)	0.42
Monocyte/lymphocyte ratio	0.25 (0.09)	0.22 (0.08)	0.19
Lymphocyte/monocyte ratio	4.38 (1.37)	4.64 (1.45)	0.49

SD: Standard deviation, SVT: supraventricular tachycardia, EPS: Electrophysiological study, * Chi-square test was performed for these parameters, and Student's t-test for other parameters

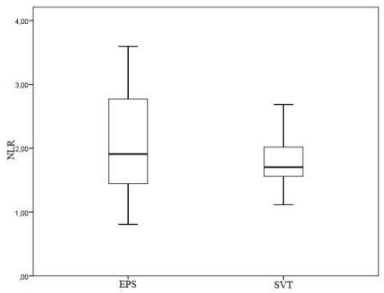

Figure 1: Comparison of the neutrophil/lymphocyte ratio between the patients with supraventricular tachycardia and the control subjects

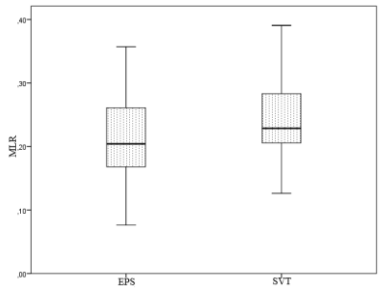

Figure 2: Comparison of the monocyte/lymphocyte ratio between the patients with supraventricular tachycardia and the control subjects

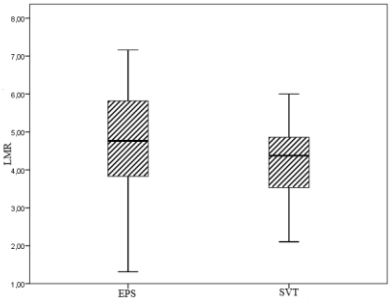

Figure 3: Comparison of the lymphocyte/monocyte ratio between the patients with supraventricular tachycardia and the control subjects

Discussion

The pathogenesis of cardiac arrhythmias is complex. In their study, Klein et al. have previously shown that inflammation plays an active role in the pathogenesis cardiac arrhythmias. As the mechanism, they have shown that inflammation markers which increase in infectious states lead to myocardial fibrosis, increased wall tension, and eventually, increases myocardial oxygen consumption. In the end, reduced coronary reserve flow and impaired intercellular action potential in myocardial cells trigger arrhythmia [6].

The three main causes of a narrow QRS tachycardia are atrial tachycardia, orthodromic AV re-entrant tachycardia, and AV nodal re-entrant tachycardia.

Antiarrhythmic drugs help control arrhythmias, but they may also cause arrhythmias, and thereby, the symptoms would also continue. Many studies recommended use of catheter ablation [7].

NLR may be associated with the onset of arrhythmias in adults, thus, this may indicate a possible inflammatory etiology. Some studies have demonstrated inflammation has important implications for risk assessment for cardiovascular diseases [8].

Elevated levels of systemic inflammation markers are associated with cardiovascular disease [9].

NLR and MLR were considered as new cardiovascular risk factors. This study aimed to show whether there was a difference between NLR and MLR values in the control and the study groups. The results of our study showed that there was no significant difference between the groups. Recent studies have demonstrated the significance of NLR in cardiovascular diseases and SVTs. There is a positive correlation between the NLR and inflammation markers [10]. Some studies have suggested that inflammatory processes contribute to atrial arrhythmias [11-12]. For example, Osmancık et al. [13] reported that atrial fibrillation is associated with the activation of inflammatory processes [e.g. higher concentrations of pro-inflammatory cytokines, interleukin-6 (IL-6), C-reactive protein (CRP)]. According to their study, successful ablation of AF together with sinus rhythm restoration and maintenance is associated with reduced serum levels of inflammation markers. In another study, Ocak et al. [14] found lymphocyte counts were similar in supraventricular tachyarrhythmia in patients with documented atrial tachyarrhythmia and healthy adults in the emergency department (ED). Aydın et al. [15] found SVT inducibility during EPS was associated with higher NLR levels.

Our results differ from those of other studies, and we believe there are two reasons for this. Firstly, the study population consisted of patients who are mainly of female gender in both the EPS and the ablation arms. Secondly, we selected the control group participants from patients who were found normal after EPS.

In the present study, there was no statistically significant difference between the groups in terms of age. Several studies have showed that hematopoiesis changes occur at different estrogen levels during menopause. Different cut-off values should be set by race and age. Despite being inexpensive and easy, the application of hematologic markers in clinical practice can be challenging due to lack of standardization and evidence [16,17].

Study limitations

The majority of our study participants were of female gender. This is a single-center, retrospective study, the number of patients is relatively small, and other inflammation markers such as TNF- α, IL- 1, and IL-6 were not measured.

Conclusion

In conclusion, there was no significant difference found NLR, LMR and MLR values in patients with study groups compared with control groups. In addition, we detected higher MLR values in patients in study group. Further large-scale, prospective, and multicenter studies are needed to confirm the association between NLR, LMR and MLR and SVT.

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Efficacy of complex decongestive therapy on breast cancer-related lymphedema: A cross-sectional study

Meme kanseri ilişkili lenfödem ve kompleks dekonjestif tedavisi etkinliği: Kesitsel çalışma

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Abstract

Aim: Lymphedema is a protein-rich interstitial fluid accumulation which occurs as a result disruption of lymphatic circulation. Breast cancer is a major reason of secondary cancer lymphedema. Breast cancer related upper extremity lymphedema result from the obstruction or disruption of the lymphatic system due to axillary lymph node dissection and/or radiation therapy of axillary region. A variety of conservative therapies have been aimed to decrease the limb swelling and its associated problems have been developed. Conservative treatments are complex decongestive therapy (CDT). The aim of our study was to investigate efficacy of CDT on the occurrence of breast cancer related lymphedema.

Methods: Between 2009 and 2018, 47 consecutive patients with histologically proven breast cancer were first treated with breast surgery, axillary lymph node dissection and radiotherapy and/or chemotherapy. These were analyzed collectively with retrospective data of our medical records who had 15-30 set of CDT and who had complete assessments before and after the treatment. CDT consists of the following components; skin care, manual lymphatic drainage, bandaging and exercises. Patients were treated with active therapy schedule (manual massage for lymphatic drainage and exercise therapy, 45-60 min per day) by the same trained physiotherapist. Volumetric quantification by circumference measurement of affected and healthy extremities was used for diagnosis and follow-up of lymphedema in all patients.

Results: The data of the 47 patients complying with the criteria specified in this retrospective study were evaluated. When the volumetric changes in the affected extremity were examined before and after lymphedema treatment, it was determined that the amount of lymphedema decreased after CDT (P=0.001). 31 (66%) patients received radiotherapy after mastectomy. When the patients were compared in terms of volumetric changes in extremities before and after CDT according to getting postoperative radiotherapy, it was determined that the changes in the patients who did not get radiotherapy were significantly higher than those getting radiotherapy (P=0.01).

Conclusion: Our study results show that CDT can be used for the management of breast cancer related lymphedema of limb. A thorough cost-effective analysis of protocol for CDT should be performed in a future study. In addition, as the factors underlying treatment delay were not included in this study, we believe future studies examining this area may be beneficial.

Keywords: Lymphedema, Complex decongestive therapy, Breast cancer

Öz

Amaç: Lenfödem lenfatik dolaşımının bozulması sonucu, proteinden zengin interstisiyel sıvının birikimiyle karakterize bir durumdur. Meme kanseri ilişkili lenfödem genellikle aksiller lenf nodu diseksiyonu ve/veya aksiller radyasyon sonucu üst ekstremitenin lenfatik drenajının bozulması nedeniyle oluşur. Tedavi yaklaşımları, ekstremitedeki şişliğin azaltılması, semptomların kontrolü ve komplikasyonların azaltılmasına yöneliktir. Bu çalışmadaki amacımız meme kanseri ilişkili lenfödem ve kompleks dekonjestif tedavisi (KDT) etkinliğini araştırmaktır.

Yöntemler: Meme kanserine bağlı olarak cerrahi müdahale, axiller lenf nodu diseksiyonu,radioterapi ve/veya kemoterapi almış ve üst ektremitede lenf ödem gelişen, 15-30 seans KDT uygulanan ve ayrıca rehabilitasyon öncesi ve sonrası değerlendirmeleri eksiksiz yapılan hastaların dosyaları değerlendirmeye alındı. Tüm hastaların lenfödemin tanı ve takibinde etkilenen ve sağlam ekstremitenin çevre ölçümleri aracılığıyla elde edilen volümetrik ölçümler kullanıldı. Hastaların tedavi öncesi ve sonrası sağlam ve etkilenen ekstremitelerinin çevre ölçümlerinden faydalanarak ekstremite volümleri hesaplandı ve kaydedildi.

Bulgular: Yapmış olduğumuz bu retrospektif araştırmada belirtilen kriterler ile uyumlu 47 hastanın verileri değerlendirmeye alındı. Lenfödem tedavisi öncesi ve sonrasındaki tutulan ekstremitedeki volüm değişimleri incelendiğinde ise KDT sonrasında lenfödem miktarının anlamlı derecede azalmış olduğu tespit edildi (P=0.001). Değerlendirmeye alınan hastalardan 31'i (%66) mastektomi sonrası radyoterapi almıştı. Hastalar postoperatif radyoterapi alma durumuna göre KDT öncesi ve sonrası ekstremitede meydana gelen volümetrik değişim açısından karşılaştırıldığında radyoterapi almayan hasta grubundaki değişimin radyoterapi alanlardan anlamlı derecede daha fazla olduğu belirlendi (P=0.01).

Sonuç: Çalışmamızın sonuçları KDT tedavisinin lenfödem tedavisinde etkin bir tedavi yöntemi olduğunu göstermiştir. Gelecek zamanda kompleks dekompresif tedavinin komponentlerinin etkinliğini değerlendirilebilmek için uzun takip süreli kontrollü çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Lenfödem, Kompleks dekompresif tedavi, Meme kanseri

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Introduction

Lymphedema is a protein-rich interstitial fluid accumulation which occurs as a result disruption of lymphatic circulation [1]. Breast cancer is a major reason of secondary cancer lymphedema. Breast cancer related upper extremity lymphedema result from the obstruction or disruption of the lymphatic system due to axillary lymph node dissection and/or radiation therapy of axillary region [2]. Breast cancer related lymphedema-associated symptoms are pain in the affected arm, skin fibrosis and impaired shoulder/arm movement altogether with worsening in their quality of life [3]. All patients with breast cancer who treated for lymph node dissection and radiation therapy has a risk of developing lymphedema, swelling of the upper extremity and concomitantly of the breast [4]. Additionally, there is a relationship between the risk of lymphedema, and treatment outcome according to the extent of lymph node dissection.

Lymphedema is considered irreversible condition. A variety of conservative therapies have been aimed to decrease the limb swelling and its associated problems have been developed. Conservative treatments are complex decongestive therapy (CDT), manual lymphatic drainage (MLD), self/partner massage, pneumatic pumps, oral pharmaceuticals and Low level laser therapy. Physical therapy treatment of patients with lymphedema is based on the principles of CDT which consists of the following components; skin care, manual lymphatic drainage, bandaging and exercises [5]. There are two phase program with an initial phase can be allowed for the reduction of lymphedema. It is followed by a maintenance phase based on compression therapy with the aid of bandages, self-lymphatic massages with regular use compression garments, skin care and remedial exercises [6]. Lymphedema cannot be completely cured and when untreated conditions, the risk of increasing over of extremity volume which leads to chronic inflammation later then fibrosis. Therefore, effective treatment of lymphedema is important for improving quality of life.

The aim of our study was to investigate efficacy of CDT on the occurrence of breast cancer related lymphedema.

Materials and methods

Between 2009 and 2018, 47 consecutive patients with histologically proven breast cancer were first treated with breast surgery, axillary lymph node dissection and radiotherapy and/or chemotherapy. These were analyzed collectively with retrospective data of our medical records. Exclusion criteria were involvement of both side, recurrence, patients treated in another center before, patients who have not completed CDT and patients who had bone metastasis.

All patients were informed about lymphedema and the therapy in the first assessment. They were also given a schedule for home exercises and thought self-massage. Patients were treated with active therapy schedule (manual massage for lymphatic drainage and exercise therapy, 45-60 min per day) by the same trained physiotherapist. The same physiotherapist made multıple part-compressive bandage therapy at the end of the day. CDT was used for 15 to 30 sessions 5 days a week according to patients' condition.

Patients' ages, the extremity involved in lymphedema, dominant extremity in use, any surgical procedure, the duration since the beginning of CDT, the duration of CDT and any previous treatment involving radiotherapy and/or chemotherapy. Volumetric quantification by circumference measurement of affected and healthy extremities was used for diagnosis and follow-up of lymphedema in all patients. Circumference measurements of all patients' affected and healthy extremities were made symmetrically in 5 cm intervals from the ulnar styloid process to the axilla pre- and post-treatment. Both extremity circumference measurements of the patients assessed and recorded pre- and post-treatment.

Statistical analysis

Statistical analyses were performed with the SPSS Software Package (version 22.00; SPSS Inc., Chicago, USA). Descriptive statistic parameters, such as frequency distribution, mean and standard deviation, were used for characterizing the study group. Mean differences of two independent groups were determined using "Student t test" when parametric test assumptions were met, while mean differences of two dependent groups were determined using "paired difference test". Additionally, strength of association between continuous variables was assessed with Spearman's correlation coefficient, while that of between discrete variables was assessed with Pearson's correlation coefficient. During analysis, a confidence level of 95% (or tolerance level of α=0.05) was deemed a statistically significant difference.

Results

The data of the 47 patients complying with the criteria specified in this retrospective study were evaluated. The mean age of the patients were 55.63 (9.60) years (min 35 - max 74 years) and the period until CDT was started was 74.25 (39.55) months (min 18, max 168 months). 28 (%59.6) patients were operated for left and 19 (40.4%) patients were operated for right breast ca and the mean BMI values of the patients were 31.34 (5.22) kg/m2. When the patients on the scope of the study were examined for comorbid diseases, one or more comorbid factors were detected in 24 (60%) patients. The most common comorbid diseases are; endocrine diseases such as diabetes mellitus, hyperlipidemia and thyroid dysfunction in 17 (41.5%) patients, cardiovascular diseases especially hypertension in 12 (30.8%) patients and pulmonary diseases in 3 (7.3%) patients. Demographic and clinical characteristics of patients are shown in Table 1.

It was determined that the affected extremity volumetric values before treatment of patients who received CDT had significantly higher than the unaffected extremity, that this difference continues after treatment too (P=0.001). When the volumetric changes in the affected extremity were examined before and after lymphedema treatment, it was determined that the amount of lymphedema decreased significantly after CDT (P=0.001) (Figure 1).

When the patients were divided into two groups according to age of under 65 years of age (37 patients, 78.7%) and 65 years of age and above (10 patients, 21.3%), there was no difference between the groups according to the change in the amount of lymphedema before and after treatment (P=0.79). In

addition, no difference was found between the groups when the changes in the amount of lymphedema before and after treatment in terms of right or left extremity affected were compared (P=0.73, Table 2).

31 (66%) patients received radiotherapy after mastectomy. When the patients were compared in terms of volumetric changes in extremities before and after CDT according to getting postoperative radiotherapy, it was determined that the changes in the patients who did not get radiotherapy were significantly higher than those getting radiotherapy (P=0.01). When the patients were compared according to getting chemotherapy, there was no difference between the groups in terms of the change in the amount of lymphedema before and after treatment. In addition, when the patients were evaluated according to the presence of comorbid diseases, it was found that there was no significant change in the amount of lymphedema before and after CDT among the patients with one or more comorbid diseases and those without any comorbid disease (Table 2).

When the patients were evaluated in terms of risk factors, there was a statistically significant strong correlation between BMI and the amount of lymphedema before and after treatment (r=0.74 and r=0.73, P=0.04) (Figure 2, 3).

Table 1: Demographic and clinical characteristics of patients

	Patient group (n=47)
Age, years, mean (SD)	55.6 (9.6)
Affected side (right/left) mean (SD)	28 (59.6%) /19 (40.4%)
BMI kg/m^2, mean (SD)	31.34 (5.22) kg/m^2
CDT sessions, mean (SD)	16.80 (3.52) (min 15, max 30)
Length of time from diagnosis to CDT (months), mean (SD)	74.25 (39.55) months (min 18, max 168 months)
Post-operative chemotherapy (n, %)	36 (76.6)
Post-operative axillary radiotherapy (n, %)	31 (66)
Comorbid disease + (total)	24 (60)
Cardiovascular disease (n, %)	12 (30.8)
Endocrine disease (n, %)	17 (41.5)
Pulmonary disease (n, %)	3 (7.3)

SD: Standard deviation

Table 2: Clinical parameters associated with lymphedema volume comparison between pre-treatment and post-treatment

	Pre-treatment lymphedema limb volume mean (SD)	Post-treatment lymphedema limb volume mean (SD)	P-value
Age			
< 65 years (n=37, 78.7%)	3.30 (0.87)	2.87 (0.73)	0.79
≥ 65 years (n=10, 21.3%)	3.47 (0.63)	2.95 (0.48)	
Effected limb			
Right upper limb (n=19, 40.4%)	3.40 (0.87)	2.89 (0.64)	0.43
Left upper limb (n=28, 59.6%)	3.29 (0.80)	2.88 (0.72)	
Radiotherapy			
Yes (n=31, 66%)	3.43 (0.96)	2.96 (0.76)	0.01 ǂ
No (n=16, 34%)	3.16 (0.44)	2.74 (0.47)	
Chemotherapy			
Yes (n=36, 76.6%)	3.28 (0.86)	2.83 (0.67)	0.38
No (n=11, 23.4%)	3.52 (0.69)	3.06 (0.70)	
1 ≤ comorbid disease + (n=24, 60 %)	3.39 (0.83)	2.92 (0.69)	0.51
Comorbid disease - (n=23, 40 %)	3.07 (0.72)	2.68 (0.59)	

SD: Standard deviation, ǂ P<0.05

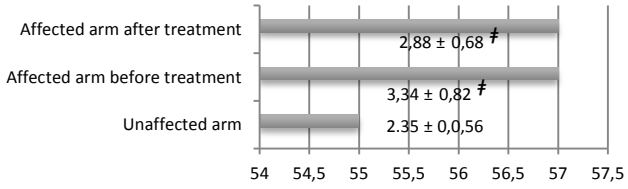

Figure 1: Comparison of affected and unaffected arm's volume between pre-CDT and post-CDT, ǂ P=0.001

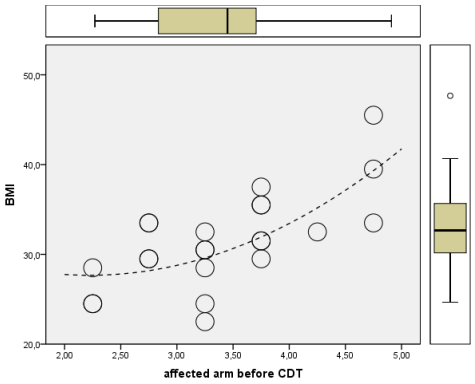

Figure 2: The relationship affected arm between BMI before CDT, ǂ (r=0.74, P=0.04)

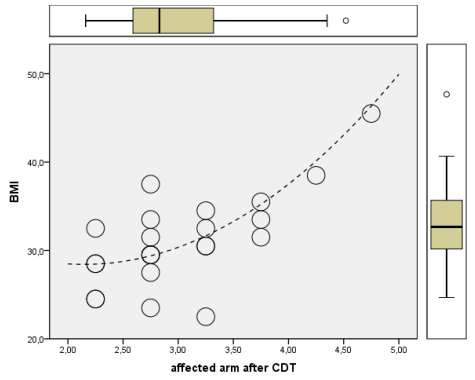

Figure 3: The relationship affected arm between BMI post CDT, ǂ (r=0.73, P=0.04)

Discussion

Lymphedema is important complications of breast cancer treatment. In the Arm lymphatic vessels were drained from the hand and forearm via superficial channels. There are also deep channels that drain via the occasional deep lymph node accompanying arteries in the forearm to the axillary nodes. Then lymph drains up the arm, passing through a few deep brachial and deltopectoral lymph nodes, before draining into the infraclavicular and axillary lymph nodes [7]. Lymphatic vessels remove circulating fluid and large molecules from the extracellular spaces and transport them to the lymph nodes. It is essential for maintain correct extracellular fluid balance and clearance of pathogenic elements. After then lymph is returned back systemic circulation via the vascular system. But in lymphedema, this normal way is impaired and excess protein rich fluid especially subcutaneous tissue. Some risk factors that may lead to developing lymphedema have been identified such as surgical removal of lymph nodes, radiotherapy to lymph node areas, obesity [8,9]. In our study, we also observed significant correlation between breast-cancer related lymphedema, and radiotherapy and obesity. Radiotherapy treatment is a risk factor of developing lymphedema; this condition may also be associated with some skin excoriation. This can decrease the transport capacity of the initial lymphatics but should slowly improve once the treatment has been completed [8]. Warren et al. [10] showed that radiotherapy to regional lymph nodes increase risk of developing lymphedema. Rupp et al. [3] collected from 385 patients data who underwent multimodal therapy for breast cancer, including breast conserving surgery, axillary dissection, and local radiotherapy and their aim is studied the effects of individual risk factors on the occurrence of breast cancer related lymphedema when breast cancer therapy included complete axillary lymph node dissection. As a result they found

association between chemotherapy and increase risk of breast-cancer related lymphedema like some studies [3,11]. Chemotherapy can lead to an enhancement of interstitial fluid filtration, capillary protein leakage and subsequently edema. In our study, this result is not in conformity with our study. We couldn't found significantly correlation between chemotherapy and lymphedema. This difference may be occurred because of our study include the relatively small and clinically diverse sample population.

