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Dergisi

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3. Lawton J, Ahmad N, Hallowell N, Hanna L, Douglas M. Perceptions and experiences of taking oral hypoglycaemic agents among people of Pakistani and Indian origin: qualitative study. BMJ 2005;30:1247-51. doi:10.1136/bmj.38460.642789.EO

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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

The effect of cold stress on right ventricular function in patients with systemic sclerosis

Skleroderma hastalarında soğuk stresin sağ ventrikülün fonksiyonu üzerine etkisi

Mustafa YILMAZTEPE, Meryem AKTOZ, Ersan TATLI, Armağan ALTUN

ABSTRACT

Objective: Pulmonary hypertension and right heart failure are poor prognostic factors in systemic sclerosis (SSc). The effect of cold stress on pulmonary vasospasm was evaluated in some trials but the results were conflicting. The aim of our study was to determine the effect of cold stress on right ventricular (RV) function.

Materials and Methods: Twenty-four patients with SSc and 24 age and sex-matched healthy controls were enrolled in the study. Transthoracic echocardiography (TTE) was performed to all patients at rest and after peripheral cold exposure. Baseline and after cold stress test TTE results were compared between the groups.

Results: Cold exposure induced changes in particularly right venticular function. Pulmonary acceleration time was significantly shortened in the SSc group (118.8±11.7ms vs 111.3±13.7ms, P<0.001). Tricuspid annular plane systolic excurison and RV fractional area change were also decreased after cold exposure in the SSc group. (23.3±1.6mm vs 21.9±1.9 mm, P<0.001; 46.3±5.8 vs 44.4±5.8,P= 0.007, consecutively). Left ventricular (LV) function did not change after cold stress (LV myocardial performance index (0.42± 0.04 vs 0.42± 0.05), P= 0.748).

Conclusion: Peripheral cold exposure caused a reduction in right ventricular function indicating pulmonary Raynaud's phenomenon as a possible contributing factor.

Keywords: Systemic sclerosis, Echocardiography, Tissue Doppler, Right ventricular function

ÖZ

Amaç: Skleroderma (SSc)'da, pulmoner hipertansiyon ve sağ kalp yetersizliği kötü prognoz göstergesidir. SSc'da soğuk stresin pulmoner vazospazm üzerine etkisi ile ilgili çeşitli çalışmalar yapılmış ancak sonuçlar çelişkili çıkmıştır. Bu çalışma ile SSc hastalarında periferik soğuk stresin sağ ventrikül fonksiyonuna etkisini araştırmayı amaçladık.

Gereç ve Yöntem: Yirmi dördü sklerodermalı, 24'ü sağlıklı toplam 48 kişi çalışmaya alındı. Her iki gruba istirahat ve periferik soğuk stres uygulama sonrasında transtorasik ekokardiyografi yapıldı. İstirahat ve soğuk stres sonrası sol ve sağ ventrikül fonksiyonu karşılaştırıldı.

Bulgular: Soğuk stresin özellikle sağ ventrikül fonksiyonunda değişikliğe yol açtığı görüldü. Pulmoner akselerasyon zamanı skleroderma grubunda anlamlı olarak kısaldı (118.8±11.7ms vs 111.3±13.7ms, P<0.001). Triküspid anuler düzlem sistolik hareketi ve sağ ventrikül fraksiyonel alan değişimi de soğuk stres ile azaldı (23.3±1.6mm vs 21.9±1.9 mm, P<0.001; 46.3±5.8 vs 44.4±5.8,P= 0.007, sırasıyla). Soğuk stres ile sol ventrikül fonksiyonunda değişiklik saptanmadı (sol ventrikül miyokard performans indeksi (0.42± 0.04 vs 0.42± 0.05), P= 0.748).

Sonuç: Periferik soğuk stres, sağ ventrikül fonksiyonunda azalmaya sebep olmuştur ve bu da pulmoner Raynaud fenomeninin pulmoner hipertansiyon gelişmesinde etken faktörlerden biri olabileceğini düşündürmektedir.

Anahtar kelimeler: Sistemik skleroz, Ekokardiografi, Doku Doppler, Sağ ventrikül fonksiyonu.

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Introduction

Systemic sclerosis is a multisystemic connective tissue disease that causes vascular damage, and fibrosis in the skin and in the visceral organs [1,2]. Pulmonary and cardiac involvement are common in systemic sclerosis (SSc). Pulmonary hypertension (PHT) and right heart failure are poor prognostic factors. PHT has worse prognosis in patients with SSc than the other types of PHT [3,4]. Early detection of PHT and right ventricular impairment is very important

because clinical findings become obvious in the advanced stages of the disease. The etiology of PHT in SSc is not well understood. Raynaud's phenomenon is the most common and cardinal feature of SSc seen in about 90% of patients [5]. It is speculated that, the increased vasospastic response as in Raynaud's phenomenon, can also be seen in pulmonary circulation and can be one of the contributing factors in the development of pulmonary hypertension [6-8].

In the present study, our aim was to investigate the effect of cold stress on right ventricular function using echocardiographic techniques.

Materials and Methods

Twenty four patients, followed by the Rheumatology Clinic and met the criteria for SSc as defined by the American College of Rheumatology [9], and 24 age-and sex-matched control subjects were included in the study. Patients with pacemaker implantation, heart failure, right or left bundle branch block, valvular heart disease, with known or suspected coronary heart disease and those using beta-blockers, prostacyclin analogs or ET-1 anatagonists were excluded; Ca – channel blocking agents were withheld one week before the study. All patients were in sinus rhythm and were asymptomatic in terms of heart failure and pulmonary hypertension. Six-minute walking test was used to estimate the functional status of the patients and transthoracic echocardiographic examination was performed to all patients.

All patients gave written informed consent. The study protocol was approved by the Local Ethics Committee and the study was conducted in accordance with the Declaration of Helsinki.

Echocardiographic Examination

Transthoracic echocardiographic examinations (Vivid 7 Pro, GE, Horten, Norway, 2–4 Mhz phased-array transducer) were performed by one cardiologist. All the images were recorded digitally and the measurements were done offline by another experienced operator, who was blinded to the patients group. The average of three values were accepted as measurement. The resting echocardiographic examination was performed after the patients had rested for 10 minutes. Data were recorded from the average of three cardiac cycles. Following the baseline examination, cold stress was applied in a similar technique as the previous studies [10 ,11]. The patients' right hand were immersed into cold water (5-10°C) up to ten minutes if tolerated. The echocardiographic measurements were recorded before the patients took their hands out of the cold water. All of the measurements were performed in accordance with the guidelines [12].

Left ventricle measurements: End-systolic and end-diastolic diameters, septal and posterior wall thickness were measured from parasternal long axis view using M-mode. To calculate biplane left ventricle ejection fraction (LVEF) end-diastolic and end-systolic volumes were measured from apical long axis 4 chamber and 2 chamber views. Left atrium diameter was measured using M-mode from parasternal long view.

Right ventricle measurements: Right ventricle end-diastolic and end-systolic area were measured from apical 4 chamber view to calculate right ventricular fractional area change (RVFAC). Right ventricular free wall thickness was measured from subcostal view. Tricuspid annular plane systolic excursion (TAPSE) was measured by M-Mode echocardiography in the apical four chamber view.

Pulsed-wave Doppler measurements: To measure early (E) and late (A) diastolic wave peak velocities, mitral and tricuspid inflow patterns were obtained from an apical four chamber view. Pulmonary acceleration time (PAAT) was measured from right ventricular outflow tract Doppler recordings.

Tissue Doppler measurements: Pulsed-TDI volume samples were gathered from lateral side of LV annulus and free wall side of the RV. Peak systolic (S'), early (E') and late (A') diastolic velocities were obtained from the mitral lateral, and tricuspid free wall annuluses. Isovolumic relaxation time (IVRT), isovolumic contraction time (IVCT) and ejection time (ET) of both ventricles were measured. Left ventricle myocardial perfomance index (LVMPI) and right ventricle myocardial performance index (RVMPI) were calculated using the formula (IVCT+IVRT)/ ET.

Global ventricular function were assessed by myocardial performance index. We used PAAT, for estimation of pulmonary hypertension [13].

Pulmonary acceleration time, IVCT and IVRT, parameteres that associated with time, were adjusted according to heart rate using the formula that Bazett described ($QTc = QT/\sqrt{RR}$) for corrected QT mesurement [14].

Interobserver and intraobserver variability was assessed for PAAT, TAPSE and RV-IVRT from the recorded images of randomly chosen 10 patients.

Statistical Analysis

Statistical analysis was performed by using SPSS 22.0. The distribution of variables were evaulated with Kolmogorov Smirnov test. Categorial data were given as counts (percentages) and were analyzed using the Chi-square test. All continuous variables were expressed as mean ± standard deviation or median (min-max) and analyzed with Mann-Whitney *U* test or independent samples t test as appropriate. Baseline and cold stress echocardiographic measurements were compared using Wilcoxon t test. Inter-observer and intra-observer reliability were evaluated using interclass and intraclass correlation coefficients. P values <0.05 were accepted to indicate statistical significance.