As mentioned, there is no cure for lymphedema, and the aim of the treatment is to reduce the swelling and to decrease discomfort. CDT can be effective in reducing arm volume. CDT consists of the following components; skin care, manual lymphatic drainage, bandaging and exercises [12]. The treatment is based on manual lymphatic drainage 5 times weekly and each treatment takes 45-60 minutes. However, standardization between different treatment locations and among treating physiotherapists does not exist. Some studies demonstrated that a reduction in upper extremity volume can be done with CDT [13-15]. In our study, results suggest that decongestive phase of therapy is effective in the maintenance of volume reduction. CDT is a combined method of treatment, and the relative efficacy of each of the components of this comprehensive treatment program has been investigated in some studies [16]. There is a debate as to which components of CDT play the most crucial and whether bandages are more effective at reducing swelling than compression hosiery. Lack of experienced therapists and inadequate resources mean that standard treatment is likely to consist of compression hosiery with advice on skin care and exercise. In case manual lymphatic drainage is not accessible, patients are often taught to perform a simplified form known as self-administered massage, however, as to which of these methods is the more effective unknown yet. These questions are required to further research investigation able to answer. This is important how we can identify the most effective physical treatment and achieve the desired clinical benefit with patient comfortable.

The main limitation of this study was the small sample size which may restrict the generalization of the results. Another limitation was the lack of adequately designed randomized controlled trials. The other one, its retrospective design prevented uniform measurement of the arm volume. And also this study had no control group; we only aimed to compare pretreatment and posttreatment status. In addition, the factors underlying treatment delay were not documented in this study. Therefore, we believe future studies for this issue may be beneficial.

In conclusion, CDT can be effectively used for the management of breast cancer related lymphedema of the limb. A thorough cost-effective analysis of protocol for CDT should be performed in a future studies.

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Kidney transplantation from living donors with multiple renal arteries

Multiple renal arterlere sahip canlı donörlerden böbrek nakli

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Abstract

Aim: Although better outcomes have been reported recently due to advances in surgical techniques, kidney artery variations are still important for good clinical results in transplantation. The aim of our study was to compare the clinical outcomes of grafts with one and two or more arteries.

Methods: Between April 2014 and January 2019, 117 patients with live kidney transplantations were evaluated retrospectively with two groups. Group 1 consisted with one artery grafts and Group 2: two or more arteries. We were evaluated clinical outcomes between groups.

Results: Among 117 recipients, there were two or more arteries in 13 cases (11.1 %). There was no significant deference between these two groups in terms of clinical outcomes during a median 27 (1-60) months of follow-up (P=0.62).

Conclusion: It appears that the presence of renal grafts with two or more arteries may not be counted as a relative contraindication for renal transplantation.

Keywords: Kidney transplantation, Multiple arteries

Öz

Amaç: Son zamanlarda cerrahi tekniklerdeki gelişmelere bağlı olarak böbrek naklinde daha iyi sonuçlar alınmasına rağmen, böbrek arter varyasyonları iyi klinik sonuçlar için halen önemlidir. Çalışmamızın amacı, bir ve iki veya daha fazla arterli greftlerin klinik sonuçlarını karşılaştırmaktı.

Yöntemler: Nisan 2014 ile Ocak 2019 arasında, canlı vericili böbrek nakli yapılan 117 hasta retrospektif olarak iki grupta değerlendirildi. Grup 1 bir arterli greft ve Grup 2 iki veya daha fazla arterli grefften oluşuyordu. Bu iki grup arasındaki klinik sonuçları değerlendirildi.

Bulgular: 117 alıcı arasında 13 (%11,1) olguda iki veya daha fazla arterli greft vardı. Ortalama 27 (1-60) aylık takip süresinde bu iki grup arasında klinik sonuçlar açısından anlamlı bir farklılık saptanmadı (P=0,62).

Sonuç: İki veya daha fazla arterli böbrek grefti kullanımının, böbrek nakli için göreceli bir kontrendikasyon olmadığı anlaşılmaktadır.

Anahtar kelimeler: Böbrek nakli, Multiple arter

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Introduction

Kidney transplantation is the treatment of choice in patients with end-stage renal disease when compared with chronic dialysis therapy in relevant to patient survival and quality of life [1].

Good outcomes due to advances at surgical techniques in last years but kidney artery variations are currently very important for clinical results in transplantation.

Variations in the number of renal arteries are common, with the reported frequency ranging between 9% and 76% [2,3].

The presence of renal artery variations in the donor kidney substantially increases the risk of complications, given the technical difficulties and longer anastomosis time [4-6].

The aim of our study was to evaluate the clinical outcomes and graft loss rates, grafts with one and two or more arteries.

Materials and methods

Between April 2014 and April 2019 at Medipol University Medical Faculty Hospital Organ Transplantation Department, Istanbul, Turkey, 117 patients with living donor kidney transplantation were studied retrospectively.

Patients were divided into two groups: Group I was formed by recipients with single renal artery grafts and Group II with multiple renal arteries. For each of these groups, the age, sex, body mass index, preoperative creatinine level, postoperative fifth days creatinine level, induction therapy with anti-thymocyte globulin (ATG), warm ischemia time, cold ischemia time, acute rejection and graft loss were compared.

Warm ischemia time was defined as the time from clamping of the renal artery to extraction of the organ from the donor's abdomen and its placement on ice. Cold ischemia time was defined as the time from placement on ice to finish the anastomosis and open the renal artery clamps.

Preoperative assessment of the renal artery, renal vein, and ureters of the donor organ was obtained computed tomographic angiography. Our surgical technique is open donor nephrectomy in multiple renal arteries patients. If there are two or more renal arteries at grafts, all of the renal arteries were anastomosed to external iliac artery separately in an end-to-side manner. Anastomoses were done by using x3.5 surgical loupes. A running suture was used to anastomose main renal artery. In other millimetric sized accessory arteries, first 7/0 or 8/0 sutures were placed separately and then tied one by one.

Statistical analysis

SPSS 22.0 (SPSS for Windows, 2007, Chicago) was used for statistical analysis. Continuous variables which have normal distribution were presented as mean (standard deviation). Statistical analysis for the parametric variables was performed by the Student's T-test. The qualitative variables were given as percent and the correlation between categorical variables was investigated by the chi-square test and Fisher's exact test. Statistical significance level was defined as $P<0.05$.

Results

The indications for kidney transplantation were; 42 (35.9%) patients had no cause, 37 (31.6%) had diabetes mellitus, 17 (14.5%) had hypertension, 15 (12.8%) had chronic glomerulonephritis, 3 (2.6%) patient had polycystic kidney disease and 3 (2.6%) other causes (Alport syndrome, vesicoureteral reflux, etc.). We used CT angiography for evaluation of the donor renal arteries (Figure 1).

Mean age of the one renal artery group was 37.4 (15.9) years; two or more renal arteries group was 35.6 (16.3) years ($P=0.76$). Sixty nine (66.3%) males and 35 (33.7%) females in one renal artery group, 9 (69.2%) males and 4 (30.8%) females patients in two or more renal arteries group ($P=0.55$).

Mean BMI of the one renal artery group was 25.1 (5.5) kg/m^2, two or more renal arteries group was 27.2 (9.2) kg/m^2 ($P=0.61$). Mean preoperative creatinine level of the one renal artery group was 8.1 (3.2) mg/dL, two or more renal arteries group was 8.7 (3.7) mg /dL ($P=0.73$). Mean postoperative first month creatinine level of the one renal artery group was 0.88 (0.25) mg/dL, two or more renal arteries group was 0.82 (0.16) mg /dL ($P=0.61$).

Induction therapy with anti-thymocyte globulin (ATG) 82 (78.8 %) patients in one renal artery group, 11 (84.6%) patients in two or more renal arteries group ($P=0.48$).

Mean Warm ischemia time was 90.5 (21-220) second in one renal artery group and 89 (32-120) second in two or more renal arteries group ($P=0.89$). Mean Cold ischemia time was 53.5 (23-120) minutes in one renal artery group and 60 (42-123) minutes in two or more renal arteries group ($P=0.02$) (Figure 2).

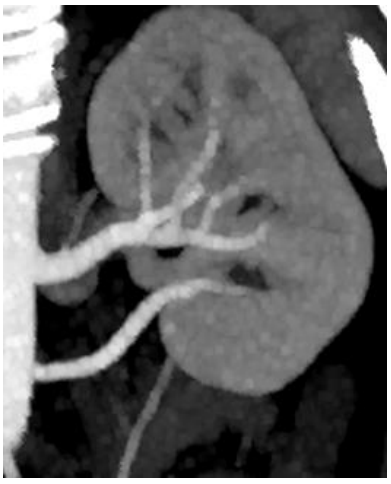

Figure 1: Computed tomographic angiography

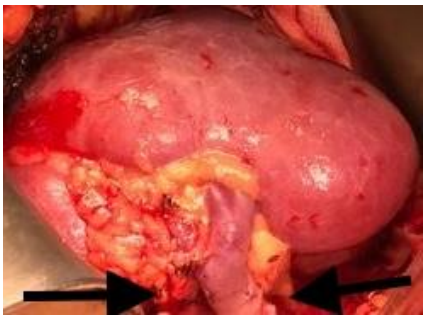

Figure 2: Graft after revascularization

Acute Rejection Rate is detected in 6 (5.8%) patients in one renal artery group, 1 (7.7%) patients in two or more renal arteries group ($P=0.57$). Graft loss occurred in 4 (3.8%) patients was only with one renal artery group ($P=0.62$) due to acute humoral rejection. Table 1 shows the comparison of demographic and clinical findings.

Table 1: Demographic and clinical data of the two groups

	One renal artery (n=104)	Two or more renal arteries (n=13)	*P*-value
Age (Years) mean (standard deviation)	37.4 (15.9)	35.6 (16.3)	0.76
Sex (Male /Female) (n/%)	69 (66.3)/35 (33.7)	9 (69.2)/4 (30.8)	0.55
Body Mass Index (kg/m^2)	25.1 (5.5)	27.2 (9.2)	0.61
Preoperative creatinine levels (mg/dL)	8.1 (3.2)	8.7 (3.7)	0.73
Postoperative first month creatinine levels (mg/dL)	0.88 (0.25)	0.82 (0.16)	0.61
Induction therapy with anti-thymocyte globulin (ATG) (yes/no) (n/%)	82 (78.8)/22 (21.2)	11 (84.6%)/2 (15.4%)	0.48
Warm ischemia time (second)	90.5 (21-220)	89 (32-120)	0.89
Cold ischemia time (minute)	53.5 (23-120)	60 (42-123)	0.02
Acute Rejection Rate (yes/no) (n/%)	6 (5.8)/98 (94.2)	1 (7.7)/12 (92.3)	0.57
Graft Loss Rate (yes/no) (n/%)	4 (3.8)/100 (96.2)	-/13 (100)	0.62

Discussion

There are several determinative factors which donor will select for transplantation. The most important one of these is anatomic abnormalities and the number of arteries, veins and ureters. Multiple methods are available for preoperative assessment of arterial supply to the kidneys, i.e., computed tomographic (CT) angiography and magnetic resonance imaging (MRI) angiography. CT angiography is reported to have a sensitivity of 91%, a specificity of 98% [7]. In our center, we used CT angiography for evaluation of the donor renal arteries.

The presence of renal artery variations in the donor kidney substantially increases the risk of complications and given the technical difficulties [8-10]. Transplanting a kidney with multiple arteries has several theoretical disadvantages. It may prolong the warm- cold ischemia time, increase the incidence of ATN and rejection episodes, decrease graft function and prolong hospitalization. Multiple renal arteries reportedly have been associated with a higher rate of vascular complications (thrombosis-stenosis), infarction, infection, and urologic complications [11,12].

Several techniques are for bench reconstruction of multiple renal arteries. The smaller artery usually is anastomosed in an end to-side fashion to the main artery. If both renal arteries are of similar size, the ends of the two vessels can be sutured together side to side or not was done reconstruction, anastomosis are one by one and end to side an external iliac artery [13,14].

In our clinic, we prefer to perform a left nephrectomy in nearly almost all living donations.

We was not done bench reconstruction of multiple renal arteries, anastomosis are one by one, end - side to external iliac artery. With polar arteries, our approach has been to anastomosis in arteries directed to the lower pole of the kidney regardless of the size because these arteries potentially the blood supply of the ureter.

In this study, there was no difference in warm ischemia times between the two groups. The duration of cold ischemia was more in two or more arteries group, but this condition did not affect acute rejection and graft loss. According to our experience, grafts with two or more arteries were not a relative contraindication for renal transplantation.

Our study has several limitations. First, this study was retrospective. Second, the number of cases was small.

Conclusion

Despite the limitations described in the Discussion section, it appears that the presence of renal grafts with two or more arteries may not be counted as a relative contraindication for renal transplantation.

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Comparison of sugammadex vs. neostigmine use in recovery of muscle relaxation related to vecuronium in obesity surgery

Obezite cerrahisinde vekuronyuma bağlı kas gevşemesinin geri dönüştürülmesinde sugammadex ile neostigmin kullanımının karşılaştırılması

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Abstract

Aim: There are many methods in anesthesia to measure the recovery after the use of neuromuscular blocking agent. Monitoring the neuromuscular function can be used to identify the residual blocks. The importance of morbid obesity in anesthesia is caused by the difficulty in succeeding sufficiency of respiration and patency of airway. There are so many methods to measure the recovery when the neuromuscular blocking agent is used. Monitoring the neuromuscular function is used to identify the residual blocks.

Methods: We designed a retrospective study with cross-sectional design. After power analysis 40 morbid obese patients operated with laparoscopic sleeve gastrectomy to treat the obesity, have been included in the study. 40 patients with sugammadex group S and neostigmine group were divided into two groups as equal.

Results: In group S, there were 14 female and 6 male having the average of 33.25 ages and the average of body mass index (BMI) as 42.96. In group N, there were 16 women and 4 men having the average of 37.55 ages and the average of BMI as 42.96. While in group S the basal train of four (TOF) value was 89.75%, in group N basal TOF was 90.65%. The duration of extubation in group S was measured 1 min and 40 sec but in group N it was measured 4 min and 39 sec. Also, the duration of recovery of muscle strength as an indicator of the recovery of basal TOF values was observed as 3 min and 15 sec in group S, and it was observed as 6 min and 18 sec in group N (P<0.001). The duration of extubation in group N was longer than in group S (P<0.001). Also, the duration of the recovery of basal TOF values as the duration of recovery of muscle strength was longer in group N than in group S (P<0.001).

Conclusions: While in the study with rocuronium, the duration of recovery of muscle strength with sugammadex got shorter 4 times, in our study this duration was become shorter 2 times. It can be explained as the long effects of vecuronium.

Keywords: Obesity, Sugammadex, Neostigmine, Deep neuromuscular blockade, Bariatric Surgery

Öz

Amaç: Nöromüsküler bloke edici ajanın kullanımından sonra iyileşmeyi ölçmek için pek çok yöntem vardır. Nöromüsküler fonksiyonun izlenmesi rezidüel blokları tanımlamak için kullanılabilir. Anestezide morbid obezitenin önemi, solunum yeterliliği ve solunum yolunun açıklığının sağlanmasındaki zorluktan kaynaklanmaktadır. Nöromüsküler bloke edici ajan kullanıldığında iyileşmeyi ölçmek için pek çok yöntem vardır. Nöromüsküler fonksiyonun izlenmesi rezidüel blokları tanımlamak için kullanılır. Bu çalışma veküronyuma bağlı kas gevşemesinde sugammadexin etkinliğinin neostigmine karşı kullanımını araştırmayı amaçlamaktadır.

Yöntemler: Bu çalışmada, Pamukkale Üniversitesi Tıp Fakültesin Hastanesi'nde, obeziteyi tedavi etmek için laparoskopik sleeve gastrektomi ameliyatı yapılan 40 morbid obez hasta retrospektif olarak değerlendirildi. Hastalar, kullanılan sugammadeks (Bridion®) (S grubu) ve neostigmin (N grubu) olarak iki gruba ayrıldı.

Bulgular: 40 hastanın toplanan verileri değerlendirilmesinde, S grubunda, sugammadeks kullanılan 14 kadın ve 6 erkek, ortalama 33,25 yaş ve vücut kitle indeksinin (BKİ) ortalaması 42,96 olarak bulundu. N grubunda ise neostigmin kullanılan, 16 kadın ve 4 erkek mevcuttu. Hastaların yaş ortalaması 37,55 ve BKİ 42,96 idi. Hastaların ek hastalıkları yoktu. Sonuçlar değerlendirildiğinde grup S' de Bazal TOF değeri %89,75 iken, grup N'de bazal TOF %90,65 idi. Operasyon sonrası uyanma döneminde S grubundaki ekstübasyon süresi 1 dakika 40 saniye iken grup N'de 4 dakika 39 saniye ölçüldü. Ayrıca, bazal TOF değerlerinin iyileşmesinin bir göstergesi olarak kas gücünün iyileşme süresi, Grup S de 3 dakika 15 saniye grup N' de ise 6 dakika 18 saniye olarak saptandı (P<0,001). Grup N'deki ekstübasyon süresi, Grup S'den anlamlı olarak daha uzundu. (P<0,001). Ayrıca, kas kuvvetinin iyileşme süresi olarak bazal TOF değerlerinin iyileşme süresi, grup N'de grup S'den anlamlı olarak daha uzundu (P<0,001).

Sonuçlar: Rokuronyum ile yapılan çalışmalarda, kas kuvvetinin sugammadeks ile düzelme süresi 4 kat azalırken, çalışmamızda bu süre 2 kat azalmıştır. Bu durum ise vekuronyumun uzun etkili kas gevşetici olması olarak açıklanabilir.

Anahtar kelimeler: Obezite, Sugammadex, Neostigmin, Derin nöromüsküler blokaj, Bariatrik cerrahi

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Introduction

Morbid obesity (defined as body mass index >40 m2/kg) in western societies is seen 2-5% frequency and it is one of the important health problems that causes physical morbidity [1,2]. Obesity surgery is an important solution for these patients [1]. Laparoscopic sleeve gastrectomy (LSG) is a kind of surgical technique in morbid obesity treatment by the resecting of stomach fundus [3]. Recent researches showed that the success in the laparoscopic surgery is developed by deep neuromuscular blockade [4]. The importance of morbid obesity in terms of anesthesia is caused by the difficulty in sufficiency of respiration and patency of airway [2].

Neuromuscular blockers are polar and hydrophilic medicines and pharmacodynamic characters can change as a result of dispersion in adipose or lean tissue in obese patients [2]. When neuromuscular blockade is made with vecuronium in obese patients, it's observed that the duration of recovery of strength of muscle become longer. The long term effect in obese patients can be explained by relatively overdose of vecuronium in lean body mass of patient.

According to increase in dose of vecuronium, duration of neuromuscular blockade, restart of mobility and spontaneous recovery takes longer [5]. The prolonged effects of neuromuscular medicines might cause residual neuromuscular paralyzing. Potentially, length of staying in operating room and post-anesthesia care unit may be shorten [6].

There are so many methods to evaluate the recovery after use of neuromuscular blocking agent. Monitoring the neuromuscular function can be used to detect residual blocks. Neostigmine edrophonium is the most used reversal agent but the use of it is limited because of the cardiovascular and gastrointestinal side effects [7]. In 2006, in anesthesia, Gijsenberg et al. [8] published an article that is defining the first human exposure of sugammadex as modified γ-cyclodextrin developed to reverse of the blockage caused by the aminosteroid neuromuscular blocking agents, especially induced by rocuronium. After injection, sugammadex capsulizes and inactivates the rocuronium (or vecuronium) which is uncombined as tight and 1:1 dissolving complexes in water. Because of that, sugammadex creates a concentration gradient favoring the movement of rocuronium (or vecuronium) from the neuromuscular junction back into the plasma, and that results function. The fast reverse of the NMB is induced by rocuronium (or vecuronium). This mechanism of action is different from neostigmine's [9].

After releasing from nerve endings, Neostigmine can reverse the acetylcholinesterase to keep the maintenance of acetylcholine at synaptic ends, It acts as a competitive inhibitor [10,11]. As a result, acetylcholine, it pushes the neuromuscular blocking agents which are at the postsynaptic nicotinic receptors in to the competition and so neuromuscular function reappears [9]. So briefly, Sugammadex is a novel γ-cyclodextrin. It's the first a new class of selective neuromuscular blocking binding agents. Sugammadex is planned to immediately deactivate the neuromuscular blocking agents acting as acetylcholine as the most common rocuronium [7]. Sugammadex is a reliable agent for rapid recovery after mid or deep relaxation of muscle related the use of vecuronium like use of rocuronium [6]. In this study, it's aimed to evaluate that whether sugammadex is more effective than neostigmine in recovery of muscle relaxation related to vecuronium in obesity surgery.

Materials and methods

In this study, 40 morbid obese patients operated as laparoscopic sleeve gastrectomy to treat the obesity, have been evaluated retrospectively in Pamukkale University Hospital. The patients have been separated into two groups as sugammadex (Bridion®) used (group S) and neostigmine used (group N). Before the operation, ages, gender, body mass index (BMI), basal train of four (TOF) values of patients were recorded. Patients were induced propofol 2 mg/kg after routinely given midazolam (3 mg) and premedication. Basal muscle strength values were recorded by using TOF monitoring. After 0.1 mg/kg vecuronium was applied having regard to their ideal weight and required muscle relaxation, the patients were intubated. Continuation of anesthesia was maintained by keeping inhalational anesthetic with sevoflurane and support of opioid preferred according to patient. During the operation, muscle strength parameters and additional dose of muscle relaxant requirements were determined by TOF device and additional dose was applied as needed. In obesity surgery patients, by anesthesia form, extubation duration and the duration of completely forming of postoperative muscle strength during on operation table, was recorded. The muscle strength recovery duration was calculated as minutes in which patients' basal TOF values recovered. At the end of the operation, anesthesia was ended by administering 2 mg/kg sugammadex to 20 patients, and 0.04 mg/kg neostigmine to the other 20 patients.

Statistical analysis

SPSS 15 package program was used to evaluate the data and $P<0.05$ was accepted as statistically significant. Continuous variables were given as mean (standard deviation (SD)) (minimum value-maximum value). Chi-square test was used to compare categorical variables. T-test was used in comparison of age, BMI, basal TOF, extubation, muscle strength recovery duration parameters between groups. In order to determine the number of patients to be included in the pre-study groups, the sample size was calculated. For this study, a minimum of 36 patients was considered to be accepted in the 95% confidence interval (Graphpad StatMate 2 Windows Program). Considering the possibility of possible loss in the process due to technical reasons, a total of 40 patients were planned to be taken to the study.

Results

In group S, there were 14 female, 6 male, at the average age of 33.25 and body mass index average (BMI) of 42.96. In the N group, there were 16 female, 4 male, at the average age of 37.55 and BMI average of 42.96 (Table 1).

As the basal TOF in Group S was 89.75%, it was 90.65% in Group N. The extubation duration was detected as 1 min. and 40 sec. in group S while the duration was 4 min and 39 sec in Group N. Muscle strength recovery duration indicating the recovery of basal TOF was in 3 min 15 sec in Group S while it was 6 min 18 sec in group N ($P<0.001$). In this study, 6 male

and 14 female in group S and 4 male and 16 male in group N, totally 40 patients were included. No significant difference was found between group S and group N in regard to age, BMI and basal TOF values (P=0.29). Extubation duration in Group N was significantly longer than group S (P<0.001). The duration of recovery of basal TOF value in group N was significantly longer than in group S (P<0.001) (Table 1).

Table 1: Analysis of the groups

	Group N (n=20)		Group S (n=20)		
	Mean (SD)	Min-Max	Mean (SD)	Min-Max	*P*-value
Age	37.55 (10.10)	19-57	33.25 (10.44)	17-49	0.19
BMI	42.97 (4.17)	35-51	42.97 (5.39)	33-59	0.99
Basal TOF (%)	90.65 (3.01)	85-96	89.80 (1.80)	85-93	0.29
Extubation Time (sec)	279 (40.54)	210-345	100.5 (27.99)	60-165	<0.001
Muscle strength return time (sec)	378.75 (59.58)	285-480	195 (38.32)	120-255	<0.001
Gender	n	%	n	%	
Female	16	80	6	30	0.39
Male	4	20	14	70	

SD: Standard deviation, Min: Minimum, Max: Maximum, sec: Second

Discussion

The increasing prevalence of obesity in developed and developing countries and the increased medical and surgical pathologies observed in these patients necessitated the treatment of obesity [3,12]. Bariatric surgery can be applied not only to decrease in weight but also applied to reduce type 2 diabetes mellitus, hypercholesterolemia, obstructive sleep apnea (OSAS), hypertension (HT), morbidity and mortality related with obesity [3]. Nowadays, laparoscopic sleeve gastrectomy is also a frequently preferred method because of similar results in terms of weight loss and improvement of comorbidities compared to the gold standard, the gastric by-pass [3]. In the basis of laparoscopic surgery, muscle relaxation is found and deep neuromuscular blockade is required for the patients having laparoscopic sleeve gastrectomy [13]. After intraoperative deep neuromuscular blockade, the use of sugammadex shortens the leaving from the operation room and ensures the confidence of patients in the postoperative period [4]. In obesity surgery, medicine applications are performed according to the ideal weight and sometimes the medication duration takes longer when the drug is taken based on normal weight. When vecuronium is used in obese patients, the recovery duration of muscle strength increases. This prolonged duration can be attributed to many reasons in obese patients. In addition to individual variability in obese patients, prolonged elimination of vecuronium in the liver, increased neuromuscular junction sensitivity in obese patients, and over dosage according to redistribution of vecuronium in obese patients are the factors that may cause prolonged recovery [14]. If the drugs are made according to the actual weight rather than the ideal weight, a relatively overdose may occur and it can cause the muscle strength recovery be prolonged [5]. In a study, in which Weinstein et al. evaluated pharmacodynamics of vecuronium and atracurium in obese patients, it was observed that the effect of vecuronium was significantly prolonged in obese patients [14]. Each 1% increase in adipose ratio was associated with a 1.1-minute elongation in the recovery time. In addition, in a recent study, it was evaluated that if sugammadex must administer according to ideal weight or normal weight. As a result of this study, it was emphasized that sugammadex must administer as 4 mg/kg according to the ideal weight but in the case of insufficiency of the medicine, it was emphasized that the addition of 35-50% dose must administer [13]. Also in this study, it was emphasized that this additional dose had no side effects. In our study, since the vecuronium was routinely medicated according to the ideal weight, the relative residual effect was not expected result. In our study, when we needed additional muscle relaxant, we applied additional doses according to the values determined with TOF device. Geldner et al. [6] evaluating the recovery of muscle strength for laparoscopic operations, identified that muscle relaxation caused by rocuronium and in the sugammadex group, the recovery was achieved in the first 5 minutes in 94% of patients and in neostigmine group it was found 20%. In this study, sugammadex was found 3.4 times faster than neostigmine in muscle strength recovery in normal weight patients. Laparoscopic techniques have been used in obesity surgery also in our study. It is important that performing the muscle relaxation until the end of surgery with regard to both for the comfort of the surgical area and for the safer reanimation of our patients. This is much more important in obese patients due to the difficulties airway management. In the study by Suy et al. [7] that they compared sugammadex and placebo, sugammadex was detected as effective in both patients medicated with rocuronium and vecuronium. Van Lancker et al. , in the study about whether sugammadex must medicate according to ideal or corrected weight in morbidly obese, detected that 2 mg/kg sugammadex provided a complete recovery in the ideal weight + 40% group [1]. Also Gaszynski et al. [15], in the study of comparison of sugammadex and neostigmine to detect postoperative residual curarization, they found that Sugammadex was more effective in reversing rocuronium induced muscular relaxation than neostigmine. When the duration of basal TOF in group used sugammadex was 2 min and 44 sec, it was 9 min and 37 sec in group used neostigmine [15].

In our study, when the duration of basal TOF related to vecuronium-induced muscle relaxation in obese patients used sugammadex was 3 min 15 sec, it was 6 min 18 sec in the group used neostigmine. In a study in Belgium in 2016 showed that sugammadex significantly shorten the operating room discharge and the length of intensive care unit stay [4]. Also in a multi centered study, in the USA in 2018, the use of sugammadex shortens the duration of mechanical ventilation in the intensive care unit after surgery [16]. In a recent study in Israel, it was reported that sugammadex administration improved the oxygen saturation during postoperative period [17]. Also in another study in our country in 2017, in which the ventilation functions in obesity surgery were detected, it's showed that the use of sugammadex has supportive effect on partial arterial oxygen pressure [18]. In patients undergoing laparoscopic obesity surgery, postoperative pain and analgesic therapy should be effective and should not cause adverse effects such as respiratory depression, hypoventilation and hemodynamic instability, nausea-vomiting, itching and delayed bowel function, and should allow early mobilization. A multimodal analgesic approach with different sites of action and different mechanism drugs appears to be a viable option in these cases [19]. In our study, in the case of muscle relaxation related to vecuronium in intraoperative period, the infusion of paracetamol intravenously was

administered along with intravenous administration of sugammadex or neostigmine. Sugammadex more rapidly and reliably reverses rocuronium-induced neuromuscular block compared with neostigmine but it is not known if subsequent patient outcomes, including nausea, vomiting and other aspects of recovery are modified. In the study that Peach et al. [20] studied on 304 patients, compared the recovery characteristics of sugammadex and neostigmine/glycopyrrolate following reversal of neuromuscular block. Twenty-four-hour recovery scores were not significantly different between groups. Reversal with sugammadex in this patient population did not reduce postoperative nausea or vomiting compared with neostigmine/glycopyrrolate. In the study performed with rocuronium, the muscle strength recovery duration was shortened by about 4 times with sugammadex but in our study this period was shortened by 2 times. This can be attributed to the prolonged effects of vecuronium.

We have shown that rocuronium as considered specific sugammadex can be also effective against vecuronium in the condition of absence of rocuronium in the laparoscopic sleeve gastrectomy surgery. Sugammadex is a rapid recovery agent against to blockage depending on rocuronium and vecuronium. We believe that our study will shed some light on the anesthetic management of obesity as the disease of the era.

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Clinical and demographic characteristics of patients with kidney disease presenting at a tertiary hospital for expert care in south-west Nigeria

Güneybatı Nijerya'da uzman bakımı için bir üçüncü basamak hastaneye başvuran böbrek hastalığı olan hastaların klinik ve demografik özellikleri

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Abstract

Aim: Although chronic kidney disease (CKD) remains an important health challenge in our environment, late presentation of the patient for nephrology care is common. We opined that dissemination of information on the sociodemographic distribution, clinical presentation and common etiology of CKD among our patient will increase individual and medical professionals' awareness of the disease. In addition, it is believed that this will ultimately result in lower threshold for screening and early referral for specialist renal care.

Methods: This was a cross-sectional descriptive study involving 152 patients with any form of renal disease either seen primarily at, or referred to the adult nephrology clinic of the hospitals between January 2013 and December 2015. The socio-demographic parameters, clinical characteristic and laboratory data were extracted with a proforma designed for data collection.

Results: Of the 152 patients analyzed, 87 (57.24%) were males. The mean age was 49.29 (15.92) years. About one quarter was within the age range 51-60 years. More than half (53.9%) were rural dweller. Common indication for referral includes abnormal renal ultrasound findings, elevated serum creatinine and urea, and abnormalities in urine analysis. Malaise, reduce urinary flow and body swelling were the common symptoms at presentation in 50.65%, 40.1% and 34.2%, respectively among the patients. The median eGFR was 18.78 (7.86-84.55) ml/min/1.73m^2. Across all age groups, majority (48.0%) presented in stage 5 CKD. Hypertensive nephrosclerosis (27.0%), chronic glomerulonephritis (14.5%) and diabetes nephropathy (9.2%) were found to be the leading causes of CKD. Majority of the patients (40.8%) were worked up for and commenced on hemodialysis soon after presentation. Among the end-stage renal disease patient, only 7 (4.6%) had renal transplantation at referred centers. Focal segmental glomerulosclerosis was the commonest histological findings among the nephrotic syndrome patient while membranous nephropathy was documented in only 2 patients.

Conclusion: Most patients present to the nephrology clinic of our hospital at advanced stage of CKD. We observed that hypertensive nephrosclerosis and glomerulonephritis are the leading causes of their kidney disease.

Keywords: Clinical profile, Demography, Chronic kidney disease, Nephrology clinic

Öz

Amaç: Her ne kadar kronik böbrek hastalığı (KBH), çevremizdeki önemli bir sağlık sorunu olsada, nefroloji bakımı için hastanın geç sunumu sıktır. Sosyodemografik dağılım, klinik prezentasyon ve KBH'ın ortak etiyolojisi hakkındaki bilgilerin yayılması, bireysel ve tıbbi profesyonellerin hastalık bilincini artıracağını belirledik. Ek olarak, bunun sonuçta tarama için daha düşük eşik ve uzman böbrek bakımı için erken sevk ile sonuçlanacağına inanılmaktadır.

Yöntemler: Ocak 2013 ve Aralık 2015 tarihleri arasında hastanelerin yetişkin nefroloji kliniğinde ya da öncelikle görülen veya herhangi bir renal hastalığı olan 152 hastayı kapsayan ve kesitsel tanımlayıcı bir çalışmadır. Sosyo-demografik parametreler, klinik özellikler ve Laboratuvar verileri, veri toplama için tasarlanmış bir proforma ile çıkarıldı.

Bulgular: Analiz edilen 152 hastanın 87'si (%57,24) erkekti. Yaş ortalaması 49.29 (15,92) idi. Yaklaşık dörtte biri 51-60 yaş aralığındaydı. Yarıdan fazlası (%53,9) kırsalda yaşayanlardandı. Yönlendirme için ortak endikasyon anormal renal ultrason bulgularını, yüksek serum kreatinin ve üre ve idrar analizindeki anormallikleri içerir. Malaise, üriner debiyi azaltan ve vücut şişmesi, hastalar arasında sırasıyla %50,65, %40,1 ve %34,2 oranında sık görülen semptomlardı. Medyan eGFR, 18.78 (7.86-84.55) ml/dk/1,73 m^2 idi. Tüm yaş gruplarında çoğunluk (%48,0) evre 5 KBH'da ortaya çıkmıştır. KBH'ın başlıca nedenleri arasında hipertansif nefroskleroz (%27,0), kronik glomerülonefrit (%14,5) ve diyabet nefropatisi (%9,2) bulundu. Hastaların çoğunluğu (%40,8) başvuru yapıldıktan kısa bir süre sonra hemodiyaliz için çalışmaya başlandı. Son dönem böbrek hastaları arasında sadece 7'sine (%4,6) sevk edilen merkezlerde böbrek nakli yapıldı. Fokal segmental glomerüloskleroz, nefrotik sendromlu hasta arasında en sık görülen histolojik bulgulardı, sadece 2 hastada membranöz nefropati kaydedildi.

Sonuç: Çoğu hasta, hastanemiz nefroloji kliniğine KBH'nin ileri evresinde başvurmaktadır. Hipertansif nefroskleroz ve glomerülonefritin, böbrek hastalıklarının önde gelen nedenleri olduğunu gözlemledik.

Anahtar kelimeler: Klinik profil, Demografi, Kronik böbrek hastalığı, Nefroloji kliniği

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Introduction

Worldwide there is a rise in the number of patients with chronic kidney disease (CKD) and consequent end-stage kidney failure. According to the reports from different countries including the United States, CKD affects 10–16% of adults around the world [1].

However, the prevalence of CKD in the early stages as well as treated end-stage renal disease (ESRD) differs from country to country. In Africa, the prevalence of the disease is estimated to be about 10.4% or more in some populations [2,3].

Chronic glomerulonephritis, diabetes mellitus and hypertension are important causes of CKD worldwide. In Sub-Saharan Africa (SSA), CKD affects mainly young adults aged 20– 50 years and is primarily due to hypertension and glomerular diseases [4]. While HIV infection and genetic disorders also contribute significantly to CKD burden, primary chronic glomerulonephritis are seen most often [5]. Due to the high cost of treatment, many patients in this sub-region cannot afford optimal treatment of CKD with consequent poor outcome. In same continent, it has been reported that there is a higher prevalence of earlier stages of CKD [6,7].

Evidences suggest that the adverse outcomes of CKD, such as end stage renal disease, cardiovascular disease, mineral bone disease and premature death can be prevented or delayed. Hence, primary and secondary prevention have been advocated in order to save cost and limit disability arising from the complication of CKD [8].

Management of kidney failure is focus on prompt diagnosis, treatment of specific etiology of the disease entity and dialysis or transplantation. Screening asymptomatic individuals at increased risk could allow early detection of CKD [8]. Strategies for early detection and intervention include laboratory measurement of serum creatinine, estimation of glomerular filtration rate (eGFR), urine analysis for blood, protein and other abnormality. Imaging of the kidney, assessment of the clinical features and complaints of the patient are important in the identification of individuals with impaired kidney function. It has been shown that prompt and adequate treatment of earlier stages of CKD including initiation of cardiovascular risk reduction is beneficial in slowing the progression toward end stage kidney disease [9].

The availability of renal care is scarce in most sub-Saharan Africa countries due to the high costs and shortage of skilled personnel. These factors in addition to late presentation of the patients are invariably responsible for high morbidity and mortality experienced in the developing countries. Early detection of CKD and referral of the patient particularly at early stages of the disease is important as renal replacement therapy is likely to be more effective if they are implemented early as indicated in the course of the disease process.

Although CKD remains an important health challenge in our environment, there is no data from this center on the characteristics of CKD patients attending the nephrology clinic. We set out to determine the pattern and clinical presentation of CKD patients at the nephrology clinic of Ekiti State University Teaching Hospital, Ado Ekiti South West Nigeria. We opined that dissemination of information on the sociodemographic distribution, clinical presentation and common etiology of CKD among our patient will in no small measure increase individual and medical professionals' awareness of the disease. In addition, it is believed that this will ultimately result in lower threshold for screening and early referral for specialist renal care.

Materials and methods

This was a cross-sectional descriptive study involving 152 patients with any form of renal disease either seen primarily at, or referred to the adult nephrology clinic of the hospitals between January 2013 and December 2015. Patients are usually registered at the clinic where biodata are documented. Clinical assessment including detailed history of the presenting complaints and examination including laboratory test are usually done and documented in individual patient's medical record. The demographic, clinical and laboratory parameters were collected with a proforma designed for data collection. Permission for the use of the data was obtained from the ethic and research committee of the hospital.

Diagnosis of CKD

The clinical profile of the patients which include history of the illness, physical examination, and laboratory investigations such as renal ultrasonography, urinalysis, and blood biochemistry was retrieved. Renal disease etiology was largely determined clinically except some cases of nephrotic syndrome where the patient had renal biopsy and histology report was available.

In this study, we adopted the following concepts and definitions; CKD was diagnosed and classified according to the KDOQI definition and staging [10]. The definition considers the persistence of kidney disease for more than three months. However, in the absence of previous data on eGFR or markers of kidney damage, chronicity was inferred from the clinical presumption of kidney disease for >3 months.

Proteinuria was defined as normal (urine dipstick negative), mild, moderate or heavy if urine dipstick reading was 1+, 2+ or ≥3+, respectively.

We entertained the diagnosis of chronic glomerulonephritis (CGN) if the patient present with hematuria, proteinuria, and reduced urine output and shrunken kidney size as well as loss of corticomedullary differentiation on ultrasound with anemia or low pack cell volume (PCV).

Hypertension was defined as the presence of a persistently elevated systolic blood pressure ≥140mmHg and/or diastolic blood pressure ≥ 90mmHg in patients aged 15 years and above, and/or the use of antihypertensive drugs and/or past medical history of systemic hypertension. Hypertension was considered as the cause of renal disease if there is history of long-standing hypertension that predated kidney disease, severe hypertension at consultation and or a familial history of hypertension. In addition, presence of mild proteinuria, evidence of left ventricular hypertrophy, hypertensive retinal changes as well as the absence of clinical renal symptoms suggestive of glomerulopathy prior to the discovery of hypertension.

Diabetic nephropathy was diagnosed if patient had a long history of diabetes mellitus, significant proteinuria, presence of other complications of diabetes mellitus with normal or increased renal sizes on ultrasound. For patient having both of

hypertension and diabetes, diagnosis of diabetic nephropathy or otherwise was presumed if there is presence of ocular manifestations of diabetes mellitus. Data on HIV/AIDS patient with renal diseases was not available at the time of data collection and hence not included in this study.

Statistical analysis

The collected data was entered into SPSS version 20 for analysis. Qualitative data were analyzed and expressed as frequency and percentage. Normal distributed continuous data were summarized as mean (SD) and non-normal data as median (IQR); the 25th-75th percentiles were specified. Tables and charts were used to illustrate the data and present the results.

Results

Among the 152 patients, there were 87 males and 65 females with sex ratio of 1.3:1. The mean age was 49.29 (15.92) years (range: 17-90 years) while about one quarter were within the age range 51-60 years. A relatively higher proportion (53.9%) lived in the rural area compared to those who resided in the sub-urban community (46.1%). Majority (19.1%) of the patients were petty traders while 16.4% and 15.8% were civil servants and self-employed, respectively as summarize in table 1.