Results

Baseline demographic and clinical characteristics

Demographic data of the subjects were given in Table I. The mean disease duration was 6.5±4.8 years (range, 1 – years). There were no differences between groups in terms of age, sex, body mass index (BMI), systolic and diastolic blood pressures, heart rate and six minute walking distance (P > 0.05).

Table I. Clinical and laboratory characteristics of the study population

	Controls	Scleroderma	
	(n=24)	(n=24)	P
Age (years)	44.3±8.0	46.8±12.3	0.160
Female/male, n/n	2/22	2/22	1
BMI, kg/m2	27±4.9	26.2±4.9	0.535
Heart rate, beats/m	80.2±11.0	79.8±8.8	0.812
SBP, mmHg	123.1±9.4	125.9±7.8	0.374
DBP, mmHg	68.2±6.4	71.3±6.5	0.131
Six-minute walking test, m	515.4±37.7	531.8±57.9	0.725
Disease duration, years	-	6.5±4.8	-
ACE inhibitor,n	0	4	0.489
Oral antidiabetic,n	0	2	0.109
Statin,n	0	2	0.489

ACE: Angiotensin Converting Enzyme, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

Echocardiographic Characteristics

The resting echocardiographic values are given in Table II. LVEF, LV end-diastolic dimension, LV mass index, LA and RA dimensions, LV E/E' and LV S' were similar in both groups. LVMPI was significantly increased in the control group when compared to the SSc group (0.43(0.35-0.54) vs 0.34(0.27-0.41), P<0.001). None of the patients had tricuspid jet velocity more than 2.8m/s, but in about 30 % of the study population tricuspid jet could not be visualized.

Table II. Resting echocardiographic characteristics of the study population.

	Controls	Scleroderma	
	(n=24)	(n=24)	P
LVEF, %	65.5 (58-77)	64.0(56-74)	0.305
LA diameter, mm	37.0 (26-40)	37.0 (28-43)	0.487
LVEDD, mm	46 (40-53)	45(38-53)	0.071
Septum thickness, mm	9 (7-10)	10(8-11)	0.138
PW, mm	9 (7-10)	9 (7-10)	0.228
LV mass, g/m2	73.5 (55-104)	74.8 (55-117)	0.415
LV E/E'	5.4 (3-9)	6.0 (4-16)	0.056
LV MPI	0.34 (0.27-0.41)	0.43 (0.35-0.54)	<0.001
RA diameter, mm	30.5 (25-36)	29.0 (27-31)	0.359
RV wall, mm	3.4 (3-4)	4.5 (3-6)	<0.001
SPAP,mmHg	24.0 (20-29)	26.0 (24-35)	0.004
RVFAC, %	49.0 (41-58)	46.5 (34-56)	<0.001
TAPSE, mm	26.0 (22-31)	23 (21-26)	0.002
RV IVCT, ms	48 (37-55)	57 (48-74)	<0.001
RV S', cm/s	15 (12-21)	13 (10-18)	<0.001
RV MPI	0.31 (0.26-0.46)	0.42 (0.33-0.53)	<0.001
RV IVRT, ms	41 (37-49)	59 (44-85)	<0.001
PAAT, ms	140 (118-170)	120 (96-140)	<0.001

E: Pulsed wave transmitral early diastolic velocity EF: Ejection fraction, E': Early myocardial diastolic velocity, IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, LA: Left atrium, LVEDD: Left ventricle end diastolic diameter, LV:Left ventricle, MPI: Myocardial performance index, PAAT: pulmonary artery acceleration time. PW: Posterior wall, RA: Right atrium, RV: Right ventricle, RVFAC: Right ventricle fractional area change, S': Systolic myocardial velocity, SPAP: Systolic pulmonary artery pressure, TAPSE: Tricuspid annular plane systolic excursion.

Pulmonary acceleration time, RVFAC, TAPSE and Rv S' were all significantly reduced in patients with SSc (120(96-140) vs 140(118-170) P<0.001, 46.5(34-56) vs 49(41-58), P=0.038, 23(21-26) vs 26(22-31) P=0.002, 13(10-18) vs 15(12-21) P<0.001, respectively). Additionally, IVCT and IVRT values were significantly higher in SSc group (57(48-74) vs 48(37-55) P<0.001, 59(44-85) vs 41(37-49) P<0.001). RV MPI, which shows globally systolic and diastolic dysfunction, was also increased compared to control group (0.42(0.33-0.53) vs 0.31(0.26-0.46), P<0.001).

Cold Stress

Cold stress echocardiographic measurements of the groups were given in Table III. RV systolic function changed in patients in the SSc group after cold stress (RVFAC, TAPSE, IVCT and PAAT), whereas no deterioration of RV function was observed in the control group. Left ventricular function was compared between the control group and SSc group during rest and after cold stress. There were no statistically significant differences in the left ventricular systolic and diastolic function in both groups during cold stress compared with the baseline values.

Reliability

Intra-observer reliability, as assessed by intra-class correlation coefficients for PAAT, RV IVRT and TAPSE, were respectively 0.96 (95% CI 0.85-0.99), 0.93 (95% CI 0.65-0.98) and 0.97 (95% CI 0.89-0.99). Inter-observer reliability, as assessed by inter-class correlation coefficients for PAAT, RV IVRT and TAPSE, were respectively 0.88 (95% CI 0.60-0.97), 0.86 (95% CI 0.52-0.96) and 0.96 (95% CI 0.86-0.99).

Discussion

The present study demonstrated that cold stress caused a reduction in right ventricular function indicating cold exposure may cause intermittent pulmonary vasospasm.

Myocardial involvement in SSc is associated with poor prognosis. Biventricular systolic and diastolic impairment has been shown in several studies [14-16]. The mechanism of right and left ventricle involvement can be different. Fibrosis due to collagen deposition is the main mechanism underlying left ventricular dysfunction, but interstitial lung disease and pulmonary hypertension also play an important role in the etiology of right ventricular dysfunction. Subclinical left ventricle dysfunction is not a rare finding [17-19]. In a recently published article of Spethmann et al., subclinical left ventricle impairment was shown using speckle-tracking echocardiography in patients with SSc [20]. Faludi et al., demonstrated that left ventricular diastolic dysfunction was highly prevalent in patients with SSc and was associated with increased risk of mortality [21]. In parallel with these studies, in the present study we also demonstrated that diastolic and systolic function of

Table III. Comparison of baseline and after cold stress echocardiographic data.

	Control (n=24)			Scleroderma (n=24)		
	Rest	Stress	P	Rest	Stress	P
HR, beats /m	80.2±11.0	82.3±11.7	<0.001	79.8±8.8	81.3±8.4	<0.001
PAAT, ms	142.0±13.5	141.0±15.4	0.116	118.8±11.7	111.3±13.7	0.001
PAATc, ms	163.4±15.6	161.9±17.5	0.544	136.6±13.8	127.9±16.1	<0.001
RVFAC,%	49.62±4.8	49.41±5.1	0.667	46.3±5.8	44.4±5.8	0.007
TAPSE, mm	25.75±2.77	25.70±2.70	0.909	23.3±1.6	21.9±1.9	<0.001
RV S', cm/s	15.04±1.75	15.16±1.55	0.512	13.5±1.8	13.2±1.7	0.210
RV IVRT, ms	41.62±3.3	42.5±4.5	0.074	58.7±7.8	59.2±8.6	0.463
RV IVRTc, ms	47.4±3.7	47.3±3.3	0.629	67.5±9.9	67.2±9.4	0.794
RV IVCT, ms	47.0±4.6	47.7±3.7	0.069	58.9±7.0	61.8±7.7	0.009
RV IVCTc	54.3±7.0	55.4±6.5	0.110	68.2±10.2	69.1±9.4	0.217
RV MPI	0.31±0.04	0.32±0.04	0.084	0.41±0.04	0.42±0.04	0.149
LVEF,%	66.3±4.9	65.8±4.7	0.175	64.9±4.2	64.4±4.1	0.327
LVE/E'	5.64±1.6	5.74±1.5	0.886	6.9± 2.6	6.9±2.10	0.548
LV S', cm/s	8.5±1.74	8.37±1.61	0.328	8.70±0.7	8.40±0.7	0.262
LV MPI	0.34±0.04	0.35±0.04	0.635	0.42±0.04	0.42±0.05	0.748

E: Pulsed wave transmitral early diastolic velocity, E': Early myocardial diastolic velocity, HR: Heart rate, IVCT: Isovolumetric contraction time, IVCTc: Isovolumetric contraction time corrected, IVRT: Isovolumetric relaxation time, IVRTc: Isovolumetric relaxation time corrected LV: Left ventricle, MPI: Myocardial performance index, PAAT: Pulmonary artery acceleration time, PAATc: Pulmonary artery acceleration time corrected, RV: Right Ventricle, RVFAC: Right ventricle fractional area change, RV S': Right ventricle systolic myocardial velocity TAPSE: Tricuspid annular plane systolic excursion.

the left ventricle, as shown by tissue Doppler derived MPI, were decreased compared to the control group.