Table 1: Distribution of socio-demographic characteristics of the patients

Parameters	Frequency (%)
Gender	
Male	87 (57.2)
Female	65 (42.8)
Rural dwellers	82 (53.9)
Age category	
≤30	23 (15.1)
31-40	22 (14.5)
41- 50	32 (21.1)
51-60	38 (25.0)
61-70	22 (14.5)
≥71	23 (15.1)
Occupational Categories	
Trading	29 (19.1)
Civil servant	25 (16.4)
Self-employed	24 (15.8)
Driving	5 (3.3)
Students	14 (9.2)
Teaching	9 (5.9)
Farming	6 (3.9)
Unemployed	12 (7.2)
Retiree	11 (7.3)
Others*	17 (11.2)

* clergy, medical personnel, aged, housewife

Yoruba tribe accounted for more than two third of the patients, though this is not unexpected as the study was conducted in predominantly Yoruba dominated region of the country.

Common indication for referral includes abnormal renal ultrasound findings, elevated serum creatinine and urea, and abnormalities in urine analysis.

Figure 1 summarizes the common symptoms among the patients at presentation. Malaise, anemia, oliguria, body swelling and frothiness of the urine were seen in 50.65%, 44.08%, 40.13%, 34.21% and 11.12%, respectively. Twelve (7.89%) patients had no complaints at presentation and were only referred on account of abnormal urinary findings (AUF). Less common clinical features include flank pain (4.61%), nocturia (11.84%), Vomiting (8.0%), bone pain (1.97%), pruritus (2.0%), and macroscopic hematuria (3.29%).

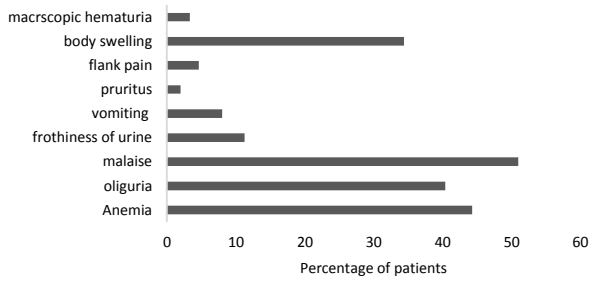

Figure 1: Common complaints by the patients at first consultation

The mean pack cell volume was 27.43 (7.38) while the median value of serum urea and creatinine was observed to be high among the patient at presentation as shown in table 2.

The median eGFR was 18.78 (7.86-84.55) ml/min/1.73m^2. Across all age groups, stage 5 disease was the commonest presentation. About half of the patients (48.0%) were in stage 5 CKD while the proportion of patient in stage 4 was 13 (8.6%).

Table 2: Distribution of clinical and laboratory data of the patients

Characteristics	Values
Age (years), mean (SD)	49.29 (15.92)
Systolic BP, mean (SD)	159.16 (38.38)
Diastolic BP, mean (SD)	99.16 (22.92)
PCV (%), mean (SD)	27.43 (7.38)
Urea (mmol/l), median (IQR)	18.00 (6-28)
Creatinine (µmol/l), median (IQR)	407.00 (89.25-950.00)
eGFR, median (IQR)	18.78 (7.86-18.80)
% with eGFR <60, mean (SD)	106 (68.4)
% with eGFR <15, mean (SD)	73 (48.0)
% treated with Hemodialysis, mean (SD)	62 (40.8)
% Transplanted, mean (SD)	7 (4.6)

eGFR in ml/min/1.73 m^2, PCV: Pack cell volume, BP: Blood pressure in mmHg

As shown in table 3, hypertensive nephrosclerosis (27.0%), chronic glomerulonephritis (14.5%) and diabetes nephropathy (9.2%) were found to be the leading causes of CKD.

Table 3: Common etiology of kidney disease among the patients

Diagnosis	Frequency (%)
Hypertensive Nephrosclerosis	41 (27.0)
Chronic glomerusclerosis	22 (14.5)
Simple renal cyst	15 (9.9)
Diabetic nephropathy	14 (9.2)
ADPKD	11 (7.2)
Nephrotic syndrome	10 (6.6)
Abnormal urinary Findings	6 (3.9)
Obstructive uropathy	5 (3.3)
Lupus Nephritis	2 (1.3)
Pyelonephritis	3 (2.0)
Malignancy	4 (2.6)
Congenital abnormality	2 (1.3)
Unknown	14 (9.2)
Others	3 (2.0)

ADPKD: Autosomal dominant polycystic kidney disease
Others include; AKI, isolated proteinuria / hematuria

Focal segmental glomerulosclerosis (FSGS) was the commonest histological findings among the nephrotic syndrome patient while membranous nephropathy was documented in only 2 patients.

Majority of the patients (40.8%) were worked up for and commenced on hemodialysis soon after presentation. Among the ESRD (stage 5) patient only 7(4.6%) had renal transplantation at referred centers.

Discussion

Clinical presentation of patient suffering from kidney disease varies according to the stage of the disease. This may range from asymptomatic apparently healthy individual without any complaint to florid uremic patients. Commonly, non-constitutional symptoms that mimic other illness may precede and be a pointer to underlying kidney failure. These symptoms

are usually overlooked until very late when the damage becomes irreversible.

Optimal management of CKD patients requires early recognition, appropriate investigation and collaboration between primary care physicians and nephrologists.

Among the patients, common indication for referral includes abnormal renal ultrasound findings, elevated serum creatinine and urea, and abnormalities in urine analysis.

Similar to other studies, there was more male sex [11-13]. The difference in the sex ratio could be a reflection of health seeking behavior among the male in addition to the increase risk factors for CKD prevalent among the male sex.

The majority of patients were seen for the first time late in their disease with chronic renal failure at which time renal replacement therapy become inevitable. About two third of the patients (68.4%) had CKD while the proportion of patients in established end stage renal disease were 48.0%.

A retrospective study conducted on medical data over a five-year period involving 301 patients with chronic renal failure by Ouattara et al. [14] showed that 82% of cases were in end-stage renal disease. Sakhuja et al. [15] reported that about two-thirds of their patients had developed ESRD at the time of the first consultation with a nephrologist. Similarly, a Cote D'Ivoire study involving 252 patients reported that nine out of ten patients were at ESRD at presentation [16]. This report is in agreement with findings by other researchers where majority of patients were seen at advanced stage of CKD due to several reasons including silent and asymptomatic nature of CKD, lack of population awareness, poorly equipped and high cost of health system [11,17-21]. However, this result is in contrast with the figure obtained in developed countries where there is good health system and better patient awareness. A systematic review of patient and health system characteristics associated with late referral in CKD carried out by Navaneethan et al. [22] showed that older age, lower socioeconomic status, less education among others were factors associated with late presentation.

Most of our patients would have patronized traditional healers, and used over the-counter drugs without improvement before resorting to consult medical practitioner. This is a common practice and a cause of late presentation to the nephrologist in our environment. The consequences of delay treatment of kidney disease are numerous. This include marked clinical and biochemical derangement in the body system. These patients will become dependent on renal replacement therapy earlier than those who started receiving specialist care at early stage of CKD.

Hypertension and glomerulonephritis were the two most common cause of CKD among our patients similar to other report [20,21]. Evidences have shown that hypertensive nephrosclerosis is a major cause of ESRD among the black race [23,24]. Research has demonstrated increasing prevalence of hypertension with age. The risk of hypertension related complications such as cardiovascular disease and CKD is equally heightened among the older adults [14,16,21,25-29].

We observed that chronic glomerulonephritis was diagnosed most often among the younger patients in this study. About 10% of the patients with CKD were classified as unknown. In our environment, establishment of the actual etiology of kidney disease is challenging. This is an important drawback to the optimal management of the patient.

Anemia is a common presenting feature among our patients as almost half of the patients (44.3%) presented with low PCV at first visit. The high prevalence of anemia is consistent with findings from other studies [11,14]. Anemia commonly occurs in CKD with onset as early as Stage 3 and increases in prevalence as CKD progresses. It is associated with increase cardiovascular morbidity and mortality.

Limitations: Lack of detailed information regarding possible causes of renal disease in many patients due to cost of renal biopsy, limited availability of diagnostic tools and laboratory support. These data may not adequately represent the situation of CKD in our general population because of small sample size and inaccessibility of renal care to the majority.

Conclusion

Most patients present to the nephrology clinic of the hospital with advanced stage of CKD, it is observed that hypertensive nephrosclerosis and glomerulonephritis are the leading causes of their kidney disease. To avert this trend, sensitization of the general population and healthcare professionals on the importance of regular routine screening and early referral of patients to the nephrologists for expert care are recommended.

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Factors affecting compliance of intraoperative frozen and final histopathology in borderline ovarian tumors: Retrospective cohort study

Borderline over tümörlerinde intraoperatif frozen ve nihai histopatolojinin uyumunu etkileyen faktörler: Retrospektif kohort çalışması

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Abstract

Aim: Frozen sections (FS) are commonly used in the course of adnexal masses operations, and it assist to select the most appropriate surgical treatment modalities in addition to intraoperative management. In this study, we aimed to investigate the effect of the demographic and obstetric characteristics as well as biochemical findings with the consistency of intraoperative FS findings with the final histopathological diagnosis in patients with borderline ovarian tumors (BOT).

Methods: This retrospective study included a total of 31 BOT patients who underwent intraoperative frozen histopathological study. The study population was divided into two groups; group 1 consisted of patients who had a positive concordance between the findings of intraoperative FS and the final histopathology, while the patients included in the group 2 had a negative concordance between the results of two examinations. We compared two groups in terms of baseline characteristics, tumor markers, tumor size, bilaterality, menopausal status and presence of ascites.

Results: There were no statistically significant differences between the two groups in terms of age, body-mass index, tumor markers (CA125, CA19-9, CEA, AFP, CA15-3, β-HCG) and tumor size (P=0.74, P=0.55, P=0.87, P=0.55, P=0.24, P=0.33, P=0.70, P=0.32 and P=0.98, respectively). Also, the presence of bilateral BOT and ascites as well as menopausal status were not different between both groups (P=0.12, P=0.60 and P=0.70, respectively).

Conclusion: Based on the study findings, we noted that patients whether had concordance or discordance with the findings of intraoperative frozen sections and the final histopathology did not differ in terms of baseline characteristics and tumor markers.

Keywords: Borderline ovarian tumor, Frozen section, Concordance

Öz

Amaç: Frozen section (FS) adneksiyal kitle operasyonları sırasında yaygın olarak kullanılır ve intraoperatif tedaviye ek olarak en uygun cerrahi tedavi yönteminin seçilmesinde yardımcı olur. Bu çalışmada, borderline over tümörlü (BOT) hastalarda demografik ve obstetrik özelliklerin yanısıra biyokimyasal bulguların intraoperatif FS bulgularla final histopatolojik tanılar arasındaki ilişkiyi incelemeyi amaçladık.

Yöntem: Bu retrospektif çalışmaya intraoperatif frozen histopatolojik inceleme yapılan toplam 31 BOT hastası dahil edildi. Çalışma popülasyonu 2 gruba ayrıldı; grup 1 intraoperatif FS bulguları ile final histopatoloji arasında pozitif uyum olan hastalardan oluşurken, grup 2'ye iki inceleme sonucu arasında negatif uyum olan hastalar dahil edildi. Bu çalışmada her iki grup temel özellikler, tümör belirteçleri, tümör boyutu, bilateralite, menopozal durum ve asit varlığı açısından karşılaştırıldı.

Bulgular: İki grup arasında yaş, vücut kitle indeksi, tümör belirteçleri (CA125, CA19-9, CEA, AFP, CA15-3, β-HCG) ve tümör boyutu açısından istatistiksel olarak anlamlı fark yoktu (sırasıyla P=0,74, P=0,55, P=0,87, P=0,55, P=0,24, P=0,33, P=0,70, P=0,32 ve P=0,98). Üstelik bilateral BOT ve asit varlığının yanı sıra menopozal durum açısından da her iki grup arasında fark görülmedi (P=0.11, P=0.60, P=0.69, sırasıyla).

Sonuç: Çalışma bulgularına dayanarak, hastaların intraoperatif FS bulgularıyla final histopatolojileri arasındaki uyum ve uyumsuzlukta temel özellikler ve tümör belirteçleri açısından farklılık olmadığını belirledik.

Anahtar kelimeler: Borderline over tümörleri, Frozen histopatoloji, Uyum

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Introduction

Borderline ovarian tumors (BOTs) are epithelial ovarian tumors that differ from both benign and malignant neoplasms of the ovaries [1]. Although the exact incidence of BOTs has not yet determined, approximately 15–20% of serious tumors are considered to be as borderline [1]. BOTs have the pathological features of both benign and malignant neoplasms, thereby making a diagnostic challenge for pathologists. Until recently, several microscopic, macroscopic, and clinical parameters have been defined to differentiate the BOTs from malignant carcinomas. BOTs can spread to the peritoneum or to the lymph nodes, and they may relapse, as similar to malignant carcinomas. Additionally, BOTs have higher rate of proliferation and nuclear atypia that includes protuberances formation [2]. However, in contrast to malign carcinomas, stromal invasion is not seen in BOTs, and the incidence rate of BOT is higher in younger patients. On the other hand, in differential diagnosis, the gray zone still appears broad.

Even though the diagnosis in other gynecologic neoplasms can be set prior to surgery, the exact diagnosis of ovarian tumors mostly cannot be made until surgery. Frozen sections (FS) are commonly used in the intraoperative treatment of adnexal masses, and it helps in selecting the most appropriate surgical treatment method. In the course of ovarian tumors surgery, the objectives of FS are to identify patients who require a more extensive operation, to separate a group that can be treated with a more limited surgery, and to separate the group that can perform fertility preserving surgery [3,4]. Considering the vast majority of patients with BOT are at reproductive age at the time of diagnosis [5], it can be said that the intraoperative FS examination becomes more important. However, BOTs constitute a subgroup of ovarian tumors with a lower accuracy for FS [3,4]. It has been reported that the sensitivity of FS examination for ovarian tumors varies from 56 to 89% [3,6].

Although several parameters have been identified to show the consistency between the FS and the final histopathological diagnosis, the role of the demographic, clinical and biochemical characteristics on the consistency remain unknown. In this study, we aimed to analyze the characteristics of patients with BOT and to demonstrate the effect of the demographic, clinical and biochemical characteristics, on the consistency of intraoperative FS findings with the final histopathological diagnosis.

Materials and methods

Study Population

This retrospective study is related to the clinical data of 31 BOT patients who underwent perioperative frozen histopathological examination between 2010 and 2017 in the obstetrics and gynecology clinics of Kafkas University Medical Faculty Hospital and Fırat University Medical Faculty Hospital. Baseline characteristics, obstetric and clinical features, pathologic reports, and operation notes were obtained from the electronic files of patients who were surgically treated due to BOTs. The approval of the local institutional review board (2019/80576354-050-99/52) has been obtained prior to the study. The types of surgical intervention included the total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, myomectomy, cystectomy, appendectomy and bilateral pelvic paraaortic lymph node dissection.

Data collection

Baseline clinical and demographic characteristics, and patients' medical data (age, body-mass index and obstetric features [gravidity, parity, menopausal status, the number of previous abortions and dilatation & curettage interventions]) were obtained from the hospital's electronic record. All blood biochemical parameters including cancer antigen-125 (CA-125), cancer antigen-19-9 (CA-19-9), carcinoembryonic antigen (CEA), alfa feta protein (AFP), cancer antigen 15-3 (CA-15-3), and βeta-human chorionic gonadotropin (β-HCG) were measured upon admission to the hospital.

Sampling of tissues and pathological examination

Medical records indicated that different specimens of FS were sampled from the surgical field. All specimens were assessed by a senior pathologist who experienced in the gynecological pathology. Medical records indicated that the excised and unfixed specimens were firstly examined macroscopically. The solid, papillary, and necrotic areas that causing suspicion of malignancy were chosen for FS analysis. At least one sample was received for each centimeter excised material to be fixed into formalin and dipped into paraffin. All samples were frozen at -25°C, and they were sliced into a thickness of 8 mm. Hematoxylin and eosin staining was carried manually out. The FS results and the final histopathological evaluation were performed by the same pathologist. Eventually, the FS results that performed on the peri-operative period were compared with the final histopathological diagnosis whether the findings were concordant or discordant (The discrepancy between an initial FS result of BOT and the final histopathological diagnosis was categorized as "discordant"). According to the FS result, a staging surgery with or without lymphadenectomy was performed depending on the histological subtype of the tumor. Patients who had a concordant (grouped as the group 1) or discordant (grouped as the group 2) results between the FS and final histopathology were compared in terms of abovementioned variables.

Statistical analysis

The statistical analysis of the data was performed by IBM Statistical Package for Social Sciences (SPSS) Statistics 20 software (SPSS Inc., Chicago, IL, USA). The normality of distribution for variables was assessed with Shapiro Wilk test. The comparison of variables with normal distribution was assessed with Student-t test, whereas variables without normal distribution were analyzed using Mann Whitney-U test and Chi-Square test. The quantitative data was expressed as the mean (standard deviation) or median (interquartile range: 25-75). The data for bilaterally and menopause were analyzed with Fisher's chi square test. *P* value less than 0.05 in confidence interval of 95% was considered as statistically significant.

Results

The study population consisted of 31 BOT patients (mean age: 47 years) who underwent peri-operative FS examination. The number of patients who had a concordance between the results of intraoperative FS and the final

histopathology was twenty (n=20, 64.5%) (defined as the group 1), while the number of patients with discordance were eleven (n=11, 35.5%) (defined as the group 2). Demographic and laboratory characteristics of all patients are listed in Table 1. There were no statistically significant differences between the two groups in terms of age (P=0.74), body-mass index (P=0.55), levels of CA 125 (P=0.87), CA 19-9 (P=0.55), CEA (P=0.24), AFP (P=0.33), CEA 15-3 (P=0.70) and β-HCG (P=0.32). The tumor size determined during the intraoperative exploration did not differ between the two groups (P=0.98) (Table 1).

Table 2 demonstrates the comparison between the obstetric profiles of both groups. There were no differences between the two groups with respect to numbers of gravidity (P=0.26), parity (P=0.40), abortion (P=0.32), and dilatation & curettage (P=0.44) (Table 2). Furthermore, there was no significant difference between the groups in terms of bilateral involvement (P=0.11), menopausal status (P=0.70), and presence of ascites (P=0.60) (Table 3).

Table 1: Comparison of data derived from groups with concordant and discordant results of frozen section and definite histopathological diagnosis

Variable	Group		*P*-value
	Concordant (n=20)	Discordant (n=11)	
Age (years)	46.3 (15.2)	44.5 (11.9)	0.74*
BMI (kg/m^2)	26.5 (2.8)	27.2 (2.5)	0.55*
CA 125 (U/ml)	61.3 (71.2)	72.5 (109.7)	0.87**
CA 19-9 (U/ml)	26.3 (67.4)	16.6 (15.8)	0.55**
CEA (ng/ml)	1.9 (1.5)	1.2 (0.5)	0.24**
AFP (ng/ml)	2.2 (1.7)	2.0 (1.8)	0.33**
CA 15-3 (U/ml)	24.1 (9.7)	20.8 (29.7)	0.70**
β-hCG (mIU/mL)	0.9 (1.9)	1.1 (1.8)	0.32**
Tumor size‡ (cm)	14.1 (9.4)	13.4 (10.6)	0.98**

Data are expressed as mean (standard deviation), * Student t test, ** Mann Whitney U test, ‡ determined via intraoperative exploration

Table 2: Comparative analysis of discrete variables in groups with concordant and discordant results of frozen section and definite histopathological diagnosis

Variable	Group		*P*-value
	Concordant (n=20)	Discordant (n=11)	
Gravidity	3 (0-9)	4 (0-14)	0.26*
Parity	2 (0-9)	3 (0-14)	0.40*
Abortion	0 (0-2)	0 (0-3)	0.32*
Dilatation & curettage	0 (0-1)	0 (0-2)	0.44*

Data are expressed as median (interquartile range), * Mann Whitney U test

Table 3: Comparative analysis of discrete variables in groups with concordant and discordant results of frozen section and definite histopathological diagnosis

Variable		Group			
		Concordant (n=20)		Discordant (n=11)	
		n	%	n	%
Bilaterality	Yes	1	5	3	27.3
	No	19	95	8	72.7
	P-value*	0.11			
Menopause	Yes	8	40	3	27.3
	No	12	60	8	72.3
	P-value*	0.69			
Ascites	Yes	2	10	2	18.2
	No	18	90	9	81.8
	P-value*	0.60			

* Fisher's Exact test

Discussion

In the present study, we focused on the potential effect of the demographic, obstetric and biochemical characteristics on the consistency of intraoperative FS results with the final histopathological diagnosis in patients with BOT. Our study demonstrated that baseline demographic, obstetric, and biochemical features of patients are not effective on the discrepancy between the FS evaluation and the final histopathological diagnosis.

Most of the adnexal masses have a diagnostic challenge in the preoperative period. Therefore, intraoperative histopathological examination has a pivotal role both in the identification of the masses and the determination of the surgical modality. FS examination has a high overall accuracy for the diagnosis of ovarian cancers; however, the diagnostic sensitivity of FS may reduce up to below 60% in BOTs surgeries [3,6]. Similar the results of previous studies, a consistent finding were found in our study as the concordance between the results of intraoperative FS and the final histopathology was 64.5%. The diagnostic difficulty in BOT patients may frequently lead the surgeon to postpone the appropriate surgical staging until the definite pathology is obtained. Nevertheless, this delay may increase the rate of re-intervention, facilitate the postsurgical tumor spread, interrupt the adjuvant treatment, and increase the psychological distress, particularly in young women with high desire for fertility [7]. Similarly, in our study, 64.5% of the patients were not in menopause, but in fertile age.