Right ventricular dysfunction in SSC is associated with poor prognosis and have more prognostic relevance than left ventricular involvement [22]. It is usually due to pulmonary hypertension caused by vascular or interstitial lung disease, additionally ischemia and fibrosis are the other possible factors that cause right ventricular dysfunction. Durmus et al., used speckle-tracking echocardiography and showed right ventricular impairment in SSc patients without pulmonary hypertension [23]. Huez et al., also demonstrated right ventricular diastolic dysfunction and claimed latent pulmonary hypertension as a possible cause [24]. Lindqvist et al., studied right ventricular function in patients with SSc and revealed impaired right ventricular diastolic function and reduced PAAT compared to control group [25]. Based on these results they implied that the cause of right ventricular diastolic impairment might be intermittent pulmonary hypertension.

There is exaggerated response to cold stimuli in SSc. Raynaud's phenomenon (RP) is the cardinal feature of SSc. Similar to RP cold induced vasospasm was demonstrated in renal [26] and coronary arteries in a subgroup of patients [27-30]. Pulmonary hypertension develops in about 10-15 % of patients with SSc. Repetitive pulmonary vasospasm has been affirmed as a possible mechanism of PHT in SSc. Whilst it is known that cold exposure increases sympathetic activation and systemic vascular resistance, the context of cold induced pulmonary vasospasm has not been proven yet [10]. Increased phosphodiesterase-1C expression and impaired production of prostaglandin I2 and an imbalance between prostaglandin I2 and thromboxane A2 were shown as the underlying mechanism of cold induced pulmonary vasospasm in patients with RP [31]. The effect of cold exposure on pulmonary circulation has been assessed in several studies with different methods and conflicting results. Several authors reported a reduction in the diffusing capacity of the lung for carbon monoxide (DLCO) [32,33]. They claimed that the decrease in DLCO after cold exposure indicated a reduction in capillary blood volume, suggesting pulmonary vasospasm. However, Lampert et al., also demonstrated a decrease in DLCO but also a reduction in mPAP and pulmonary vascular resistance, and pointed out that intrapulmonary blood redistribution may be the underlying mechanism that caused diminished DLCO [34]. Mukerjee et al., evaluated right ventricular function using cardiac catheterization after 2 minutes of cold stress, and found no differences whereas Sakamoto et al., found an increase in pulmonary hypertension in a subgroup of patients [11,8]. In a recently published study, Keir et al., implied pulmonary vasospasm as a possible explanation to worsening symptoms in a subgroup of patients after exposure to cold [6].

Detection of patients with cold induced pulmonary vasospasm and demonstrating the relation with overt pulmonary hypertension may provide a new perspective in the prevention of SSc related pulmonary hypertension. To the best of our knowledge, this is the first study investigating right venticular function after cold stress using echocardiography. In the present study, cold stimuli caused a significant reduction in the parameters of right ventricular systolic function, as TAPSE, RVFAC, IVCT and PAAT, however, there were no changes in left ventricular function after cold stress. One can argue that, whether such a short time of cold exposure can change RV function or not. Pulmonary circulation is a low pressure system and RV thickness is about 1/3 of LV, causing RV more sensitive to changes in afterload. Ischemia, fibrosis and pulmonary hypertension are the possible underlying mechanisms for the deterioration in right ventricular function in SSc, however as shown in the present study, solely decrease in RV function after cold stress, cannot be explained by cardiac Raynaud's phenomenon, ischemia or fibrosis. These results indicated that cold induced pulmonary vasospasm may be the cause of changes in RV function, however, further larger scale studies with follow-up are needed to put forth the association between intermittent pulmonary vasospasm and pulmonary hypertension and the underlying patophysiological mechanism.

The first limitation of our study is that we evaluated right ventricular function by transthoracic echocardiography. Despite all efforts, as in all studies based on echocardiography, echocardiograpic measurements have high intra and inter observer variability and we cannot exclude that the significant but small changes found in the present study could be a result of intra-observer variability. Cardiac MRI or right heart catheterization would have given us more objective data but we chose echocardiography since it is a non-invasive, and a low-cost method and can be used for screening. Novel echocardiographic techniques as strain imaging and 3D echocardiographic imaging could also be used, but unfortunately we did not have that opportunity. The second limitation of the present study is that, although the measurements were done offline by a cardiologist who was

blinded to the patients groups, the operator who performed the echocardiography was not blinded. The other important limitation of our study is small number of patients, and lack of follow-up of patients.

Conclusion

Cold stress induced pulmonary RP may contribute to the development of PHT. Although, we were able to demonstrate that peripheral cold exposure caused a reduction in isolated right ventricular function by transthoracic echocardiography the lack of right heart catheterization or novel imaging modalities to assess right heart function, prevented us to imply more definitive conclusions. Further studies with larger sample size and follow-up are needed to detect the effects of cold stress on PHT and right heart function.

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Surgical outcomes of patients with non-small cell lung cancer following neoadjuvant treatment

Neoadjuvant tedavi sonrası küçük hücreli dışı akciğer kanseri olan hastaların cerrahi sonuçları

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ABSTRACT

Objective: Although, anatomical resection of non-small cell lung cancer (NSCLC) following neoadjuvant therapy is still controversial, it is a widely accepted approach for thoracic surgery practice. The aim of this study is to briefly evaluate clinical results, long term survival, and factors affecting survival of the patients with locally advanced NSCLC, pancoast tumour and lung cancer with solitary brain metastasis, who have been operated at our institution following neoadjuvant therapy.

Materials and Method: Between March 2006 and March 2012, 70 patients with NSCLC diagnosis who underwent anatomic pulmonary resection following neoadjuvant therapy were included in the study.

Results: A three year survival (39%) and a 5-year survival (29%) were 16±6.8 and 37±9.89 months, respectively. The mean survival was found to be 37.15±3.06 months. When survival rate was evaluated according to localization of tumor, it was lower in central and left upper lobe tumors compared to other anatomical localizations (P=0.042). The mean 5-year survival times were 50.00±5.65 months in stage 0 patients, 35.39±5.85 months in stage 1 patients, 37.40±6.89 months in stage 2 patients and 21.44±3.10 months in stage 3 patients.

Conclusion: We can achieve significant survival results by the anatomical pulmonary resection following neoadjuvant therapy.

Keywords: Non-small cell lung cancer, Neoadjuvant therapy, Chemotherapy, Radiotherapy, Surgery

ÖZ

Amaç: Neoadjuvan tedaviyi takiben küçük hücreli dışı akciğer kanseri (KHDAK)'nin anatomik rezeksiyonu halen tartışmalı olsa da, torasik cerrahi uygulamada yaygın kabul gören bir yaklaşımdır. Bu çalışmanın amacı, neadjuvan tedaviyi takiben kurumumuzda cerrahi operasyon uygulanan lokal ileri evre KHDAK'i, pancoast tümörü ve soliter beyin metastazı olan akciğer kanseri hastalarının klinik sonuçlarını, uzun dönem sağkalımını ve sağkalımı etkileyen faktörleri kısaca değerlendirmektir.

Gereç ve Yöntem: Mart 2006 ve Mart 2012 tarihleri arasında neoadjuvan tedaviyi takiben anatomik pulmoner rezeksiyon uygulanan 70 KHDAK tanılı hasta çalışmaya alındı.

Bulgular: Üç yıllık sağkalım (% 39) ve 5 yıllık sağkalım (% 29) sırasıyla 16±6,8 ve 37±9,89 ay idi. Ortalama sağ kalım 37,15±3,06 ay olarak bulundu. Sağkalım oranı tümörün anatomik lokalizasyonuna göre değerlendirildiğinde santral ve sol üst lob tümörlerinde daha düşüktü (P=0,042). 5 yıllık ortalama sağkalım süreleri evre 0 hastalarda 50,00±5,65 ay, evre 1 hastalarda 35,39±5,85 ay, evre 2 hastalarda 37,40±6,89 ay ve evre 3 hastalarda 21,44±3,10 ay idi.

Sonuç: Neoadjuvan tedaviyi takiben anatomik pulmoner rezeksiyon ile önemli sağkalım sonuçları elde edebiliriz.

Anahtar kelimeler: Küçük hücreli dışı akciğer kanseri, Neoadjuvan tedavi, Kemoterapi, Radyoterapi, Cerrahi

Introduction

Although, anatomical resection of non-small cell lung cancer (NSCLC) following neoadjuvant therapy is still controversial, it is a widely accepted approach for thoracic surgery practice. The use of trimodality treatment has increased after publications supporting neoadjuvant therapy [1,2].

Oncological control of locally advanced stage III NSCLC is extremely difficult, despite all new treatment modalities. Recent studies have shown that neoadjuvant chemoradiotherapy positively affects the rates of resectability in patients with locally advanced stage III NSCLC and offers better results than the surgery-only groups [3]. Publications

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regarding the effect of neoadjuvant therapy on the pancoast tumours also favored trimodality treatment [4,5].

The aim of this study is to briefly evaluate clinical results, long term survival, and factors affecting survival of the patients with locally advanced NSCLC, pancoast tumour and lung cancer with solitary brain metastasis, who have been operated at our institution following neoadjuvant therapy.