The sensitivity of FS for patients with BOT may be attributed to several parameter including pathologist experience [8,9], the mucinous histopathology and size of the tumor [1,10]. It has been established that the cut-off tumor size for increased discrepancy of FS for ovarian tumors ranges from 10 to 20 cm [11,12]. The vast majority of cases (94%) of discordant diagnosis occur in tumors with a size of more than 13 cm [13]. In our study, the FS evaluation was performed by senior pathologists experienced in gynecological pathology, and the mean size of the tumors was 13.83 cm. Although the experience of pathologists seems to be satisfactory, the concordance between the results of intraoperative FS and final histopathology was 64.5 % in the study.

There are contradictory data in the literature regarding the association between the consistency of intraoperative FS results with the final histopathological diagnosis and demographic and biochemical characteristics in patients with BOT. In a study conducted by Tempfer et al. [8] reported that there was no relationship between age, the presence of bilateral tumor, and CA 125 level with the concordance of FS analysis. In another study, a good correlation was observed between serum CA 125 level and FS accuracy, especially in patients with an advanced stage of BOTs [2]. On the other hand, CEA and CA 15.3 were not found to be correlated with BOTs, but CA 19-9 was partially associated with the mucinous subtype of BOTs [2]. However, we did not found any association between the consistency of intraoperative FS results with the final histopathological diagnosis and any biochemical marker including CA 125, CA 19-9, CEA, AFP, CA 15-3 and β-HCG.

There is a limited data regarding the relationship between obstetric features and the concordance of intraoperative FS results. The present study showed that the obstetric profile was not associated with the consistency between intraoperative FS results and the final pathological diagnosis. Bilaterality of the tumor, or ascites in the abdomen, which are easily detectable by the diagnostic tools, does not seem to aid the accuracy of FS.

Limitations

Our study has certain limitations. Our study had a retrospective design, and it was based on the patient file analyses. The sample size is a quite small; hence the prognostic data could not be introduced due to low number of patients

Conclusion

In patients with BOT, an unsatisfactory examination finding of FS may result in a repeated surgical intervention,

which probably leads to worse outcomes, especially in vulnerable or morbid subjects. Reducing the discrepancy between the peri-operative FS and the final histopathological diagnosis could assist to choose a suitable surgery method. This study, investigating the effects of obstetric history, demographic characteristics, and biochemical characteristics on the FS discordance, revealed that the abovementioned parameters did not effect on the discordance between the FS evaluation and the final histopathological diagnosis.

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Living donor liver transplantation in hepatocellular carcinoma: A single-center experiences

Hepatosellüler karsinomda canlı vericili karaciğer nakli: Tek merkez deneyimi

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Abstract

Aim: Hepatocellular carcinoma (HCC) is the most common primary solid tumor of the liver. Hepatitis B virus (HBV) infections, Hepatitis C virus (HCV) infections and at alcoholism can be seen. The aim of this study was to evaluate living donor liver transplantation in hepatocellular carcinoma.

Methods: This is a retrospective cohort study. Between April 2014 and December 2017 at Medipol University Medical Faculty Hospital Organ Transplantation Department, 38 patients in living donor liver transplantation for HCC were evaluated.

Results: The mean patient age was 58.0 (9.9) (20–74) years; 31 (81.6%) of the 38 were male. The mean MELD score was 14.2 (8–32). Outside Milan criteria (P=0.003), poorly differentiated and cholangiocarcinoma tumor component (P=0.003) appears to be worse in living donor liver transplantation in hepatocellular carcinoma.

Conclusions: In this study, outside Milan criteria, poorly differentiated and cholangiocarcinoma tumor component appears to be worse in living donor liver transplantation in hepatocellular carcinoma.

Keywords: Hepatocellular carcinoma, Living donor liver transplantation

Öz

Amaç: Hepatosellür karsinom (HCC) karaciğerin en sık görülen primer solid tümörüdür. Hepatit B virus (HBV) enfeksiyonları, hepatit C virus (HCV) enfeksiyonları veya alkolizm zemininde de görülebilir. Bu çalışmanın amacı, HCC nedeniyle canlı vericili karaciğer nakli yapılan hastaların değerlendirilmesidir.

Yöntemler: Retrospektif kohort çalışma planlandı. Nisan 2014 – Aralık 2017 tarihleri arasında Medipol Üniversitesi Tıp Fakültesi, Organ Nakli Merkezi'nde HCC nedeniyle canlı vericili karaciğer nakli yapılan 38 hasta değerlendirildi.

Bulgular: Ortalama yaş 58,0 (9,9) (20-74) yıldı; 38 kişiden 31'i (%81,6) erkekti. Ortalama MELD skoru 14,2 (8–32) idi. Milan kriterleri dışında (P=0,003), kötü farklılaşmış ve kolanjiokarsinom tümör bileşeni (P=0,003), olan hepatosellüler karsinomda canlı vericili karaciğer naklinde daha kötü görünmektedir.

Sonuçlar: Bu çalışmada Milan dışı, az differansiye ve kolanjiokarsinom komponenti olan tümörlerin daha kötü olduğu görünmektedir.

Anahtar kelimeler: Hepatosellüler karsinom, Canlı vericili karaciğer nakli

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Introduction

Hepatocellular carcinoma (HCC) is the most common malignant solid tumor of the liver, and the seventh most fatal cancer worldwide [1]. HCC is threefold more common in males than females [2]. The etiology usually involves hepatitis B infection hepatitis C infection and liver cirrhosis caused by alcoholism [3, 4].

Percutaneous alcohol injection (PAI), transarterial chemoembolization (TACE), radiofrequency ablation (RF), and microwave coagulation are local ablative treatments. Surgical resection in patients with adequate liver size without cirrhosis, and liver transplantation (LT) for those with extensive cirrhosis, are curative [5, 6]. The aim of this study was to evaluated living donor liver transplantation in hepatocellular carcinoma.

Materials and methods

Between April 2014 and December 2017 at Medipol University Medical Faculty Hospital Organ Transplantation Department, Istanbul, Turkey, 38 patients in living donor liver transplantation for HCC were studied retrospectively.

Thirty eight patients with living donor liver transplantation were evaluated demographic features, recurrence rates and mortality rates.

Post-transplant follow-up

In our center, Immunosuppression regimens were based on calcineurin inhibitor (tacrolimus or cyclosporine), mycophenolate mofetil and corticosteroids in pediatric recipients. Patients received control once a week for the first month after discharge, and every 15 days for the second month and monthly after that period. Every 3 months abdominal magnetic resonance imaging and thorax computed tomography was performed in these patients.

Statistical analysis

SPSS 22.0 (SPSS for Windows, 2007, Chicago) was used for statistical analysis. Continuous variables which have normal distribution were presented as mean (standard deviation). Statistical analysis for the parametric variables was performed by the Student's T-test. The qualitative variables were given as percent and the correlation between categorical variables was investigated by the chi-square test and Fisher's exact test. Statistical significance level was defined as $p<0.05$.

Results

The mean patient age was 58.0 (9.9) (range 20–74) years; 31 (81.6%) of the 38 were male. The mean Model for End-Stage Liver Disease (MELD) score was 14.2 (8–32). In terms of etiological factors, 14 patients (36.8%) had HBV infections, 12 (31.6%) had cryptogenic, 8 (21.1%) had HCV infections, and 4 (10.5%) had alcohol-induced liver cirrhosis.

Figure 1 shows patient survival by the Milan criteria. Survival was significantly higher in patients whose tumors met the criteria than in those whose tumors did not (43 vs. 18 months, $P=0.003$).

Figure 2 shows patient survival by tumor grade; survival was significantly higher in patients with well-to-moderately differentiated than poorly differentiated carcinomas or tumors with cholangiocarcinoma components (45, 18, and 20 months, respectively, $P=0.003$).

The mean follow-up time was 18.5 months (7–44 months). Recurrence developed in 16 patients (42.1%) and 15 (39.4%) died by 44 months. The overall survival rate was 86.9% for the first year and 60.6% for the first 4 years.

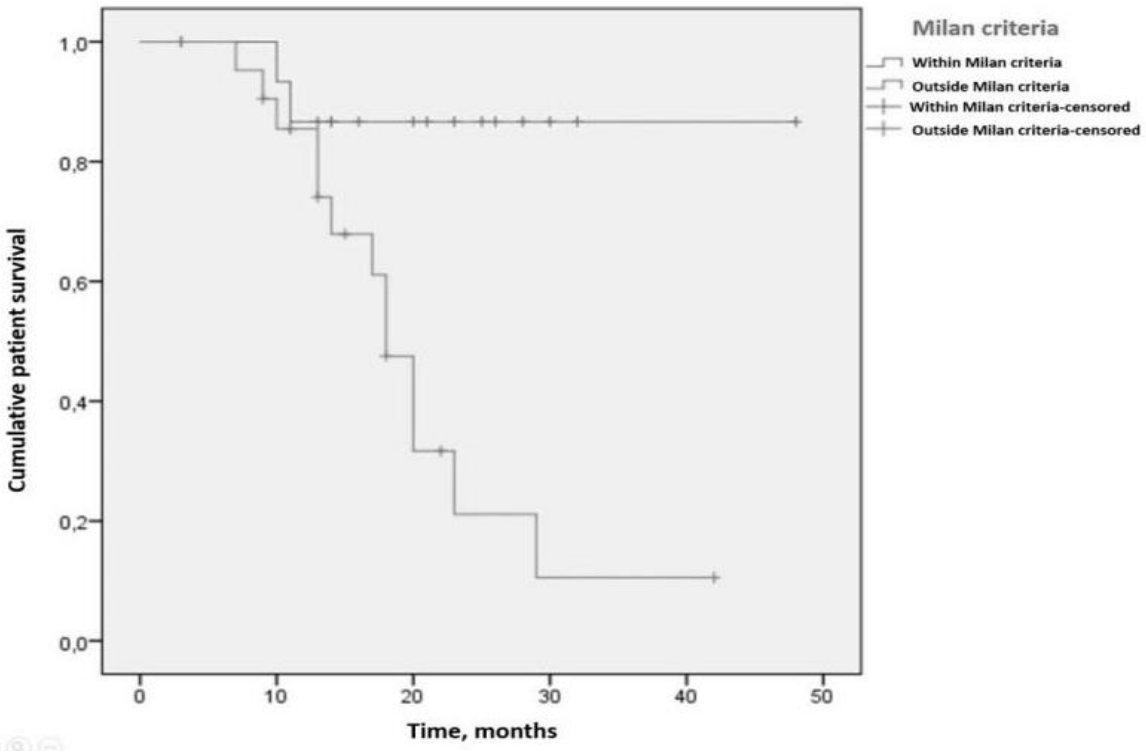

Figure 1: Patient survival by the Milan criteria

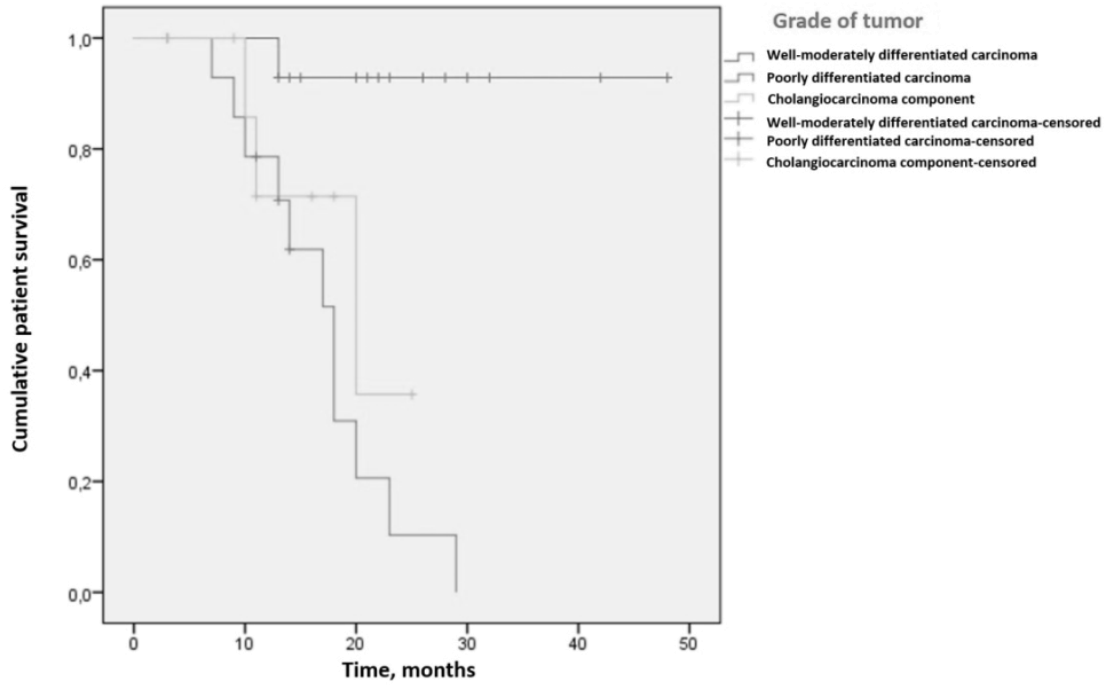

Figure 2: Patient survival by tumor grade

Discussion

Hepatocellular carcinoma is the most common malignant solid tumor of the liver, and the seventh most fatal cancer worldwide [1]. Males constitute 75% of all patients [2]. More than 80% of hepatocellular carcinomas develop on the surface of a cirrhotic liver; the annual incidence in cirrhotic patients is 1–6% [7,8]. In non-Western countries, HCC is associated with HBV infection [9-12] and, in Western countries, with alcohol-induced cirrhosis and HCV infection [13]. In our study, 14 patients (36.8%) had HBV infections, 12 (31.6%) had cryptogenic, 8 (21.1%) had HCV infections, and 4 (10. 5%) had ethanol-induced liver cirrhosis. Hematogenous spread is more common than lymphatic spread [14,15].

It is very important to evaluate both primary HCC and recurrence. Pre-transplant sensitivity of CT is about 70%. Gadolinium enhancement increases MRI sensitivity. In highly suspicious cases, Positron Emission Tomography combined with a Computed Tomography (PET/CT) and whole-body bone scintigraphy are valuable [2]. In our clinic, every 3 months, abdominal magnetic resonance imaging and thorax computed tomography was performed in these patients.

Local ablative treatments are used to treat HCCs in patients not suited to resection or transplantation. The treatments include PAI, TACE, RF, and microwave coagulation. If liver reserve is lacking because of cirrhosis, or if multiple lesions are present, surgical resection is usually not feasible. LT is highly effective and curative in those with both cirrhosis and HCC [5,6]. In this study, six patients who did not meet the Milan criteria exhibited significant tumor regression after TACE, and then underwent living donor LT.

Literatures have identified the male gender, multiple tumors, multiple lobe involvement, tumor size, metastasis, and lymphovascular invasion as poor prognostic factors [16-19]. Ernesto et al. [20] found that poorly differentiated tumors >5 cm in diameter featuring lymphovascular invasion were poorly prognostic. Mohamed et al. [21] found that many relapsed tumors were poorly differentiated and exhibited lymphovascular invasion. Tumor cells may exhibit a wide range of differentiation [22,23]. Those with intrahepatic cholangiocarcinomas are contra-indicated for liver transplantation because of early recurrence and poor prognosis [24,25]. The rarest malignant liver tumor is combined hepatocellular carcinoma and cholangiocarcinoma (1% of all liver cancers). The 5-year survival rate of such patients (determined via pathological examination after transplantation) ranges from 8–85% [26]. If HCC is not treated, the 5-year survival rate is <5% [27]. Mazzaferro et al. [28] defined the Milan criteria in 1996. The Milan criteria are cirrhosis associated with a single small tumor ≤5 cm in diameter or up to three tumors <3 cm in diameter, with no vascular invasion or extra-liver metastasis. Such patients exhibited very good results after LT [28]. In most studies, the 5-year survival rates were >70% and the recurrence rates <15% [29,30].

Here, recurrence developed in 16 patients (42.1%) over the 44-month follow-up time. Two underwent resection. Fifteen patients (39.4%) died. The overall survival rate was 86.9% for the first year and 60.6% for the first four years.

Our study has several limitations. First, this study was retrospective. Second, the number of cases was small.

Conclusion

Despite the limitations described, outside Milan criteria, poorly differentiated and cholangiocarcinoma tumor component appears to be worse in living donor liver transplantation in hepatocellular carcinoma.

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Does neutrophil-lymphocyte ratio show recurrence in patients who underwent curative resection for non-muscle-invasive bladder cancer?

Nötrofil lenfosit oranı, küratif rezeksiyon ile tedavi edilen yüzeyel mesane kanserinde rekürrensi gösterir mi?

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Abstract

Aim: The role of inflammation is a critical component of tumor progression and the neutrophil-lymphocyte ratio (NLR) reflects inflammatory status. We aimed to determine the clinical significance of the preoperative NLR in patients with non-muscle-invasive bladder cancer (NMIBC).

Methods: A total of 178 patients, who underwent curative transurethral resection of bladder tumor (TURBT) for NMIBC between 2011 and 2016 in the urology department of Pamukkale University and Uludağ University were included in the study. Data including clinical characteristics, surgery, pathology, and follow-up were obtained from a retrospectively maintained database. Patients were divided into groups according to pre-operative NLR values (h-NLR group: ≥2.5, l-NLR group: NLR <2.5). Their cut-off values were determined through receiver operation characteristics curves analysis. Recurrence rates of the patients were determined in the 1st year follow-up. For further analysis, all of the patients were allocated according to their risk ratio according to European Organization for Research and Treatment of Cancer (EORTC) tables as low, intermediate and high, and all of the groups have been evaluated according to the risk ratio.

Results: NLR patients (55.6% of the cases) were associated with worse risk of bladder cancer recurrence as compared to l-NLR group (P=0.005). Kaplan-Meier plots illustrated that higher pre-operative NLR had decreased disease-free survival (DFS). Low pre-operative PLR and NLR levels correlated with recurrence.

Conclusion: The present research shows that NLR is a prognostic indicator in NMIBC. Calculating NLR value might be useful at predicting recurrence in NMIBC patients.

Keywords: Bladder cancer, Recurrence, Neutrophil-lymphocyte ratio

Öz

Amaç: Enflamasyon, tümörün ilerlemesinin kritik bir bileşenidir ve nötrofil lenfosit oranı (NLR), enflamasyonun bir göstergesidir. Bu araştırmanın amacı; NLR'nin yüzeyel mesane kanserinde (NMIBC) prognostik bir gösterge olup olmadığını göstermekdir.

Yöntemler: Pamukkale ve Uludağ Üniversitesi Üroloji Anabilim Dalları'nda 2011-2016 yılları arasında yüzeyel mesane kanseri nedeni ile, sadece küratif amaçlı transüretral mesane rezeksiyonu uygulanan (TUR-M) toplam 178 hasta çalışmaya dahil edildi. Hastaların klinik ve patolojik verileri retrospektif olarak incelendi. Ameliyat öncesi nötrofil/lenfosit oranına (NLR) göre NLR ≥2.5 (h-NLR) ve <2.5 (l-NLR) olacak şekilde iki gruba ayrıldı. Ayrıca hastalar daha ileri analiz için, Avrupa Üroloji Derneği risk sınıflamasına göre düşük, orta ve yüksek riskli mesane tümörü olarak alt gruplara bölündü ve kendi içinde ayrıca değerlendirildi. 1. Yıl sonunda nüks oranları belirlendi ve rekürrens oranlarına göre istatiksel analiz uygulandı. NLR 2,5 cut-off değerine göre toplam hastalıksız geçen süre Kaplan Meier eğrisi kullanılarak analiz edildi.

Bulgular: Yapılan değerlendirmeler ile h-NLR hastaları (%55,6), l-NLR hastalarına göre istatiksel anlamlı olarak yüksek rekürrens oranlarına sahipti (P=0.005). Kaplan-Meier analizi sonucunda, h-NLR'nin hastalıksız geçen süreyi önemli ölçüde azalttığını ve rekürrensi arttırdığını göstermiştir.

Sonuç: NLR'nin, NMIBC hastalarında tümör rekürrensi değerlendirmesinde kullanılabilecek, faydalı bir biyobelirteç gibi görünmektedir.