Materials and Methods

Between March 2006 and March 2012, 70 patients with NSCLC diagnosis who underwent anatomic pulmonary resection following neoadjuvant therapy were retrospectively reviewed. Ninety-one patients undergoing neoadjuvant therapy were included in the study, but only 76.9% (n=70) of them underwent anatomical pulmonary resection. Twenty-one patients were excluded from the study due to the progression or no change on their nodal status and size of the tumour despite the neoadjuvant treatment.

The inclusion criteria were as follows: 1. radiological or histological diagnosis of a single-station mediastinal lymph node involvement, 2. centrally located or locoregional advanced stage NSCLC, 3 pancoast tumour, 4 synchronous solitary brain metastasis.

The exclusion criteria were: 1. chemotherapy or radiotherapy for other malignancies, 2. adjuvant chemotherapy and/or radiotherapy, 3. presence of unresectable tumor despite neoadjuvant therapy, 4. psychologically unsuitability for completing the regimen.

The mediastinal status of the patients was confirmed by mediastinoscopy for histological diagnosis and radiologically interpreted by computed tomography (CT) or positron emission tomography (PET) before neoadjuvant treatment.

Neoadjuvant chemotheraphy regimen

Cisplatin (60-75 mgr/m2) + docetaxel (75 mgr/m2) or cisplatin (60-75 mgr/m2) + gemcitabin (1gr/ m2) in standard treatment protocol was received as total 6 cycles, of which 3 cycles preoperatively and 3 cycles postoperatively.

Neoadjuvant radiotheraphy regimen

4000-4600 cGy of radiotheraphy with 200 cGy daily fraction dosages was performed preoperatively for clinically T4 (Ct4) tumours and total dosage was completed to 6000-6600 cGy postoperatively. The protocol was different for pancoast cases. 4600 cGy of radiotheraphy with 250 cGy daily fraction dosages was performed preoperatively and total dosage was completed to 6600-7000 postoperatively.

Evaluation after neoadjuvant treatment

All cases were re-evaluated according to the surgical and radiological aspects after the neoadjuvant treatment. CT and PET were used for the majority of the cases but re-mediastinoscopy was required in few selected patients for the evaluation. Patients who had no lymph node invasion or metastasis were selected for anatomical pulmonary resection.

All data were evaluated in terms of age, sex, comorbidities, smoking , FEV1 value, localization of the tumour, type of the resection, regimen type, clinical staging before and after treatment, pathological staging after surgery, histological type, clinical response, morbidity, mortality, lenght of hospital stay, recurrence, clinical follow-up and survival. This study was approved by the Institutional Ethics Committee.

Statistical Analysis

Descriptive statistics for continuous variables were reported as means and standard deviation (SD) with 95 % confidence interval (CI). Apart from descriptive statistical methods, Kruskal Wallis was used for the comparison between groups. The Mann-Whitney U test was used to compare differences between two independent groups. Wilcoxon sign test was used for intra-group comparisons. Chi-square test, Yates corrected chi-square test and Fisher's exact test was used in the comparison of qualitative data. Kaplan-Meier analysis and Log Rank (Mantel-Cox) were used for survival analysis. In this study, the maximum type I error was 0.05, and the level of significance was accepted as $P< 0.05$. All analyses were performed using Number Cruncher Statistical System (NCSS) and Power Analysis and Sample Size (PASS) statistical software (Utah, USA).

Results

Study was designed with 91 patients receiving neoadjuvant treatment. Unfortunately, 21 inoperable patients who had progression despite neoadjuvant therapy were excluded from the study. The age of the patients varied from 41 to 76

years (mean 56.31±7.36 years). Sixty-five of the cases were male (92.9%) and 5 (7.1%) were female.

In terms of neoadjuvant treatment, fifty patients (71.4%) were treated with chemotherapy, 11 patients with (15.7%) chemoradiotherapy, and 9 patients with (12.9%) radiotherapy. Chemotherapy and radiotherapy regimens are shown in Table I.

Table I. Chemotherapy and radiotherapy regimens

		Min-Max	Mean±SD
Radiotherapy Dosage		30.00–66.00	47.20±10.23
		N	%
Chemotherapy Cycle	2	3	4.9
	3	51	83.6
	4	3	4.9
	6	4	6.6
Type of Chemotherapy	Cisplatin-Docetaxel	52	85.2
	Cisplatin-Gemcitabin	6	9.8
	Cisplatin-Paclitaxel	2	3.2
	Cisplatin	1	1.6

The exclusion of N2 disease after neoadjuvant therapy was provided by mediastinoscopy in 37 (53%) patients and radiological evaluation in 33 (47%) patients. Clinical staging is described in Table II.

Table II. Clinical staging

		Before Neoadjuvant Therapy		After Neoadjuvant Therapy	
		N	%	N	%
T	T0	-	-	24	34.2
	T1	9	12.8	20	28.5
	T2	22	31.4	17	24.2
	T3	24	34.2	9	12.8
	T4	15	21.4	-	-
N	N0	17	24.3	26	57.8
	N1	2	2.9	1	2.2
	N2	50	71.4	17	37.8
	N3	1	1.4	1	2.2
M	M0	67	95.5	44	100
	M1	3	4.5	-	-
Clinical Staging	2B	7	10.0		
	3A	54	77.1		
	3B	6	8.6		
	4	3	4.3		

T:Tumour, N: Nodal cT4:clinically T4, M: Metastasis

Tumors were located at the right upper lobe in 30 patients (43.5%), hilar in 16 patients (23.2%), left upper lobe in 15 patients (21.7%), left lower lobe in 5 patients (7.2%) and right lower lobe in 3 patients (4.3%).

Resection following neoadjuvant treatment was planned for 30 patients (42.8%) with pathological N2 invasion, 19 patients (27.1%) with radiological N2 invasion, 10 patients (14.2%) with cT4 tumor, 8 patients (11.4%) with pancoast tumour, and 3 patients with solitary brain metastasis. Lobectomy was conducted in 37 patients (52.9%), pneumonectomy in 22 patients (31.4%) and bilobectomy in 11 patients (15.7%). 6 of the patients (8.6%) underwent sleeve resection.

On TNM staging after resection, there were 13 patients in stage IA (18.5%), 7 in stage IB (10%), 9 in stage IIA (12.8%), 13 in stage IIB (18.5%), 18 in stage IIIA (25.7%) and 1 in stage IIIB (1.4%). The pathological results of the other 9 patients (12.8%) were reported as complete response. Of 70 patients included, 65 patients (92.6%) had R0 resection and 5 patients had R1 resection. No tumor was detected in the histological examination of 9 patients (12.8%) due to the complete response to treatment. Pathological staging is shown in Table III.

Table III. Pathological staging

		After Surgery	
		N	%
T	T0	9	12.8
	T1A	18	25.7
	T1B	6	8.5
	T2A	10	14.2
	T2B	1	1.4
	T3	20	28.5
	T4	6	8.5
N	N0	45	64.3
	N1	14	20.0
	N2	11	15.7
M	M0	70	100
Pathological Staging	0	9	12.8
	1A	13	18.5
	1B	7	10
	2A	9	12.8
	2B	13	18.5
	3A	18	25.7
	3B	1	1.4

T:Tumour, N: Nodal cT4:clinically T4, M: Metastasis

When the pathological staging after neoadjuvant therapy was compared with the clinical staging before neoadjuvant therapy, there were complete response in 9 patients (13%), partial response in 40 patients (57%), no response in 20 patients (29%), and progression in one patient (1%).

The 30-day morbidity rate was 36%. The most common causes of major morbidity were pneumonia (11.4%) and postoperative bleeding (10%). The most common cause of minor morbidity was prolonged air leak (12.8%). No statistical difference was detected between the types of neoadjuvant treatment and air leak (P>0.05). The postoperative 30-day mortality rate was 4% (3 cases). No statistical difference was detected between type of neoadjuvant therapy, type of resection and postoperative early mortality (P>0.05). Intensive care unit (ICU) was required for 14 patients (20%) in the postoperative period. No statistical difference was detected between the ICU necessity and the type of the resection (P>0.05).

Mean length of the hospital stay was 8.851 ± 1.10 days (2-74 days) and mean follow-up period was 18.86±18.28 months (1-60.5). Recurrence was detected in 21 patients (30%) during the follow-up period. Fourteen of these patients (20%) were distant metastasis, and 7 (10%) were local metastasis. Recurrence rate was high in patients who received chemotherapy as neoadjuvant therapy and was statistically significant (P<0.05). There was no statistically significant difference in patients who received radiotherapy or chemoradiotherapy (P>0.05). In terms of resection type, recurrence rate was statistically significant only in the patients who underwent lobectomy (P<0.05).

During the follow-up period, we experienced cancer related mortality in 33 (47%) patients and non-cancer mortality in 3 patients (4%). A 3-year survival time (39%) and 5-year survival time (29%) were 16±6.8 and 37±9.89 months, respectively. Mean survival time was 37.15±3.06 months. When the survival rates were evaluated according to localization of the tumor, the central and left upper lobe tumours had lower survival rates than the others (P=0.042).

In terms of neoadjuvant indication and survival, the mean survival was 43.99±8.54 months in cT4, 37,48±4,17 months in N2 disease, 22.05±9.34 months in pancoast and 16.33±3.08 months in solitary brain metastasis. Neodajuvant indication and survival is shown in Figure 1.

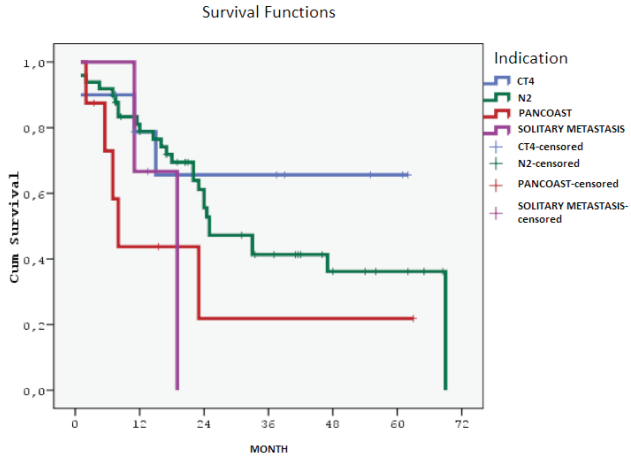

Figure 1. Survival rates according to indication

Regarding the relation between neadjuvant treatment type and survival; the mean survival was 40.67±4.08 months in chemotherapy, 24.49±9.96 months in radiotherapy and 19.88±4.25 months in chemoradiotherapy. Neodajuvant treatment type and survival is shown in Figure 2.

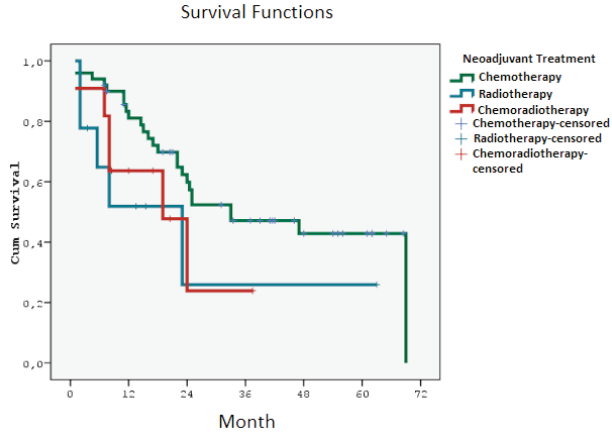

Figure 2. Relationship between type of neoadjuvant treatment and survival rate

If we examine the survival rates according to the type of resection, mean survival time was 33.35±4.59 months in lobectomy, 40.81±7.0 months in pneumonectomy and 36.39±6.89 in bilobectomy. Mean survival was significantly lower in left pneumonectomy (18.08±2.55 months) in comparison to right pneumonectomy (56.18±9.70 months) (P=0.021).

In the evaluation of a 5-year follow-up period; mean survial time was 50.00±5.65 months in stage 0. 35.39±5.85 months in stage 1, 37.40±6.89 months in stage 2, and

21.44±3.10 months in stage 3. Pathological staging and survival is shown in Figure 3.

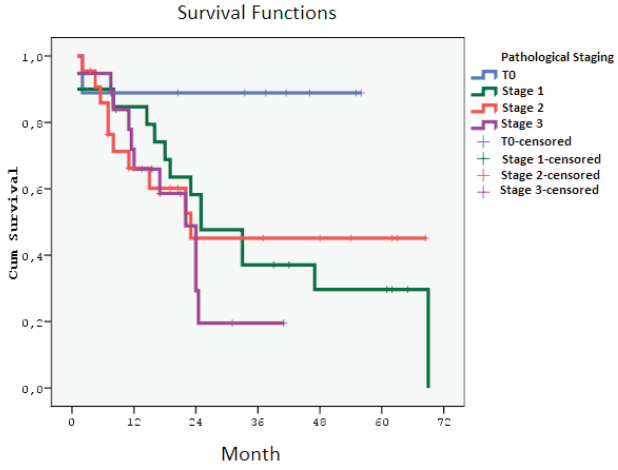

Figure 3. Pathological staging and survival rates

Discussion

The determination of appropriate patients to benefit from surgical resection after neoadjuvant therapy is still controversial. Some authors reported that clinical response after neoadjuvant treatment and the eradication of the disease with the operation were sufficient for the surgical outcome [6,7].

It is put forward that neoadjuvant treatment increases the resectability rates by taking part in the reduction of the tumour size and helping in annihilation of the micrometastatic disease. It is also important that neoadjuvant treatment can be performed in the highest dosages and easily tolerated when compared to adjuvant treatment [8]. It is difficult to determine the proper treatment modality because of having clinically heterogeneous pattern. Radiologically suspicious or histologically proven N2 disease, inoperable disease due to tumor size or localization, pancoast tumor or solitary brain metastasis were included in the study.

Resection of N2 disease after neoadjuvant chemotherapy increases long-term survival compared to medical treatment alone [7,9]. Cerfolio and colleagues reported that a 5-year survival rate after resection of non-suspicious N2 disease following neoadjuvant treatment was 42% [10]. In our study, a 5-year survival rate for N2 disease patients who underwent resection following neoadjuvant treatment was 46.9%.

Takeda et al., published a study reporting that tumour localization was not effective on survival and prognosis [9]. In contrast to this publication, the survival rates of the central and left upper lobe tumors were found to be significantly lower in our study (P=0.042).

The addition of preoperative radiotherapy to chemotherapy is thought to provide more successful outcome and more aggressive locoregional control than neoadjuvant chemotherapy alone [6]. High preoperative radiation dose increases the incidence of complete response [10,11]. Jacklitsch and colleagues pointed out that complete resection following neoadjuvant treatment have the key role in the increased long-term survival [12]. In our study, we did not detect a statistical difference between the types of neoadjuvant treatments and survival rates (P=0.122). Although, it was not statistically significant, survival rates were higher in the patients who received neoadjuvant chemotherapy alone.

In terms of survival rates according to the type of resection, no statistical difference was detected in our study (P=0.579). Deslauriers and colleagues reported that patients with N2 disease who underwent sleeve lobectomy or pneumonectomy after chemoradiotherapy had poor prognosis and unsatisfactory results [13]. Despite the high morbidity and mortality reports of pneumonectomy in the previous publications, we did not detect any results favoring high mortality, morbidity and poor prognosis in our study. In contrast to related literature, we found out that survival rates were higher in the pneumonectomy patients. Kim et al., published that although there was no statistically significant difference in terms of survival between the lobectomy and the pneumonectomy patients, lobectomy patients had more survival time than the pneumonectomy patients [14]. Some authors also reported that right pneumonectomy patients had higher postoperative morbidity rates without the statistical reflection on the survival rates [14-16]. When pneumonectomy patients were evaluated in terms of the side; contrary to current opinion, our study showed better survival in right pneumonectomy (P=0.021). In our belief; the reason for this outcome comes from performing more detailed preoperative evaluation of patients who are planned for right pneumonectomy.

Cerfolio and friends reported that most common major morbidities were pneumonia and respiratory distress [10]. We found out that pneumonia and hemorrhage were the most common major morbidities.

A 5-year survival rate after primary surgical resection in stage IIIA patients with N2 nodal invasion was 17-20%. It is reported by many publications that a 5-year survival was increased up to 19-45% by the help of the multimodality treatment. International Association for the Lung Cancer Staging Commitee published a multi-center study about patients with N2 and N1 disease who recevied neoadjuvant treatment. In the comparison of the patients with single N2 nodal disease and N1 disease who received neoadjuvant therapy, the same survival rates were achieved [17]. Borri and colleagues reported that long-term survival was only achieved in the patients receiving neoadjuvant therapy [18]. Our study revealed similar results with the other series focusing on multimodality treatment in NSCLC patients. Some studies reported that a 5-year survival was 3-10% in stage III patients receiving adjuvant chemotherapy [11,19]. Borri and colleagues advocated that even with R1 resection, the patients had better survival rates (22%) in comparison to adjuvant chemotherapy [18]. Decaluwe et al., published a series of 92 patients who underwent resection following neoadjuvant treatment and reported complete resection rate of 68%. When compared to this publication, our study revealed a complete resection rate of 95% [20].

The increase in the stage of the disease results with decrease in the survival rates [14]. Similarly, there was a decrease in survival curve in our study. Kim and colleagues found out a significant difference between the pathological T variant and the survival [14]. When we evaluated T variants in our study; T1 and T2 had the similar mean survival times but T3 and T4 patients showed significant decrease in terms of mean survival times.