Anahtar kelimeler: Mesane kanseri, Rekürrens, Nötrofil-lenfosit oranı

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Introduction

Clinical features of bladder cancer are heterogeneous, and 70% of cases are non-muscle-invasive bladder cancer (NMIBC) at the time of the diagnosis [1,2]. Despite appropriate treatment, these tumors develop recurrence rates ranging from 30% to 80% within 5 years, and progress to muscle-invasive disease up to 45%. The risk classification of NMIBC and its association with recurrence are determined according to the European Organization for Research and Treatment of Cancer (EORTC) tables [3]. To calculate the risk of recurrence and progression, NMIBC are divided into three groups: low, intermediate and high-risk. Number of tumor, tumor size, T category, World Health Organization (WHO) grade, and the presence of concurrent carcinoma in situ (CIS) are used to determine cancer risk [4]. However, despite the accurate calculation of risk analyzes, recurrence and progression is still unpredictable. In this case, it is necessary to investigate new clinical, molecular, biological, and environmental factors in order to make the risk calculation the most accurate. Inflammation is a critical component of tumor progression. The systemic inflammatory response (SIR) is associated with outcome in a variety of malignancies [5]. For example, as a SIR marker, incorporating C-reactive protein (CRP) and serum albumin, correlates with outcome in patients undergoing cancer treatment [6,7]. Elevated pre-operative or pre-treatment neutrophil to lymphocyte ratio (NLR) detected in peripheral blood are simple SIR markers, which have been identified in various malignancies [8,9]. Recent papers studied on NLR and recurrence showed that preoperative NLR was associated with the risk for disease recurrence, cancer-specific mortality in patients with NMIBC [10]. The aim of this study was to examine whether NLR could be useful inflammatory biomarkers for the risk of recurrence and progression with NMIBC.

Materials and methods

Data source and selection criteria

The medical records of 439 consecutive initially diagnosed NMIBC patients who underwent transurethral resection were obtained. Exclusion criteria in patient selection: Patients with hematological disorders, active infection, immune deficiency, history of additional cancer, with incomplete resections, patients with missing data in our electronic medical record system and patients undergoing intravesical treatment with Bacille Calmette-Guerin (BCG). After exclusion criteria, 178 patients were included in the study and data obtained from 178 patients, who underwent transurethral resection of bladder tumor (TURBT) (curative only and not diagnostic) for NMIBC between 2011 and 2016 in the urology department of Pamukkale University and Uludağ University were evaluated retrospectively in the study after approval for the study was granted by the Committees on Medical Ethics (PAU/Application Admission no: 60116787-020/29221). Data including; clinical characteristics, surgery, pathology, and follow-up were obtained from a retrospectively maintained database. To determine the clinical T stage of a bladder tumor according to the 2002 Union International Contre le Cancer (UICC) TNM classification, all patients was histologically confirmed by TURBT. The pathology reports, including carcinoma in-situ (CIS), were recorded and the patients were grouped as low-, intermediate- and high-risk. In the first and second year, the patients were followed-up every three months and in the third year patients were followed-up every six months in our institution. The number of white blood cells was determined by a hemocytometer from the peripheral blood obtained at the time of surgery prior to surgery, and the serum NLR values were calculated. Univariate and multivariate Cox regressions were performed to assess the predictive capability for recurrence, versus and in conjunction to the pathologically based EORTC score, among additional statistical analyses. This regression resulted in only NLR 2.5 as a significant variable (P=0.005). The patients were divided into 2 groups according to NLR values (NLR ≥2.5 (h-NLR) and <2.5 (l-NLR) before surgery. Recurrence rates of the patients were evaluated at the 1st year follow-up. For further analysis, all patients were grouped into low, medium and high groups according to recurrence risk groups by the EORTC tables. The cut off value was determined as 2.5 and the groups were evaluated within themselves.

Statistical analysis

All statistical analyses were carried out using Stat View 5.0 for Windows (SAS Institute, Cary, NC, USA). NLR values were compared using the Mann-Whitney U-test. Fisher's exact probability test was used to determine the significance of differences between two groups. Survival probabilities were calculated using the product limit method of Kaplan and Meier, considering overall cancer free survey. The influence of each significant predictor identified by univariate analysis was assessed by multivariate analysis using Cox's proportional hazards model. The influence of each clinicopathological variable on the risk of high NLR was assessed by logistic regression analysis. All P values less than 0.05 were considered statistically significant.

Results

l-NLR group included 79 patients, and l-NLR group consisted of 99 patients. There were no statistically significant differences between two groups in terms of age, height and BMI. The mean neutrophil lymphocyte ratio was 1.89 in l-NLR group and 3.58 in h-NLR group. No statistically significant difference was found between the groups in terms of gender, ASA, mitomycin, smoking history, BCG, Carcinoma in-situ, Ta0-Ta1 and risk categories (Table 1).

41 of the patients who had recurrence in the first year were in the l-NLR group and 71 of them were in the h-NLR group with, and this difference was significant (P=0.005) (Table 2).

When compared to the NLR of patients with tumor recurrence status; 10 patients (62.5%) with non-recurrence in the low-risk group were predominant in the l-NLR group and there was no statistically significant difference (P=0.05). In the medium-risk group; 8 patients (57.1%) with non-recurrence had a majority in the l-NLR group and 8 patients (61.5%) in the h-NLR group had recurrence and this was not statistically significant (P=0.050). In the high-risk group; twenty-nine patients (59.2%) in the l-NLR group and 54 patients (77.1%) in the h-NLR group were predominant in the presence of relapse,

and there was statistically significant difference between these data (P=0.029). Regarding the NLR of all patients without any risk category difference, 41 patients (51.9%) with recurrence were found in l-NLR group, while this number was 71 (77.1%) in h-NLR group. This difference was significant (P=0.005).

Table 1: Demographic data of the patients

		Groups l-NLR NLR <2.5	h-NLR NLR ≥2.5	*P*-value
n (%)		79 (44.4)	99 (55.6)	
		Mean (SD)	Mean (SD)	
Age		70.06 (12.45)	69.77 (10.39)	0.87
Weight		77.83 (11.21)	76.71 (14.58)	0.55
BMI (Body mass index)		27.35 (4.17)	27.12 (5.9)	0.77
NLR (Neutrophil-lymphocyte ratio)		1.89 (0.45)	3.58 (1.92)	
		n (%)	n (%)	
Sex	Female	8 (38.1)	13 (61.9)	0.35
	Male	71 (45.2)	86 (54.8)	
ASA	1	14 (53.8)	12 (46.2)	0.52
	2	57 (43.5)	74 (56.5)	
	3	8 (38.1)	13 (61.9)	
Mitomisin	No	69 (46.3)	80 (53.7)	0.21
	Yes	10 (35.7)	18 (64.3)	
Smoking	yes	28 (41.2)	40 (58.8)	0.33
BCG	No	47 (45.6)	56 (54.4)	0.41
	Yes	32 (42.7)	43 (57.3)	
Carcinoma in-situ	No	76 (45.8)	90 (54.2)	0.14
	Yes	3 (25)	9 (75)	
Ta 0- T 1	No	55 (46.6)	63 (53.4)	0.25
	Yes	24 (40)	36 (60)	
Risk Category	Low risk	16 (50)	16 (50)	0.47
	Medium Risk	14 (51.9)	13 (48.1)	
	High Risk	49 (41.2)	70 (58.8)	

SD: Standard deviation

Table 2: Recurrence rates of patients according to NLR

		l-NLR group n (%)	h-NLR group n (%)	*P*-value
Status	No recurrence	38 (57.6)	28 (42.4)	0.005
	Recurrence	41 (36.6)	71 (63.4)	

Table 3: Risk category and NLR evaluation

Risk category	Recurrence	Groups l-NLR	h-NLR	*P*-value
		n (%)	n (%)	
Low risk	No	10 (62.5)	7 (43.8)	0.24
	Yes	6 (37.5)	9 (56.3)	
Medium risk	No	8 (57.1)	5 (38.5)	0.28
	Yes	6 (42.9)	8 (61.5)	
High risk	No	20 (40.8)	16 (22.9)	0.03
	Yes	29 (59.2)	54 (77.1)	
Total	No	38 (48.1)	28 (28.3)	0.005
	Yes	41 (51.9)	71 (71.7)	

We observed that the recurrence rate of l-NLR group was less than h-NLR in the follow-up period of 36 months (Figure 1).

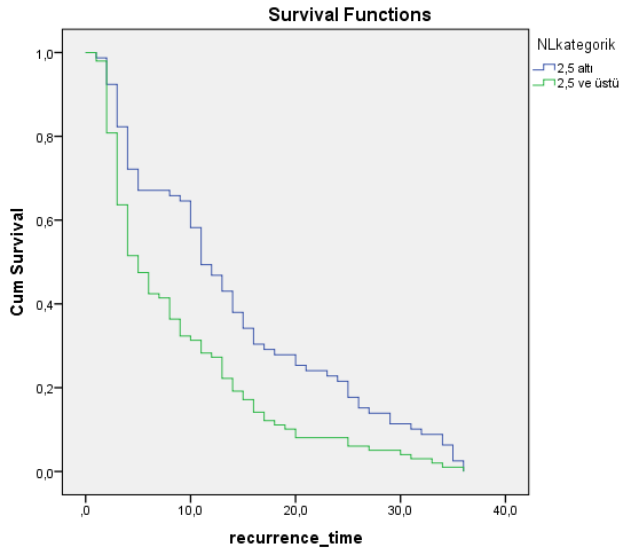

Figure 1: Kaplan-Meier survival curves, stratified by recurrence period neutrophil-lymphocyte ratio

Discussion

In order to predict recurrence and progression in NMIBC, EORTC tables were established; parameters such as tumor count, tumor size, previous recurrences, presence of T1 disease, presence of carcinoma in the site (CIS) and the degree of tumor were used. However, these evaluations are still lacking due to unpredictable factors. However, different biomarkers have been used to facilitate recurrence prediction in bladder cancer and to increase patient comfort by reducing the number of control cystoscopy. Urine cytology is a biomarker used for this purpose; ImmunoCyt (Diagnocure Inc., Quebec City, Canada) [11,12], the nuclear matrix protein-22 (Matritech, Newton, MA, USA) [13], fluorescence in situ hybridization (FISH) analysis (Urovysion Systems Vume Abbott Laboratories, Abbott Park IL, USA), urinary epidermal growth factor receptor and epithelial cell adhesion molecules were performed in many countries [14,15]. However, it is very important to use biomarkers in the methods to be used, to be cost effective and to use in practical use [16]. In addition, biomarkers should be able to be used at the same time in diagnosis and follow-up. The N/L ratio was a low prognostic indicator in colorectal cassettes, gastric carcinoma, renal cell cancers and ovarian cancer. [8,17,18]. In literature, it was reported that use of N/L ratio is effective in various conditions, e.g., cardiovascular problems [19,20]. In this study, our aim was to determine the predictive value of the preoperative N/L ratio for predictable tumor recurrences in NMIBC.

Systemic inflammation is known to increase in recurrence and progression in different types of cancer [2]. The prognostic value of leukocytosis and C-reactive protein (CRP) in cancer is poor [21]. The N/L ratio in the preoperative period is known to be used to predict recurrence in NMIBC [22,23]. Tachibana et al. [24] showed that bladder cancer cells produce granulocyte colony stimulating factor (G-CSF) receptors and this shows us that inflammation is important in the progression of bladder cancer. However, neutrophil vascular endothelial growth factor (VEGF) allows a proliferation of the tumor by secreting a proangiogenic factor [25]. The N/L ratio was determined as an independent prognostic factor in patients who underwent radical cystectomy (RC) between these inflammatory parameters [26]. In addition, the N/L ratio; it is an easy to detect biomarker that can be easily calculated by looking at cheap, peripheral blood. In this study, we evaluated whether the preoperative N/L ratio in 178 patients could predict recurrent disease based on the cut-off value of 2.5. In our study, we excluded all TURBT operations which were not completed (incomplete TURBT) in order to rule out all external factors.

Gondo et al. [26] reported that using the cut-off value of 2.5, and suggested that the N/L is an independent prognostic factor ratio for disease-related survival risk in bladder cancer patients treated with radical cystectomy. Krane et al. also reported the association of the high NLR value before the radical cystectomy has generally been associated with worse overall survival. Also they found that patients with a NLR >2.5 had a significantly higher likelihood of extravesical disease at radical cystectomy, suggesting that they may benefit from neoadjuvant chemotherapy [27]. In a recent study; Marchioni et al. [28] determined the cut-off value to be 2 and this value was

associated with upper urothelial cancer progression. Mano et al. [29] showed in their study, include 107 NMIBC patients, the value of NLR >2.41 is associated with disease progression; >2.43 was associated with disease recurrence. In our study, 2.5 cut-off value was associated with disease recurrence similarly to Mano's study. In addition, all risk groups were evaluated separately and the progression was statistically significant in the high risk group but not in other groups. Although the N/L ratios in the low and intermediate risk groups did not show statistical significance, they supported the numerical results of our study.

The most important aspect of this study is the separation of NMIBC patients according to the risk categorization and the high number of exclude criteria. In this way, the N/L ratio of all risk groups was evaluated based on the cut off value 2.5. In addition, the long-term follow-up of the patients in the Kaplan-Meier curve; when the cut-off value was 2.5, it was observed that the recurrence rate was significantly less in patients with N/L ratio <2.5 in 36 months follow-up. Cho et al. [18] patients with a high N/L ratio indicated relative lymphocytopenia. And as a result of this, it can cause an immune response and this allows potential tumor progression and worsens the prognosis.

This study has some limitations. The number of patients included in the study was low due to the design of the study retrospectively, and eligibility criteria for inclusion were comprehensive. In addition, because the follow-up times were relatively short and operator-dependent TURBT and pathologist-dependent pathological evaluations were affected by the results.

Conclusion

The present research shows that NLR is a prognostic indicator in NMIBC. It is found that the N/L ratio may be used as a predictor of recurrence patients with NMIBC, because it's easily accessible. However, randomized-controlled studies and prospective studies with a higher number of patients are needed for validation.

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Critical stab injury due to anatomical variation caused by retroperitoneal lipoblastoma: A case report

Retroperitoneal lipoblastomanın neden olduğu anatomik varyasyona bağlı kritik bıçakla yaralanma: Olgu sunumu

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Abstract
Lipoblastoma and lipoblastomatosis are rare soft tissue neoplasms that are derived from fetal adipose tissue and that are seen in infants and young children. They transform into mature lipomas as the patients age. We present a 23 years old male patient stabbed from left abdominal flank and had a lipoid lesion on the right side of retroperitoneum. Due to malposition of intraabdominal organs in the stabbing site, patient had various vascular and serosal injuries as well as intestinal perforations.
Keywords: Lipoblastoma, Stab wound, Computed tomography

Öz
Lipoblastoma ve lipoblastomatozis, fetal yağ dokudan köken alan nadir yumuşak doku neoplazileri olup süt çocuklarında ve küçük çocuklarda görülür. Hasta yaşı ilerledikçe matür lipomlara dönüşürler. Retroperiton sağ yarısında lipoid lezyona sahip karın sol yandan bıçaklanan 23 yaşındaki erkek hastayı sunduk. Bıçaklanma düzeyindeki intraabdominal organların malpozisyonu nedeni ile hastada, vasküler ve serozal yaralanmaların yanı sıra intestinal perforasyon mevcut idi.
Anahtar kelimeler: Lipoblastoma, Delici kesici alet yarası, Bilgisayarlı tomografi

Introduction

Retroperitoneal fat containing lesions represent wide spectrum of entities. Lipomas are frequently seen as an intraabdominal mass however, if the origin is retroperitoneum, lipoma can hardly be the diagnosis [1,2]. List of differential diagnosis is reduced when pediatric population is considered. The condition of abdominal wall muscles can give clue about the mass as it has been shown that, in rare diseases, abdominal wall atrophy is secondary to fetal abdominal distention [3]. Lipoblastoma and lipoblastomatosis are rare soft tissue neoplasms that are derived from fetal adipose tissue and that seen in infants and young children [1]. We present a case who is 23 years old male stabbed from left abdominal flank and had a lipoid lesion on the right side of retroperitoneum. Due to malposition of intraabdominal organs in the stabbing site, patient had various vascular and serosal injuries as well as intestinal perforations.

Case presentation

A 23 years old male was admitted to emergency room with stab wound. He had no history of previous surgery. Perinatal and childhood history was uneventful. Physical examination revealed left flank stab wound with minimal leakage of blood and abdominal distention. He had a body temperature of 37.6 °C, blood pressure of 100/70 mmHg, and heart rate of 110 beats per minute. Laboratory test results showed decreased hemoglobin levels (10.3 g/dL, range: 12.9–18.1) as well as red blood cell count ($3.80x10^6$ /uL, range: 4.06–6.13).

Abdominal ultrasonography was performed to investigate the extent of the injury. Sonographic result revealed intra-abdominal, peri-intestinal fluid collection with mildly increased wall thickness of left sided intestinal loops. Furthermore, there was a large echogenic mass with obscured borders that was located in the right upper and lower quadrant. Abdominal computed tomography (CT) examination was performed to solve the ambiguity.

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CT images showed a mass with fat density which filled the right side of the abdomen (Figure 1A). There were no any intestinal or colonic loops on the lesion side. Atrophy of the abdominal wall muscles and septa in the mass were also detected (Figure 1B). Imaging findings on the left side were concordant with sonographic results (Figure 1C).

Patient was immediately prepared for laparotomy. On the right side, a bulky retroperitoneal mass composed of fat was observed (Figure 2A). The whole mass was extracted (Figure 2C) and sent for histopathologic examination. Result was consistent with mature encapsulated lipoma. On the left side, at the level of the stab wound entry, six distinct intestinal perforation sites along with injured mesentery were detected (Figure 2B). Resection and anastomosis were performed. Additionally, various serosal injuries involving the caecum, ascending and descending colon were observed. Bleeding from small mesenteric vessels was also controlled. Postoperative course of the patient was uneventful. The written consent was obtained from the patient presented in this study.

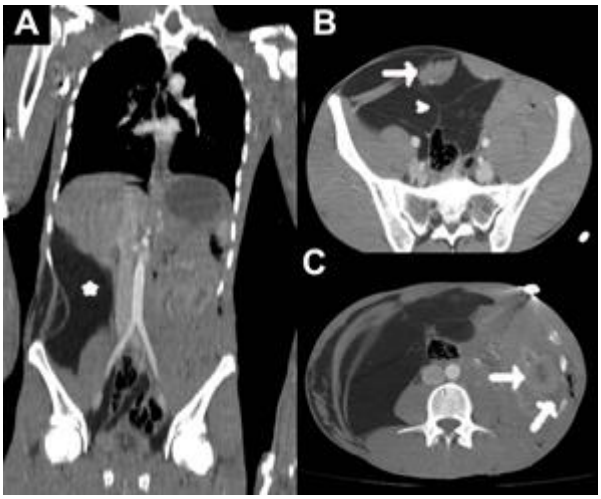

Figure 1: Coronal CT image (A) shows a fat density mass on the right side (asterisk) with all intestinal and colonic loops are seen on the left of abdomen. Axial image from pelvic level (B) shows right sided atrophy of the abdominal wall muscles (arrow) and septa within the lipoid mass (arrowhead). At the level of stab wound, axial image (C) shows increased wall thickness of the intestinal loops along with peri-intestinal fluid collection (arrows).

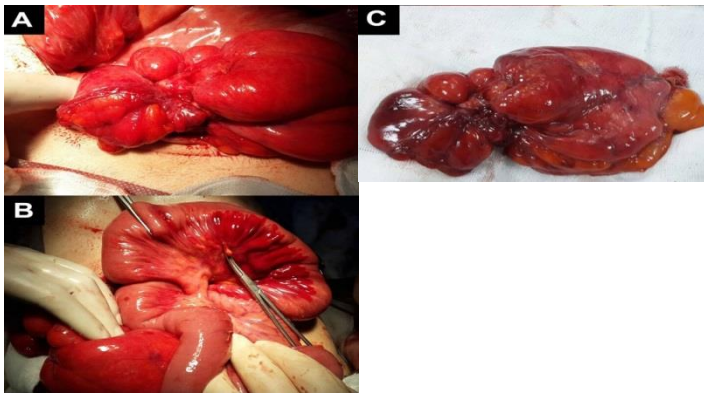

Figure 2: Photos taken during laparotomy. Macroscopic view of the mass before (A) and after resection (C). One of injured intestinal loop along with its mesentery (B).

Discussion

In this paper, we demonstrated a case of intestinal malposition due to an intraabdominal mass and critical damage from stabbing due to presence of such anatomical variation. In our case, many bowel loops were injured due to stabbing. Even the caecum, which should have been localized on the right side of the abdomen, was injured. This is unlikely to be happened in a normal individual who had caecum at the right and stabbed from the left. Our patient had right sided lipoblastoma, which displaced the entire bowel including caecum and made the left sided stabbing to cause more damage than expected.

Penetrating trauma to the back or flank less likely poses a significant injury compared to anterior abdominal wounds [4]. However, these injuries can be challenging by means of imaging techniques and clinical evaluation. Focused abdominal sonographic examination for trauma as well as physical examination is unreliable in retroperitoneal imaging [4]. For patients who have sustained a penetrating injury to the abdomen, treatment choice is always non-operative follow-up unless patient is unevaluable, presence of hemodynamic instability, peritonitis, or evisceration. Patients who represent those findings should undergo immediate exploration whereas imaging should be performed to remaining. If the injury mechanism is an abdominal gunshot wound, situation can be easily delineated by CT because trajectory of the foreign body and crossings of this trajectory to intraabdominal structures can be determined. However, the lack of soft tissue disruption makes visualizing the tract of the stab wound and any associated injuries difficult and renders the role of CT imaging less potent [5]. On the other hand, CT imaging is useful for investigating the presence of other comorbid situations and accompanying anatomical variations as in our case.