In the evaluation of N variant, mean survival time was 37.54±4.35 months in patients with N0 disease, 44.77±8.40 months in patients with N1 disease and 25.68±3.63 months in patients with N2 disease. We believe that increase in the survival time of N1 patients may be related to the lack of subgroups. We did not detect any statistical difference when we compared N status and survival rates (P=0.969). Researchers believe that N2 disease is the continuation of the N1 disease and both of them need adjuvant chemotherapy in the postoperative period. In the light of this general opinion; when they evaluate the comparison between N status and survival rates, they count N1+N2 patients as one group (N1+N2) and compare them with N0 disease. One study detected a significant difference in survival between patients with N0 and N1 positive and patients with N2 positive. According to the results of this study, a 5-year survival rate was 53% in patients with N0 or N1, and 10-16 % in patients with N2 positive [21,22]. We did not detect a similar relationship in our study. Some authors reported that multiple N2 lymph node positivity adversely affected the survival rates. Unfortunately, these studies did not include patients who received neoadjuvant theraphy [22,23]. Port and colleagues presented that they could not detect any significant difference in terms of survival rates between patients with multiple N2 nodal invasion and patients with single N2 nodal invasion [7]. We also could not detect any significancy in our study, either.

Conclusion

In locally advanced NSCLC, we can obtain considerable survival results by the help of the anatomical resection following neoadjuvant theraphy. However, surgical difficulties due to the neoadjuvant therapy, complexity in the designation of the real stage, toxicity of the treatment modality and difficulties during follow-up period are the limitations and the challanges of the multimodality treatment approach.

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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Efficacy of topical clobetasol propionate in the treatment of idiopathic granulomatous mastitis

İdiyopatik granülomatöz mastit tedavisinde yerel klobetazol propionatın etkinliği

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ABSTRACT

Objectives: To evaluate the efficacy of topical clobetasol propionate 0.05% pomade in the treatment of idiopathic granulomatous mastitis.

Patients and Methods: Twenty-one idiopathic granulomatous mastitis patients' clinical and histopathological findings were retrospectively reviewed. Those patients excluded from other etiologies were categorized as idiopathic granulomatous mastitis and treated with topical clobetasol propionate 0.05% pomade as an initial treatment.

Results: All 21 patients with a final diagnosis of idiopathic granulomatous mastitis were women with the average age of 36.2+/-5.2 years. Of the 21 patients; erythema, induration and pain problems of 6 (28.5%) patients totally resolved without recurrence in 3 months follow-up period. Erythema, induration and pain problems of 7 (33.5%) patients were minimalized and stay stable in 3 months follow-up period. The symptoms of 8 (38%) did not change under topical clobetasol propionate treatment. None of the patients developed side or adverse effects due to topical steroid treatment and 6 of 18 patients with non-steroidal anti-inflammatory drugs (NSAIDs) complained of gastric pain.

Conclusion:Topical steroid treatment is a safe treatment option for idiopathic granulomatous mastitis patients before systemic steroid and immunosuppressive treatments and also surgery.

Keywords: Idiopathic granulomatous mastitis, Granulomatous mastitis, Mastitis, Topical Steroid, Steroid

ÖZ

Amaç: İdiyopatik granulomatöz mastit tedavisinde topikal klobetazol propiyonat %0,05 pomadın etkinliğini değerlendirmek.

Hastalar ve Yöntemler: Klinik ve histopatolojik olarak idiyopatik granülomatöz mastit tanısı konulan 21 hastanın dosyası retrospektif olarak incelendi. Altta yatan başka patoloji saptanmayan hastalar idiyopatik granülomatöz mastit olarak sınıflandırıldı ve ilk tedavi olarak topikal klobetazol propiyonat % 0,05 pomad uygulandı.

Bulgular: İdiyopatik granülomatöz mastit tanılı 21 kadın hastanın yaş ortalaması 36,2 ± 5,2 yıldı. Yirmi bir hastanın 6 (% 28,5)'sının eritem, sertlik ve ağrı problemleri tamamen geriledi ve 3 aylık takip döneminde tekrarlamadı. Hastaların 7 (% 33,5)'sinde eritem, sertlik ve ağrı şikayetleri tama yakın geriledi ve 3 ay süreli takiplerinde artış izlenmedi. Sekiz (%38) hastada iyileşme gözlenmedi. Hastalarda yerel steroid tedavisine bağlı yan etki görülmezken, ek olarak non-steroid antiinflamatuvar (NSAI) ilaç kullanan 18 hastanın 6'sında mide ağrısı şikayetleri gelişti.

Sonuç: Yerel steroid tedavileri idiyopatik granülomatöz mastit tedavisinde etkili ve güvenli tedavi seçenekleridir.

Anahtar kelimeler: İdiyopatik granülomatöz mastit, Granülomatöz mastit, Mastit, Yerel steroid, Steroid

Introduction

Idiopathic granulomatous mastitis (IGM) is a benign inflammatory condition of the breast with unknown etiology. Several mechanisms have been proposed, including autoimmune process, infectious diseases and hormonal distruption [1]. The localized autoimmune inflammatory response to retained milk secretions in the duct has been postulated in the pathogenesis of IGM [2-4]. IGM occurs most commonly in parous young women, it may be seen also in nulliparous women and rarely men [5,6]. There is no increased risk of subsequent breast cancer in patients with IGM [7]. The breast mass, abscesses, erythema, induration and tenderness are the common clinical findings

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of IGM. The nipple retraction, sinus formation, fistula and axillar adenopathy may accompany these findings. The malignancies, bacterial mastitis, tuberculosis, sarcoidosis, deep fungal infections, foreign body granulomas and autoimmune diseases should be considered in the differential diagnosis of IGM [1,2,4]. The challenging diagnosis of IGM requires exclusion of all other possible disorders with a multidisciplinary approach. There are studies reporting about association between IGM and *Corynebacterium kroppenstedtii* infection and elevated prolactin levels [8,9].

The treatment options are controversial. The reports of spontaneous remissions lead observation or conservative treatments such as symptomatic treatments, systemic antibotics, steroids and immunsuppressive drugs [10]. In some reports; for recurrent cases excision of the affected tissue have been proposed as a treatment option [10].

Material and Methods

We conducted a retrospective study to evaluate the efficacy of topical clobetasol propionate 0.05% pomade in the treatment of IGM. The files of 21 IGM patients treated with topical clobetasol propionate at least for 2 months in the general surgery and the dermatology outpatient clinics from April 2014 to July 2017 were analyzed. The patients were included in this study if they had histopathologic confirmation of granulomatous mastitis and excluded the other possible disorders by breast ultrasonograpy, polymerase chain reaction (PCR) for *Mycobacterium tuberculosis*, chest radiography, bacterial and fungal tissue cultures. Those in whom no underlying etiology was found were categorized as having IGM and treated with topical clobetasol propionate with or without oral non-steroidal anti-inflammatory drug (NSAID) at least 2 months.

All statistical analyses were performed with the Statistical Package for Social Sciences (SPSS) Statistics 20.0 software. The descriptive data were analyzed according to the frequency, percentage, average and standard deviation. Chi-Square and Mann – Whitney U tests were used to compare qualitative data.

Results

The files of 21 patients with IGM those applied topical clobetasol propionate 0.05% pomade twice a day, at least for 2 months were analyzed retrospectively. Eighteen of 21 patients were also treated with oral steroidal anti-inflammatory drugs (NSAIDs). The most common presenting symptoms and signs were unilateral erythema, infiltration, massand mastalgia in the patients. All patients had the histologic findings consistent with granulomatous mastitis without caseous necrosis. All had normal chest radiography. The breast cancer was assessed in all patients with ultrasonographic imaging.

No identifiable etiology was found in any of the patients who were diagnosed with IGM. All patients were women with an average age of 36.2+/ – 5.2 years. None of them has personal or family history for the breast cancer or tuberculosis. Six of 21 (28.5%) were cigarette smokers. Six of 21 (28.5%) used oral contraseptives at any time in the last 3 years. All women had nursed their children with double breast at least 4 months. Three (14.3%) women presented during breastfeeding. None of 21 patients were pregnant at the time of presentation. There were abscess drainage histories in 4 of 21 (19%) patients. None of the patients except 1 had systemic symptoms. One patient suffered coexisting erythema nodosum and artralgia. All patients had erythema, infiltration and tenderness on affected breast's skin. All patients except 1 had unilateral findings. Nine patients had abscess and fistula formation. The patient characteristics are summarized in Table I.

Table I. Characteristics of patients with idiopathic granulomatous mastitis (n=21)

	Min	Max	Average	Standard Deviation
Age	26	47	36.2	5.2
Duration of disease (month)	3	36	11.22	9.05
Number of pregnancy	1	4	2.76	1.38
Time from last pregnancy (month)	14	180	75.00	36.29
Total breasfeeding duration (month)	4	72	24.73	12.37

All histopathological examinations were established with ultrasound-guided tru-cut biopsy. The initial treatment with topical clobetasol propionate 0.05% pomade was given to all patients for at least 2 months. Of the 21 patients; 6 patients' (28.5%) erythema, induration and pain totally resolved within 2 months of treatment without recurrence after 3 months off-therapy period. Seven patients' (33.5%) erythema, induration and pain resolved with minimal erythema and induration and did not worsen for 3 months follow-up period. Eight patients' (38%) symptoms did not improve with topical clobetasol propionate treatment. Total 62% of patients had complete or partial remission off-therapy. None of the patients developed side or adverse

effects due to topical steroid treatment. Six of 18 patients treated with NSAID had complaints of gastric pain.

Discussion

Idiopathic granulomatous mastitis (IGM) is a chronic inflammatory disorder of the breast tissue without proven etiology [1,2,4]. Although, patients do not have systemic findings, in some reports erythema nodosum and arthritis were associated with IGM [11]. IGM is generally seen in young-or middle-aged women unilaterally after giving birth. Autoimmune reactions against milk which leak from breast lobules is the suspected mechanism of the disease. The patients generally present with breast mass that should be differentiated from breast cancer by imaging and histopathological examination.

The IGM shows non-caseating granulomatous inflammation in the lobules on histopathological examination. After exclusion of malignancies, etiology for granulomatous mastitis as Mycobacterium infections, foreign body granulomas, fungal infections, Corynebacterium infection, sarcoidosis, Sjögren's disease, vasculitis and other autoimmune diseases should be evaluated. Clear screening for differential diagnoses leads for the diagnosis of IGM. The combination of clinical history, histopatology, laboratory and imaging findings with multidisciplinary approach is critical in the diagnosis and treatment of the IGM.

There is no consensus on treatment however, step by step treatment by antibiotics, steroids and then immunosuppressives and finally excision is suggested in the literature. The prognosis of the IGM is variable.

The successful results with systemic corticosteroid therapy was first reported in1980 [12]. There are 1 case report and 1 prospective and 1 retrospective study by the same group in the literature on IGM treatment with topical steroid therapy [13-15]. The latest report analyzed topical prednisolone 0.125% pomade from 28 patients with biopsy-proven IGM, retrospectively. After initial complete remission, during 4 months follow-up period, only 10.7% of the patients had disease recurrence in whom a repeated course of topical prednisolone treatment resulted with complete healing in most patients. According to results of this study, topical steroid treatment seemed to be very effective in the treatment of IGM [15].

A meta-analysis in 2017 reviewed the complete remission (CR) and recurrence rates of various reported treatments for IGM [10]. According to this study; a pooled estimate of complete remission and recurrence rates for surgical managements were 90.6% and 6.8%, oral steroids were 71.8% and 20.9%, oral steroids+surgical managements were 94.5% and 4%, oral steroids+methotrexate were 71.4% and unknown, observation were 95.1% and 9.2% and finally of topical steroids were 98.8% and 14.3%, respectively. All the studies about topical steroid efficacy in the treatment of IGM which also analyzed in this meta-analysis were mentioned above [14,15]. This meta-analysis assessed 4 reports of observation in IGM [16-19]. The number of patients were between 3 and 8 in the 3 of these 4 reports [16,18,19]. There were 27 patients,with 100% CR rate and 11.1% recurrence rate during average 7.4 months follow-up period, in the report of Bouton et al. [17].

The success rate of observation without treatment, topical steroids and advanced treatment options were reported similar and high in the literature. Despite the fact that strength of topical clobetasol propionate is superior than topical prednisolone, the remission rates are inferior relatively in our study. This might be due to lower number of patients, shorter medication period, resistance of our cases or the prolonged activity of various antibiotics those used in previous study. Our study has a 62% total complete and partial remission rate and it is still an effective response result for IGM.

There is still no consensus on how to manage this benign condition properly. This is mostly due to its rarity and lack of well-designed studies. Previous studies and our study showed that topical steroid treatment is a safe alternative for the modalities with more adverse event risks such as systemic steroid, immunsuppressive agents and surgery . In the light of recent studies surgical treatments and medical treatments with possible side effects might be reserved for those in whom conservative modalities such as observation and topical steroids are not effective or who ask to have a rapid amelioration.

The limitations of our study are retrospective design of the study, the lack of longer follow-up period and the lack of an observational arm results. Our study and previous studies show the necessity of the randomised, placebo controlled studies and that it is worth observing and/or trying topical steroids in the treatment of IGM before advanced options in the selected cases.

Conclusion

Our study suggests to treat IGM with topical steroids before the options with more adverse event risks and also less cosmetic results as systemic steroids, immunosupressive agents and surgery.

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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

The seasonality in the diagnosis of acute leukemia: A single center data from Turkey

Akut lösemi tanısında mevsimsel dağılım: Türkiye'den tek merkez verisi

Rafet EREN, Mehmet Hilmi DOĞU, Şermin ALTINDAL, Osman YOKUŞ, Elif SUYANI

ABSTRACT

Objectives: The seasonality in the diagnosis of acute leukemias (ALs) has been conceived ever since and the results have been confounding between summer and winter peaks since those times. To our knowledge, the seasonality in the diagnosis ALs has not been explored in our region and we aimed to investigate for a seasonal accumulation in the diagnosis of AL patients.

Materials and Methods: A hundred and sixty-two patients who were diagnosed with either acute myeloid leukemia (AML) or acute lymphocytic leukemia (ALL) between November 2012 and October 2017 were included in the study. The data regarding the gender, age, type of leukemia and the time of admission were noted from files of the patients.

Results: The median age of the patients was 51.5 years (range, 17-85) with 64 (39.5%) female, 98 (60.5%) male. Most of AL patients were diagnosed in August (21,13%) and the least in June with 6 (3.7%) patients. According to the seasons; 39 (24.1%) patients were diagnosed in winter, 40 (24.7%) patients in spring, 40 (24.7%) patients in summer and 43 (26.5%) patients in autumn (P>0.05).

Conclusion: We could not determine any seasonality in the diagnosis of ALs, both AML and ALL, in our study.

Keywords: Acute myeloid leukemia, Acute lymphoblastic leukemia, Seasonality

ÖZ

Amaç: Akut lösemilerin (AL) tanısında mevsimsel değişkenlik olabileceği uzun süredir düşünülüyor olsa da yapılan çalışmaların sonuçları yaz ve kış pikleri arasında çelişkilidir. Bilindiği kadarıyla bölgemizde AL tanısında mevsimsel değişkenlik incelenmemiştir. Bu çalışmada AL hastalarının tanısında mevsimsel bir birikim olup olmadığını araştırmayı amaçladık.

Yöntemler ve Gereçler: Kasım 2012 ile Ekim 2017 tarihleri arasında akut myeloid lösemi (AML) veya akut lenfositik lösemi (ALL) tanısı alan 162 hasta çalışmaya dâhil edildi. Cinsiyet, yaş, lösemi tipi ve hastaneye yatış bilgileri hasta dosyalarından edinildi.

Bulgular: Hastaların medyan yaşı 51,5 idi (aralık: 17-85). 64 hasta (%39,5) kadın, 98'i ise (%60,5) erkekti. AL tanısı alan 21 hasta (%13) ile en sık Ağustos ayında iken, 6 hasta (%3,7) ile en nadir Haziran ayındaydı. Mevsimlere göre incelendiğinde, 39 hasta (%24,1) kış, 40 hasta (%24,7) ilkbahar, 40 hasta (%24,7) yaz ve 43 hasta (%26,5) ise sonbahar mevsiminde tanı almıştı (P>0,05).

Sonuç: Hem AML hem de ALL açısından bakıldığında, çalışmamızda AL tanısında herhangi bir mevsimsel değişkenlik belirleyemedik.

Anahtar kelimeler: Akut myeloid lösemi, Akut lenfoblastik lösemi,Mevsimsel dağılım

Introduction

Acute leukemias (ALs) are the hematological malignancies characterized by abnormal proliferation of blasts derived from either a hematopoietic myeloid precursor or a hematopoietic lymphoid precursor or both. While, the most common type of AL in adults is the acute myeloid leukemia (AML) with an incidence of 5-8/100.000 [1,2], acute lymphoblastic leukemia (ALL) is encountered less frequently with an incidence of 1.28/100000 [3]. Although, ALs are rarely seen, they remain to have an acute onset and a clinical course with high morbidity and mortality rates in adults, despite the significant improvements in treatment modalities [1-3]. The acute onset nature of ALs has raised

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the question whether the diagnosis of ALs shows a seasonal variation or not. Hence, the seasonality in the diagnosis of ALs has been conceived ever since [4-8] and the results have been confounding between summer and winter peaks since that time [9-14].

To our knowledge, the seasonality in the diagnosis ALs has not been explored in our region. In this study, we aimed to investigate whether there is a seasonal accumulation in the diagnosis of AL and if there is, its possible causes including sunshine exposure and infection epidemics.

Materials and Methods

A hundred and sixty-two patients diagnosed with either AML or ALL (except secondary AML, acute promyelocytic leukemia or ALL with type 3 blast) between November 2012 and October 2017 at Marmara University Hospital Hematology Department were included in the study. The data regarding the gender, age, type of leukemia and the time of admission were noted from files of the patients.

Statistical Analysis

Statistical evaluation was made by SPSS 22 program. Data were described as numbers and percentage or median and range, when appropriate. x^2 Fisher's exact test was used for evaluating categorical values. All P-values were 2-sided with statistical significance at 0.05 alpha levels.