Lipoblastomas commonly presents with painless mass in asymptomatic children. However, older patients have a more mature lipoblastoma in which immature fat cells are replaced by mature ones [1]. Furthermore, circumscribed form of lipoblastoma mimics the typical lipoma with its well-defined borders. Lipoblastomas differ from lipomas by having fibrous septa which retain as the patients ages [1]. Although histopathologic examination was consistent with lipoma in our case, imaging and histopathologic characteristics such as retroperitoneal location, retained fibrous septa, atrophy of the abdominal wall muscles and presence of external capsule indicate that this lipoma was the transformed form of lipoblastoma.

Lipoblastoma is a rare retroperitoneal lipoid mass and that transforms into lipoma in adulthood. CT imaging is helpful in the diagnosis. Adjacent structures should be examined carefully as they provide useful information about the origin and the extent of the mass.

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Superior mesenteric artery syndrome with superior mesenteric artery thrombosis: A case report

Superior mezenterik arter sendromlu hastada superior mezenterik arter trombozu birlikteliği: Olgu sunumu

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Abstract

Superior mesenteric artery (SMA) syndrome is a rare syndrome with symptoms including nausea, vomiting and epigastric pain. SMA syndrome is also known as Wilkie's syndrome, mesenteric root syndrome, chronic duodenal ileus syndrome. SMA syndrome is vascular compression of the third part of the duodenum between the SMA and the aorta. In this article, we will present an adult patient with SMA syndrome who was admitted to the emergency service with abdominal pain and associated thrombosis of her superior mesenteric artery, demonstrated by computed tomography. Since SMA syndrome is rare and symptoms are not frequent, some diagnostic difficulties might happen and this will lead unnecessary long-term symptomatic treatments for the patient. In such patients, mesenteric artery thrombosis should be considered in differential diagnosis of abdominal pain.

Keywords: Superior mesenteric artery syndrome, Superior mesenteric artery thrombosis, Acute abdomen, Wilkie's syndrome

Öz

Superior mezenterik arter (SMA) sendromu; bulantı, kusma ve epigastrik ağrı gibi semptomları olan nadir bir sendromdur. SMA sendromu ayrıca Wilkie sendromu, mezenterik kök sendromu, kronik duodenal ileus sendromu olarak da bilinir. SMA sendromu, duodenumun üçüncü bölümünün SMA ile aort arasındaki vasküler kompresyonudur. Bu yazıda, acil servise abdominal ağrı ve bilgisayarlı tomografi ile gösterilen superior mezenterik arterinin ilişkili trombozuyla başvuran SMA sendromlu yetişkin bir hastayı sunacağız. SMA sendromu nadir olduğundan ve semptomların sık görülmediğinden, bazı tanısal zorluklar ortaya çıkabilir ve bu hasta için gereksiz uzun süreli semptomatik tedavilere yol açacaktır. Bu hastalarda, karın ağrısının ayırıcı tanısında mezenterik arter trombozu düşünülmelidir.

Anahtar kelimeler: Superior mezenterik arter sendromu, Superior mezenterik arter trombozu, Akut abdomen, Wilkie sendromu

Introduction

Superior mesenteric artery (SMA) syndrome is characterized by compression of duodenum between the aorta and superior mesenteric artery and causing duodenal (+/- stomach) dilation. Superior mesenteric is separated from aorta with an angle of 45 degrees and if this angle drops below 20 degrees, clinical SMA syndrome manifestations appear. These angle values are valid for adult patients, for pediatric patients' values are lower [1]. However narrow superior mesenteric angle alone is not sufficient to explain symptoms and one should know that patients with low body mass index and children with narrow superior mesenteric artery angles may not display typical symptoms [2]. Carl Freiherr von Rokitansky first identified SMA syndrome in 1861 however, its pathology was obscure until 1927 when Wilkie published the first series of 75 patients [3].

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Case presentation

82-year-old woman patient admitted to our emergency service with abdominal pain, nausea, and vomiting after the meal. In her background, she had hypertension and stroke history, which she experienced 1 year ago. With mesenteric ischemia in her pre-diagnosis, the patient underwent computed tomography (CT) angiography. Her CT of the abdomen showed compression of third part of duodenum between the aorta and superior mesenteric artery, apparent narrowed duodenum lumen in that level and distended stomach and especially first proximal part of the duodenum (Figure 1, 2). In addition, there is no transfer of contrast agent because of thrombus from the level which duodenum passes between the aorta and superior mesenteric artery and from 3 cm distal to the orifice of superior mesenteric artery.

The patient was operated due to the mesenteric ischemia. In observation, from the 40th cm of Treitz ligament, all small intestines with half of the transverse colon were necrotic. Subtotal resection of the small bowel and the right hemicolectomy was performed. The patient died at postoperative 3rd week due to cardiopulmonary arrest. Written informed consent was obtained from the patient's legal representative.

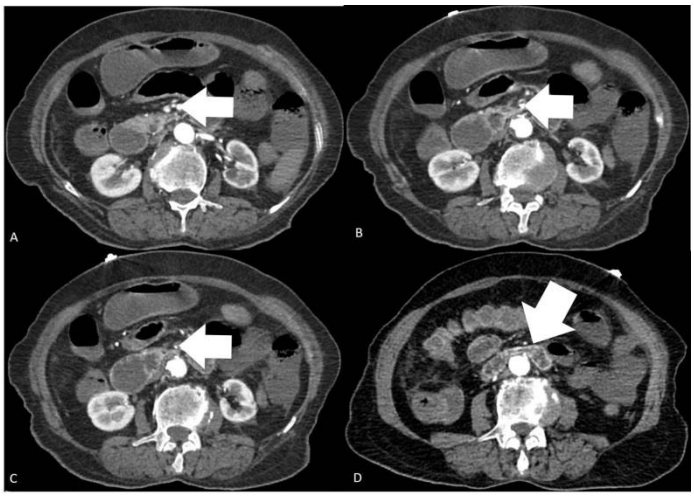

Figure 1: A: Contrast enhanced abdominal computed tomography shows patent superior mesenteric artery (arrow), B, C: Contrast enhanced abdominal computed tomography; there is thrombosed superior mesenteric artery (arrow), D: There is a narrow segment of duodenum between superior mesenteric artery and abdominal aorta (arrow)

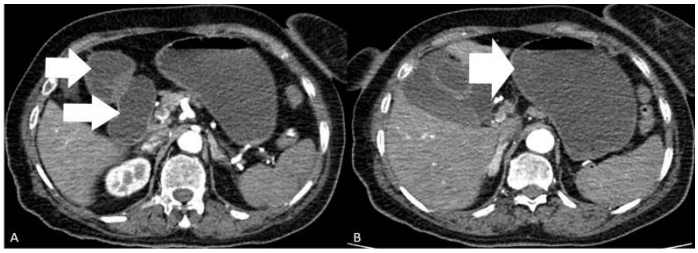

Figure 2: A, B: Contrast enhanced abdominal computed tomography; there are dilated duodenal segments and dilated stomach (arrow)

Discussion

The detection rate of SMA syndrome is 0.3% in patients who undergo upper gastrointestinal system examination with barium [4]. However, the rate of the symptomatic patient was very low. This syndrome was more frequently seen in women. Although there is no specific age range, it was seen most often in early adulthood. The most common comorbid conditions are mental and behavioral disorders like eating disorders and depression, tuberculosis and infectious diseases such as acute gastroenteritis, muscular dystrophy, neurological diseases such as Parkinson's disease and cerebral palsy [5].

Delay in SMA diagnosis may cause severe dehydration, electrolyte abnormalities, hypokalemia, rupture acute gastric or intestinal perforation, gastric distention, spontaneous upper gastrointestinal hemorrhage, hypovolemic shock, aspiration pneumonia, and sudden cardiovascular events [6]. Retroperitoneal fat and lymphatic tissue normally serves as a cushion for the duodenum, prevents the duodenum compression by the superior mesenteric artery. Lack of this structure, which serves as cushion and narrowing of the angle of superior mesenteric artery, leads to the syndrome.

SMA syndrome may be acute or chronic (congenital). Congenital causes can be listed as high insertion of the field ligament of Treitz of duodenojejunal flexure, SMA origin with short distance and the pressure as a result of peritoneal adherence linked with duodenum intestinal malrotation [7]. The causes of the acute form of SMA syndrome can be considered as long-term rest in the bed, spinal cord injury, spinal surgery for scoliosis, left nephrectomy. Even though many clinical conditions can be observed together, the combination of the SMA thrombosis is a rare condition that establishes a ground for the mesenteric ischemia in the acute period. Conservative treatment approaches are tried often. Generally, pediatric cases and acute presentation of SMA syndrome respond better to conservative treatment compared to chronic presentation of SMA syndrome. In pediatric cases, 6-week conservative treatment is recommended [8]. The aim of conservative treatment in SMA is making the underlying causes better and prevention of the weight gain. In acute cases, conservative approaches may be successful including relaxation of the bowel, fluid replacement, parenteral nutrition, correction of electrolyte balance and nasojejunal nutrition [9]. If the conservative approach is not successful or it is not applicable because of the severe disease, surgical interventions are necessary. The most common operation for SMA syndrome is duodenojejunostomy. In 1907, it has been tested by Bloodgood for the first time [10]. The aim of the open or laparoscopic surgery is providing the anastomosis between duodenum and jejunum thus to bypass the area, which is pressed by aorta and SMA [6].

In conclusion, the presence of SMA syndrome and thrombosis is rare clinical condition however since it might be overlooked because of its non-frequent and nonspecific symptoms, the differential diagnosis should be considered. Radiological methods including Barium X-rays, computed tomography, CT angiography and magnetic resonance imaging angiography can be used in diagnosis.

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Case report
Olgu sunumu

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A case of epidermal inclusion cyst which causes open roof deformity in the nasal bone

Nazal kemikte açık çatı deformitesine neden olan epidermal inklüzyon kisti olgusu

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Abstract

Epidermoid cysts; in the midline of the body is composed of internal keratin filled cysts. They occur when the branch arches are not fully closed. They usually have limited involvement. They occur mostly in the genital area and rarely hold the head and neck region. Nasal dorsum involvement is very rare. In this case report, we present a case of epidermal cyst that disintegrates the nasal bone at the age of 33 and forms an open roof deformity.

Keywords: Epidermal cyst, Nasal bone, Open roof deformity

Öz

Epidermoid kistler; vücudun orta hattında oluşan içi keratin dolu kistlerdir. Brankial arkların tam olarak kapanmamasıyla oluşurlar. Genellikle sınırlı tutulumları vardır. En çok genital bölgede görülürler ve nadiren baş ve boyun bölgesinde bulunurlar. Nazal dorsum tutulumu çok nadirdir. Bu olgu sunumunda, 33 yaşında nazal kemiği destrükte eden ve açık çatı deformitesi oluşturan bir epidermal kist vakasını sunuyoruz.

Anahtar kelimeler: Epidermal kist, Nazal kemik, Açık çatı deformitesi

Introduction

Cysts in the mid-fascial region are divided into three groups as dermoid, epidermoid and teratoid cysts. Dermoid cyst contains skin inserts, all three germ leaves (such as muscle, bone, gastrointestinal system epithelium), the teratoid cyst contains only the multilayer squamous epithelium, and is called epidermoid cyst if it does not contain skin attachments [1].

Epidermal inclusion cysts; they are frequently seen in the head, neck, face, behind the ear, chest, genital area. They are round shapes and contain dermis remnants. Epidermal cysts are formed by pathological migration of epidermal elements below the dermis. They contain cheese-like secretions. Parotid and jaw region cases have been reported in the head and neck region [2].

The diagnosis of cysts is made by ultrasound (USG), computed tomography (CT) and magnetic resonance imaging (MR). Histopathological examination is important in definitive diagnosis. Pericapsular excision is sufficient for its treatment; but it is impossible to take the whole epithelial layer completely. Recurrences are rare. They do not destroy the bone. They don't spread [3].

Epidermal cysts of the nasal region are rare. Cysts formed in this region can form the tract and open to the skull base or sinuses. Mostly they do not come out of the skin. Nasal dorsum cyst after rhinoplasty is mentioned in the literature [4-6]. It has not been reported that epidermal cysts are destroying bone. In this presentation, we present a 33-year-old patient with open roof deformity that completely obscures the superior wall of the bone in the nasal bone radix section.

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Case presentation

A 33-year-old female patient was admitted to our clinic with the complaint of swelling in the upper part of her nose which had been growing slowly for 2 years. There was no color change in the skin. USG reported as 3x3 cm cystic formation in the nasal dorsum. The patient underwent excision of the cystic mass by introducing dorsum with a classical inverse V incision of rhinoplasty (Figure 1). After the cyst was removed, it was found to infect the region, eat the bone in the nasal bone radix area and cause open roof deformity. The area was cleaned and the roof was closed with oblique and lateral osteotomies. The patient was closed with sutures in the rhinoplasty. Histopathologic diagnosis of the excised cystic mass was defined as epidermal inclusion cyst. There were no postoperative complications. The written consent was obtained from the patient presented with images in this study.

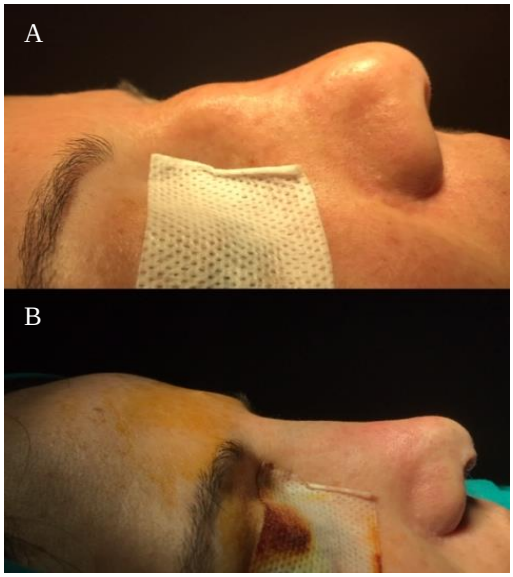

Figure 1: Before (A) and after (B) operation

Discussion

Dermoid, epidermoid and teratoid cysts occur congenitally due to disturbances in epithelial migration. Dermoid cysts contain skin inserts; while epidermoid do not contain skin attachment. Teratoid cysts originate from three germ leaves. There are many theories about etiology. The most accepted of these; the first and second branch arcs are formed by epidermal tissue debris around the midline closure [7].

They can occur in many parts of the body. Generalities occur with adolescence. The most reported cases are in the genital area (testis and ovary). Head-neck welds are around 5% of all cysts [8]. Epidermal inclusion cysts are less than dermoid cysts and they are mostly located in the submental region. Several cases have been reported in areas such as parotid, jaw and zygoma [9].

Epidermoid cysts do not open to the outside in the nasal region; they show the continuity of the sinus to the base and the base of the head. The first choice is USG. CT and MR are useful to find where the tract is opened in large masses. CT is very important in diagnosing and detecting intracranial spread [10,11]. Diagnosis is difficult in cysts that do not leave the nasal cavity. In this case, the differential diagnosis should be differentiated from the hemangioma and the encephalocele [12].

In order to prevent recurrence in the treatment, it is necessary to remove the entire tract and the wall of the cyst [12]. As the external approach can be used in the cysts, incisions used in rhinoplasty can also be used. In our case, a "İnverse V İncision" was performed due to the patient's cosmetic anxiety.

Recurrence of epidermal cysts is rare [13]. Epidermal cysts may rarely undergo malignant transformation. Cystic macular malignant cells are seen in the differential diagnosis of these cases [12]. In our case, superficial tissue USG 3x3 cm skin horse cystic formation was found. Histopathological examination revealed squamous epithelial cells. Histopathological examination revealed epidermal inclusion cyst. No recurrence was detected at follow-up of 2 years.

Open roof deformity; is usually a complication of rhinoplasty surgery. It occurs when the upper wall of the nasal bone is removed and osteotomy is not performed. Medial, oblique and lateral osteotomies are performed to reconstruct the deformity [14]. The most striking point in our case was bone involvement. The nasal bone radix region was completely destructed and it caused the open roof deformity. This deformity was reconstructed with oblique and lateral osteotomy. Bone involvement and destruction have not been previously reported in the literature [15-17].

In conclusion, epidermal inclusion cysts can be found in many parts of the body. Head and neck localizations are rare and most often occur in the jaw. Nasal bone involvement has not been previously reported in the literature. In surgery, the excision of the cyst wall and removal of the tract are sufficient.

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Case report
Olgu sunumu

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Transient neonatal diabetes mellitus caused by a novel mutation in the ABCC8 gene

ABCC8 geninde yeni bir mutasyonun neden olduğu geçici neonatal diyabet

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Abstract

Neonatal diabetes mellitus is a rare monogenic form of diabetes that develops in the first 6 months of life. Neonatal diabetes mellitus is commonly divided in two groups as transient and permanent. Genetic and epigenetic anomalies of chromosome 6q24 locus are responsible for 70% of transient neonatal diabetes mellitus cases. Incidence of macroglossia, umbilical hernia, cardiac and renal anomalies is increased in transient neonatal diabetes mellitus patients. Mutations in the genes (ABCC8 and KCNJ11) encoding two protein subunits (SUR1 and Kir6.2) of ATP-sensitive potassium channels constitute the second common cause of transient neonatal diabetes mellitus. In this article, we present a case with homozygous missense mutation (DNA expression: c1456> T), which was found in the ABCC8 gene in a 3.5-month-old patient with no congenital anomalies, leading to transient neonatal diabetes mellitus.
Keywords: Neonatal diabetes, ATP-sensitive potassium channel, ABCC8 gene

Öz

Neonatal diyabet, yaşamın ilk altı ayında ortaya çıkan ve diyabetin nadir görülen monojenik bir formudur. Genel olarak geçici ve kalıcı diye iki gruba ayrılır. Geçici neonatal diyabetli olguların %70'inden kromozom 6q24 lokusun genetik ve epigenetik anomaliler sorumludur. Bu olgularda makroglossi, umlikal herni, kardiyak ve renal anomali sıklığı artmıştır. ATP duyarlı potasyum kanallarının iki protein alt birimini (SUR1 ve Kir6.2) kodlayan genlerdeki (ABCC8 ve KCNJ11) mutasyonlar geçici neonatal diyabetin ikinci sık nedenini oluşturmaktadır. Bu yazıda konjenital anomalilerin eşlik etmediği, 3.5 aylık bir hastada ABCC8 geninde yeni saptanan ve geçici neonatal diyabete yol açan homozigot missense mutasyonlu (DNA tanımlaması: c1456>T) bir olgu sunulmuştur.
Anahtar kelimeler: Neonatal diabet, ATP duyarlı K kanalı, ABCC8 geni

Introduction

Neonatal diabetes mellitus (NDM) is a monogenic form of diabetes often occurring in the first 6 months of life, characterized by severe hyperglycemia. NDM continues for at least 2 weeks and requires insulin treatment for blood glucose regulation [1]. The frequency of NDM has been reported to be 1:100,000-400,000 [2]. While 90% of NDM cases are transient or permanent, the remaining 10% is associated with mutations that effect organs other than the pancreas and hence present syndromes whose spectrum of clinical and radiologic features provide clues to the cause [3]. Transient neonatal diabetes mellitus (TNDM) typically occurs within the first several days or weeks of life and the recovery often occurs within a mean period of 12 weeks. However, TNDM may recur in approximately half of the cases, particularly in adolescent or young adult patients [4].

In this report, we present an infant with TNDM caused by a novel mutation in the ABCC8 gene who recovered at the age of two years.

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Case presentation

The patient was born at 39 weeks gestation with 3200 g birth weight by normal spontaneous vaginal delivery. The parents of the patient were first-degree cousins. An uncle and aunt had been diagnosed with Type 2 diabetes after the age of 40 years, who had previously undergone oral antidiabetic therapy. At the age of 3.5 months, the patient was admitted to another center with the complaints of vomiting and diarrhea and the patient was referred to our hospital due to persistent hyperglycemia. On initial physical examination revealed that weight was 6 kg (33^{rd} percentile), length was 62 cm (60^{th} percentile), dry mouth, and signs of mild dehydration. There was no dysmorphism. All systems examinations were normal. Laboratory investigation revealed that blood glucose 594 mg/dl, glucose-positive and ketone-negative urine, and normal venous blood gas values (pH: 7.38, HCO3: 20.3 mmol/L). Kidney and liver function tests, electrolytes, and complete blood count (CBC) were all normal and anti-GAD antibodies were negative. Glycosylated hemoglobin level (HbA1c) was 11.2%. However, despite the presence of hyperglycemia, C-peptide (0.52 ng/ml, normal range: 1.1-4.4 ng/ml) and the insulin (2.34 mIU/L, normal range: 2.6-24.6 mIU/L) levels were low. Based on these findings, NDM was considered and thus was started on subcutaneous Neutral Protamine Hagedorn (NPH) insulin therapy with a divided dose of 0.5 IU/kg/day. On day 7, the patient was discharged after the stabilization of blood glucose levels and the parents were informed about diabetes.

As the patient had a normal birth weight and no concomitant congenital anomalies, TNDM Type 2 was considered. Subsequently, in the genetic analysis performed in the molecular genetic laboratory, a homozygous missense mutation was detected in the ABCC8 gene (DNA identification: c.1456C>T). The arginine residue at codon 486 is highly conserved across species and current evidence suggests that the p.R486W mutation is pathogenic. This homozygous missense mutation was not found in the Human Gene Mutation Database (HGMD and Locus-specific databases and was interpreted as "disease-causing'' by the Mutation Taster Software (test score: 0.999) (http://www.mutationtaster.org). Both parents were heterozygous carriers for the same mutation. The patient was not brought for regular follow-up examinations. The result of the genetic analysis for the patient was obtained when the patient reached the age of 18 months. After the detection of the ABCC8 gene mutation, sulfonylurea treatment was planned to start at hospital because of the hypoglycemic side effects of the sulfonylureas. However, her parents refused hospitalization; the treatment was continued with insulin. The HbA1c level was 7.6 when the patient was 18 months of age. During this period, it was noticed that the patient needed less insulin. When the patient reached the age of two years, the insulin treatment was terminated. Currently, the patient is four years old with normal blood glucose and HbA1c levels. Depending on this outcome, the patient was considered as having TNDM. Written informed consent was obtained from the patient's family for publication of this case report.

Discussion

Neonatal diabetes mellitus, which leads to hyperglycemia in the neonatal period, usually manifests with severe dehydration attacks in the first weeks of life and is extremely rare compared to other forms of diabetes. The main reason for severe dehydration in affected children is osmotic diuresis. There is poor weight gain despite good nutrition. If diagnosis is delayed without consideration of potential causes, NDM can lead to severe dehydration and life-threatening ketoacidosis [5]. The case presented in this report presented with signs of acute gastroenteritis and mild dehydration and the diagnosis of NDM was established based on the detection of persistent hyperglycemia. In 70% of TDNM cases, the "imprinted" locus of chromosome 6q24 is responsible for the genetic and epigenetic anomalies. These cases are known as TNDM Type 1 (TNDM1) and mostly recover within a mean period of 3 months, which can also be prolonged to up to 48 months [4,5]. Docherty et al. [5] evaluated TDNM1 patients and reported that macroglossia was detected in approximately 50%, umbilical hernia in 25%, cardiac and renal anomalies in 9%, hand anomalies in 8%, and hypothyroidism in 4% of the patients. Remission, when it occurs, is usually around 3 months and about half of these patients will revert to varying degrees of hyperglycemia in the teen years or later.

A second form of TNDM is named TNDM2 which is distinguished from TNDM1 due to the defects in the 6q24 region and includes the mutations in the ATP-regulated potassium channel involving predominantly mutations in ABCC8 (SUR1) and KCNJ11 (Kir6.2), with a small minority being due to recessive insulin gene mutations and mutations in transcription factor HNF1β and SLCA2A, which together account for 30% of TNDM [3,6]. TNDM2 occurs due to the mutations in the genes regulating insulin secretion rather than the expression of imprinted genes. Compared to TNDM1, it has been shown that TNDM2 patients have a greater birth weight, are diagnosed with diabetes mellitus at a later period, remit later and have recurrence earlier [3,7]. In our patient, since the patient had a normal birthweight and did not have congenital anomalies, TNDM Type 2 was considered. Moreover, the genetic analysis indicated homozygous missense mutation in the ABCC8 gene (DNA identification: c.1456C>T). Literature shows that determining ABCC8 or KCNJ11 mutations in NDM is highly important in the management of the treatment process since most mutations in the ATP-associated potassium channels respond to sulfonylurea treatment [7,8]. Therefore, insulin therapy is the initial treatment of choice in patients diagnosed with NDM, which can be followed by sulfonylurea therapy depending on the diagnostic tests performed for molecular examination [7]. In our patient, we also planned sulfonylurea treatment depending on the results of the genetic analysis but we continued the insulin therapy since the parents of the patient refused hospitalization. Therefore, we could not evaluate the response of the ABCC8 gene mutation in our patient to sulfonylurea treatment, which could be accepted as the limitation of our study.

In conclusion, we determined a novel mutation in the ABCC8 gene leading to TNDM. Mutations in the ABCC8 and KCJN11 genes should be considered in the absence of congenital anomalies, such as macroglossia and umbilical hernia, with a

normal birth weight and a later NDM diagnosis. In such cases, the treatment and the long-term follow-up of the patient should be planned based on the mutation detected in molecular examination.

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Infarction of Percheron artery: A rare case report

Percheron arter enfarktı: Nadir görülen bir olgu sunumu

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Abstract

The thalamus has strategic nuclei, which are divided into different functional classes and manage important cortical functions in harmony with each other. The mechanism proposed in the bilateral paramedian thalamic infarction is an occlusion of a single undifferentiated thalamo-perforating artery which is an anatomic variant. This artery, called the Percheron artery, appears from the first segment of the posterior cerebral artery and gives bilateral medial thalamic perforating branches. Bilateral paramedian thalamic infarction causes specific clinical signs and symptoms such as changes in consciousness ranging from lethargy to coma, vertical gaze paralysis, ocular congestion loss and amnesia. In this case we aimed to present clinical and radiological features of a rare condition with infarction of Percheron artery.

Keywords: Percheron artery, Infarct, Magnetic resonance imaging

Öz

Talamus farklı işlevsel sınıflara ayrılan ve önemli kortikal işlevleri birbiri ile uyum içerisinde yöneten stratejik çekirdeklere sahiptir. Bilateral paramedian talamik infarktta öne sürülen mekanizma bir anatomik varyant olan, santral ayrışmamış tek bir talamo-perforan arterin oklüzyonudur. Percheron arteri olarak isimlendirilen bu arter posterior serebral arterin ilk segmentinden çıkar ve bilateral medial talamik perforan dalları verir. Bilateral paramedian talamik infarkt letarjiden komaya kadar değişen bilinç değişiklikleri, vertikal bakış paralizileri, oküler konverjans kaybı ve amnezi ile karakterli spesifik klinik belirti ve bulgulara neden olur. Bu vakada, nadir görülen bir durum olan percheron arter enfarktının klinik ve radyolojik özelliklerini sunmayı amaçladık.

Anahtar kelimeler: Percheron arter, İnfarkt, Manyetik rezonans görüntüleme

Introduction

The thalami and midbrain arterial supply is provided by perforating branches from the posterior cerebral artery and the posterior communicating artery. Although there are significant variations and overlaps, the thalamic vascular supply is classically categorized into 4 territories: anterior, paramedian, inferolateral and posterior [1]. Gerard Percheron described four anatomical variants of arterial supply to the paramedian thalami, including the artery of Percheron (AOP), a rare variant of paramedian arterial supply in which a single dominant thalamoperforating artery arises from the P1 and bifurcates to supply both paramedian thalami and, in some cases, the rostral mesencephalon [2,3]. In addition to the paramedian thalami, the paramedian thalamic arteries supply the medial areas of the upper brainstem: the interpeduncular nucleus, the decussation of the superior cerebellar peduncles, the medial part of the red nucleus, the third and fourth cranial nerve nuclei and the anterior portion of the periaqueductual grey matter [2,3].

Typical symptoms of bilateral paramedian thalamic infarcts due to occlusion of AOP are vertical gaze palsy, memory impairment, akinetic mutism, confusion, drowsiness, hypersomnolence, or coma. Patients with bilateral paramedian thalamic infarcts accompanied by rostral midbrain lesions also have hemiplegia, cerebellar ataxia, movement dysfunctions and oculomotor deficits [4]. In this case we aimed to present clinical and radiological features of a rare condition with infarction of Percheron artery.

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Case presentation

A 70-year-old woman was brought to the hospital by her relatives because she could not wake up in the morning. On the physical examination of the patient, lethargy, power loss on the right side of the body compared to the left side and right central type facial paralysis were reported. The patient, who could walk, eat, dress herself, know his relatives and speak before, also was complaining about vision impairment. Intracranial hemorrhage was suspected in the patient with hypertension and brain computed tomography (CT) was performed. Brain CT was reported as normal (Figure 1). Diffusion-weighted magnetic resonance imaging (MRI) was performed on the patient who suspected of having a stroke (Figure 2). In the medial section of the bilateral thalamus, more prominent on the right side, the mesencephalon and the periaqueductal area, diffusion restriction consistent with acute infarction was observed by the diffusion weighted MRI (acute infarction in the field of Percheron artery irrigation). She was followed up for 1 day in intensive care unit and two days in a neurology service. When the patient's general condition improved, he was discharged with antiaggregant therapy. Written informed consent for this report was obtained from the patient.

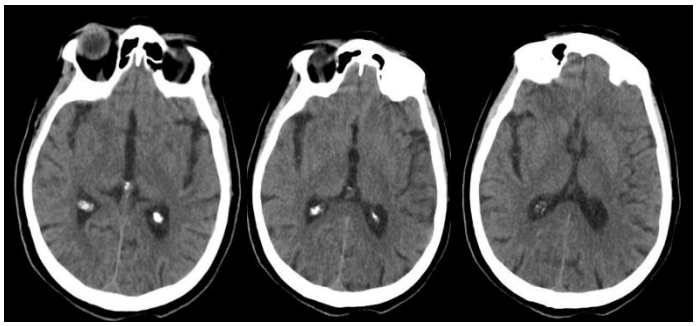

Figure 1: Brain computed tomography was normal.

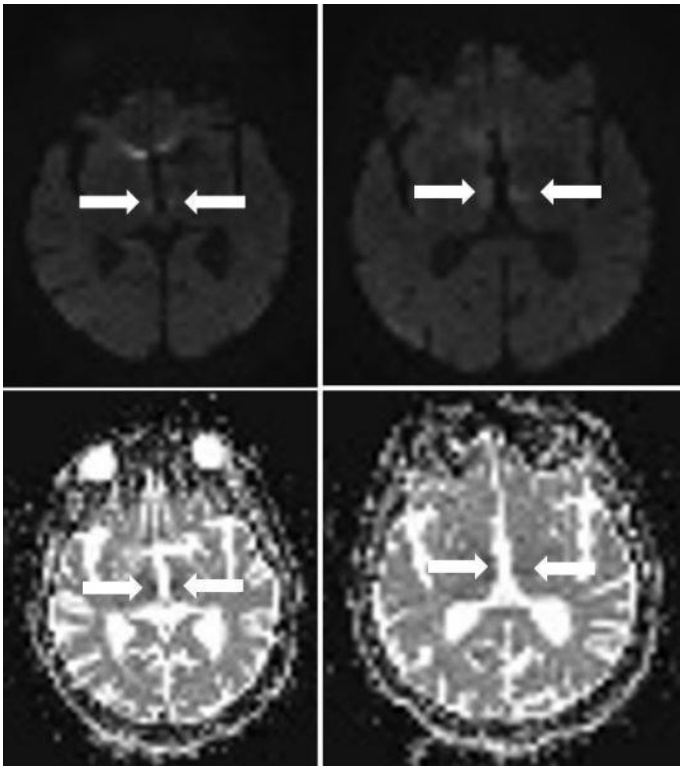

Figure 2: Diffusion-weighted magnetic resonance imaging shows bilateral restriction on medial section of thalami

Discussion

Lazzaro et al. [5] identified 4 ischemic patterns in the Percheron artery occlusion. Approximately 43% of patients showed ischemic damage in bilateral paramedian thalamus and midbrain. In 38% of patients, only the paramedian thalamus was shown to be affected with no damage in the midbrain. Up to 14% of patients have shown that anterior thalamic nuclei are also affected by ischemic damage in addition to paramedian thalamus and upper midbrain. In the least common pattern (5%), bilateral thalamus and anterior thalamus were ischemically affected however midbrain was protected. They also found a sign ("V" sign) which was previously undetected and recognized as a supporting factor in the AOP infarcted cases with midbrain involvement by fluid attenuated inversion recovery (FLAIR) and in the DWI sequences. The "V" sign appears as a distinct pattern of V-shaped hyperintensity on axial FLAIR and / or DWI along the pial surface of the midbrain adjacent to the interpeduncular fossa [2,5]. Treatment of AOP infarction involves thrombolysis and intravenous heparin therapy followed by prolonged anticoagulation [2,6]. However, because of the frequent delay in the diagnosis of AOP infarct, thrombolysis treatment is not available because the therapeutic window is narrow. This is a clear indication that early detection is important for the application of treatment [6]. Among the vascular etiologies of bilateral thalamic lesions, there are the ‘top of the basilar’ syndrome and deep cerebral venous thrombosis [6-8]. Deep cerebral thrombosis may result in bilateral symmetric involvement of the thalamus and basal ganglion in some rare cases [8-10]. Wernicke's encephalopathy, neoplasms, infections, Wilson's disease and osmotic myelinolysis should also be considered in differential diagnosis [8,11]. Several researchers have reported that CT scanning in AOP infarction is normally assessed [3,6,12,13]. However, it has also been reported that the initial MRI is normal. This is an indication that normal MRI at the beginning cannot exclude the diagnosis [13,14]. Therefore, it may be valuable to repeat the radiological evaluation in patients with normal baseline evaluations of suspected AOP occlusion [14].The prognosis of thalamic infarcts in general is relatively good in terms of mortality and permanent motor deficits. A study of the long-term prognosis of 15 patients with AOP infarcts described positive outcomes when the Modified Rankin Scale (mRS) score was ≤2. In this study, 67% of patients with bilateral paramedian thalamic infarction without midbrain involvement received a positive outcome. In contrast, only 25% of patients with combined bilateral thalamic and rostral midbrain infarction had positive results. This suggests that the prognosis of the AOP infarcts, which do not have midbrain involvement, are generally good [15].

Percheron artery is a rare anatomic variant with a single dominant thalamoperforator artery. In addition, involvement of the anterior thalamus is rare. Symptoms of AOP may vary depending on the size and distribution of the infarct. Therefore, these differences in clinical symptoms as well as the presence of radiological difficulties make it difficult to diagnose. In addition, the fact that doctors do not have enough knowledge and awareness about the diagnosis of this condition is another factor that makes it difficult to recognize. Repeated CT and MRI may be important in clinically suspected cases of AOP infarction. We

also believe that case reports such as ours will contribute significantly to the literature in raising awareness about such rare occurrences.

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Magnetic resonance imaging findings of elastofibroma dorsi: A case report

Elastofibroma dorsi manyetik rezonans görüntüleme bulguları: Olgu sunumu

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Abstract

Elastofibroma dorsi (EFD) is a rare soft tissue tumor. In people who work with arm power, excessive rubbing of the scapula to the chest wall or genetic factors is held responsible for its formation. Thoracic computed tomography (CT) and magnetic resonance imaging (MRI) are the most commonly used imaging modalities for diagnose of EFD. MRI and CT imaging can distinguish EFD with the support of clinical findings. It is necessary to avoid unnecessary interventional procedures in asymptomatic elderly patients who are thought to be EFD and only follow-up is sufficient in these cases. This article aimed to present MRI findings of a 61-year-old male patient suffering from EFD with literature review.

Keywords: Magnetic resonance imaging, Chest, Surgery, Elastofibroma dorsi

Öz

Elastofibroma dorsi (EFD), nadir görülen bir yumuşak doku tümörüdür. Kol gücü ile çalışan insanlarda, skapulanın göğüs duvarına aşırı sürtünmesi veya genetik faktörler oluşumundan sorumlu tutulur. Torasik bilgisayarlı tomografi (BT) ve manyetik rezonans görüntüleme (MRG) EFD tanısında en sık kullanılan görüntüleme yöntemleridir. BT ve MRG EFD 'yi klinik bulguların desteği ile ayırt edebilir. EFD olduğu düşünülen asemptomatik yaşlı hastalarda gereksiz girişimsel işlemlerden kaçınmak gerekir ve bu vakalarda sadece takip yeterlidir. Bu yazıda EFD'den muzdarip 61 yaşında bir erkek hastanın MRG bulgularını literatür taraması ile birlikte sunmayı amaçladık.

Anahtar kelimeler: Manyetik rezonans görüntüleme, Toraks, Cerrahi, Elastofibroma dorsi

Introduction

Elastofibroma dorsi (EFD) is a rare, benign, solid, slow-growing, encapsulated soft tissue tumor that is frequently seen in the subscapular region of the chest wall. It cannot be distinguished easily [1,2]. The lesion was named as EFD due to its characteristic subscapular-infrascapular location [1,3]. However, although it is rarely, elastofibroma (EF) can also be seen outside this site. In this situation, only the lesion is called EF and the lesions located in the subcapsular region are called EFD. Other areas reported for EF are lateral chest wall, deltoid muscle, axilla, thoracanter major, around olecranon, foot, tricuspid valve, tuberositas ischi, inguinal region, omentum majus, stomach, rectum, spinal canal, sclera, orbita and mediastinum [1,4-7]. In this report, 61-year-old male patient suffering back pain because of EFD is presented.

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Case presentation

A 61-year-old male patient was admitted to the clinic with complaints of swelling on his back for a long time. On his physical examination, there was a palpable mass on the chest wall. Chest X-ray was normal. Chest magnetic resonance imaging (MRI) was performed to patient. There was a heterogeneous mass lesion on the left side of the chest wall, 90x76x31 mm in size, which was located longitudinally between the ribs and serratus anterior muscle and isointense with muscles. Mass-localization and imaging findings were compatible with EFD (Figure 1). Informed consent was obtained. The mass was totally excised. Histopathologic diagnosis was confirmed as elastofibroma dorsi. The patient had no complaints postoperatively.

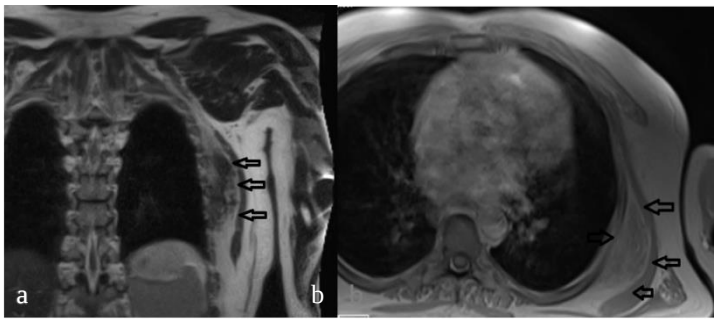

Figure 1: In the chest magnetic resonance imaging, there is a heterogeneous mass lesion which was located longitudinally between the ribs and serratus anterior muscle at the left side and isointense with muscles. a: Coronal plain, b: Axial plain

Discussion

A rare, benign tumor of the connective tissue, EFD is located below the scapula. It emerges as a soft tissue mass that pushes the scapula out [7]. Although it is seen as an asymptomatic swelling, in some cases it causes increasing pain, discomfort or tension in periscapular region in addition to limitation in shoulder movements [2,8]. Rarely, an annoying click during the shoulder movement can be felt. Although it is known to enlarge slowly, Turna et al. [9] reported a case with radiological doubling time as short as 25 days.

Many opinions have been proposed to explain the pathogenesis of the EFD. The first of these is the recurrent minor trauma suggested by Jarvi, that occurs in the subcapular region by rubbing the lower edge of the scapula to the chest wall [8,10].

When the EFD, which is unilateral in 90% of the cases, is bilateral, the two lesions may be synchronous or asynchronous [11,12]. Although it is reported that there are 8-12 times more than females in males, the reason for this frequency is not mentioned [10,13]. It was reported that the lesion is seen after 5th decade and our case was also 61 years old [14].

Chest radiographs, ultrasonography, computed tomography (CT) and MRI are useful for diagnosis. On chest X-ray, a soft tissue tumor can be seen in the chest wall. On ultrasonography, there is a mass-like appearance in the form of linear and curvilinear hypoechoic lines sprinkled in the echogenic fibroelastic background, and the multilayer appearance is characteristic. On CT, EFD is observed as a heterogeneous soft tissue mass and contains linear low density areas depending on adipose tissue. Distinction from environmental muscle plans is poor. In MRI, EFD is in the form of a soft tissue mass with heterogeneous intensity and fat-related linear hypointense opacities. In T1 and T2-weighted images, the form of soft tissue mass with high or medium intensity, straight and curved linear regions is characteristic. According to some authors, biopsy is not necessary for diagnosis [15-17,20,21].

In the differential diagnosis, lipoma, hemangioma, metastatic or primary sarcoma, desmoid tumor, subcapsular bursa prominence, neurofibroma, scatricial fibroma, fibrous histiocytoma, fibromatosis and fibrolipoma should be considered. Needle aspiration or incisional biopsy can be performed to confirm diagnosis; however, excisional biopsy should be preferred [1,3,15,18,20,21].

Surgical total excision of the EFD is the recommended treatment modality. However, It is also recommended to avoid surgery especially if the lesions are asymptomatic and smaller than 5 cm [1,19-21]. There were no reports of local recurrence after surgery except one case [1,3,20,21].

EFD is an under diagnosed lesion which should be considered in the differential diagnosis of soft tissue tumors of the scapular region. Its diagnosis is easy when the clinical presentation and the radiological characteristics are typical. Recently, authors recommend biopsies only for atypical cases.

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