Results

The median age of the patients was 51.5 years (range 17-85) with 64 (39.5 %) female, 98 (60.5 %) male. The subtype of 110 (67.9 %) patients were AML and 52 (32.1 %) were ALL (Table I). The distribution of the leukemias according to the months is presented in Figure 1. When the patients were evaluated separately as AML and ALL, no seasonal accumulation was observed (Table II). The diagnosis of AL was most frequent in August with 21 /13 %) patients and least in June with 6 (3.7 %) patients. According to the seasons; 39 (24.1 %) patients were diagnosed in winter, 40 (24.7 %) patients in spring, 40 (24.7 %) patients in summer and 43 (26.5 %) patients in autumn (P>0.05). The distribution was similar when subgroup analysis were done based on gender and leukemia subtype.

Table I. Patient characteristics

	N=162
Gender, n, (%)	
Female	64 (39.5 %)
Male	98 (60.5 %)
Age, years, median, (range)	51.5 (17-85)
Leukemia subtype, n, (%)	
AML	110 (67.9 %)
ALL	52 (32.1 %)

ALL: acute lymphocytic leukemia; AML: acute myeloid leukemia

Table II. Distribution of months of diagnosis in patients with AML and ALL

		AML		ALL	
		n	%	n	%
Months of Diagnosis	January	11	10.0%	4	7.7%
	February	7	6.4%	4	7.7%
	March	12	10.9%	5	9.6%
	April	3	2.7%	9	17.3%
	May	9	8.2%	2	3.8%
	June	3	2.7%	3	5.8%
	July	6	5.5%	7	13.5%
	August	16	14.5%	5	9.6%
	September	10	9.1%	4	7.7%
	October	10	9.1%	3	5.8%
	November	14	12.7%	2	3.8%
	December	9	8.2%	4	7.7%

ALL: acute lymphocytic leukemia; AML: acute myeloid leukemias

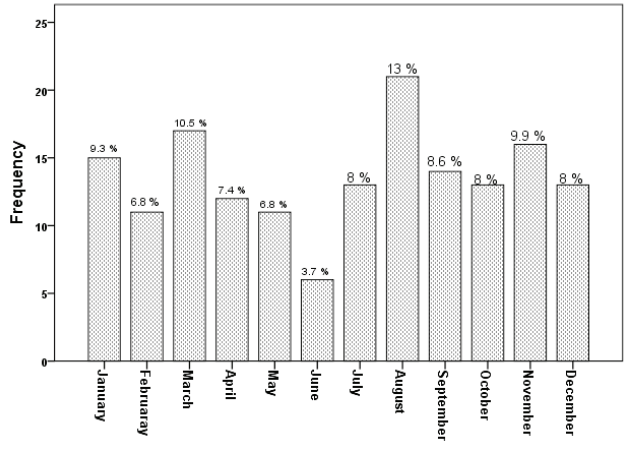

Figure 1. Distribution of the diagnosis of leukemias according to the months

Discussion

The pathogenesis of ALs comprises complex sequence of events including chromosomal translocations and/

or inversions and/or point mutations, all of which alter the proliferation and differentiation of the hematopoietic precursor cells [1-3]. The triggering factor, which initiates those events, has not been elucidated so far. It has been suspected that viruses could be one of the potential triggering factors linked to ALs. The role of JC virus, Ebstein-Barr virus, cytomegalovirus, human herpes virus 6 and 7, and parvo virus B19 has been investigated as an etiologic factor in AL and among them parvo virus B19 was found to be potentially involved in the etiology of AL [15-19]. Actually, the data regarding the role of viruses, especially the ones causing respiratory infections which are mostly encountered in winter, is obscure in occurrence of ALs. Hereby, seasonality of ALs has been an intriguing topic thus we also investigated it in our clinics. However, we could not demonstrate a seasonal variation in the diagnosis of ALs. Similarly, subgroup analysis according to subtype of AL and gender did not show any seasonal variation in the diagnosis of ALs. When the patients were evaluated in general, the least common month of diagnosis was June. This could be due to the population of Istanbul moving temporarily to other cities for vocational purposes.

The seasonality in diagnosis of ALs particularly ALL has been investigated with studies including quite enough number of patients [9-14, 20]. Gao et al., investigated variation in the seasonal diagnosis of ALL in 3 different regions of the World, which allowed a more accurate evaluation, because the selected regions were located located on different altitudes and had entirely different climates [9]. While there was no seasonal peak in the diagnosis of ALL in Singapore and the United States, a winter peak was observed in Sweden where seasons differ prominently unlike the climate of other selected regions. Similarly Timomen et al., also found a winter peak in the diagnosis of ALL patients in a study from Finland [10]. Furthermore, they investigated the association between the peak and influenza epidemic, which has been the basis for the seasonality postulate in the diagnosis of ALs. And they demonstrated that more ALL were diagnosed during influenzae epidemics. On the other hand, their analysis did not reveal those findings for AML. Another considerable point is that, due to the presence of winter peak in the diagnosis of ALL in the North areas of the World, they hypothesized that vitamin D deficiency might be associated with the initiation of the disease because of the sunlight deprivation in winter. Eatough et al., studied the seasonality in the diagnosis of acute monocytic leukemia in England which is also located in the North part of the World, and determined a peak in February and March [11]. In terms of AML, Calip et al., found a winter peak in the diagnosis of AML in a quite high number of patients in different regions of the United States [12]. In contrast to former studies, Badrinath et al., demonstrated a summer peak in the diagnosis of ALL in England [13]. Ross et al., also demonstrated a summer peak in the diagnosis of ALL in the United States with a high number of patients [14]. Gao et al., showed that there was not a prominent seasonal variation in the diagnosis of ALL in a meta-analysis [20]. But, the meta-analysis was quite heterogeneous regarding the age of the patients. After all these conflicting results we could not determine any seasonality in the diagnosis of ALs, both AML and ALL, in Turkey.

Although limited number of patients and patients being from a single center seem to be the limitations of this study, our hospital is located in Istanbul which is the most crowded city of Turkey and has received a major of influx from nearly all parts of Turkey. So, our study population can be the representative of Turkey. In fact the most significant limitation of this study similar to the other ones, is the lack of antecedent infection history of the patients.

In conclusion, given the complexity of the pathogenesis of AL, achievement of a precise conclusion about the seasonality in the diagnosis of ALs could not be feasible despite the studies including large number of patients.

Conflict of Interest

The authors declare that they have no conflict of interest

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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Dimensions and pattern of growth of the femoropatellar groove: A digital metric study on adult and fetal femora

Femoropatellar oluk boyutları ve büyüme paterni: Erişkin ve fetal femoral kemik üzerinde dijital metrik bir çalışma

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ABSTRACT

Objectives: A detailed knowledge about the anatomy of the femoropatellar groove (FPG) and its articulation is essential for the better understanding of the patellar stability. Therefore, the present study was carried out to describe the morphology of FPG in adults and the pattern of its growth in fetuses.

Materials and Methods: Thirty-seven adult dry femora of unknown age and 24 fetal femora of known gestational age were included in the study. The dimensions of FPG and its angulations were calculated digitally using Image J software and were analyzed statistically.

Results: The femoropatellar angulation ranged from 136.38° to 142.38°. The dimensions and angulation were correlated with the gestational age. The dimensions of FPG and the altitude of lower end of the femur increased significantly with the gestational age ($P<0.05$). There was also a significant negative correlation between the femoropatellar angulation and the gestational age ($P<0.05$).

Conclusion: This study provides a database for the parameters of the adult femora. It also describes the pattern of growth of the lower end of fetal femur. These findings are essential in determining the patellar stability during walking.

Keywords: Femoropatellar groove, Fetus, Femur, Patella, Gestational age

ÖZ

Amaç: Femoropatellar oluğun ve eklemlerinin anatomisinin detaylı bir şekilde bilinmesi, patellar stabilitenin daha iyi anlaşılmasını sağlar. Bu nedenle, bu çalışma yetişkinlerde FPG morfolojisini ve fetüslerde büyümenin paternini tanımlamak için yapılmıştır.

Gereçler ve Yöntemler: Çalışmaya, yaşları bilinmeyen 37 erişkin kuru femur ve 24 gestational yaşı bilinen fetal femur dahil edildi. Femur ve angülasyonlarının boyutları Image J yazılımı kullanılarak dijital olarak hesaplandı ve istatistiksel olarak analiz edildi.

Bulgular: Femoropatellar angülasyon 136.38 ° ila 142.38 ° arasındaydı. Boyutlar ve angülasyon gebelik yaşı ile korelasyon göstermektedir. FPG'nin boyutları ve femurun alt ucunun yüksekliği, gebelik haftası ile anlamlı olarak artmıştır ($P<0.05$). Ayrıca, femoropatellar angülasyon ile gestasyonel yaş arasında anlamlı negatif korelasyon saptanmıştır ($P<0.05$).

Sonuç: Bu çalışma yetişkin femur parametreleri için bir veritabanı sağlar. Bu aynı zamanda fetal femurun alt ucunun büyüme paternini de açıklar. Bu bulgular, yürüme sırasında patellar stabiliteyi belirlemede esastır.

Anahtar kelimeler: Femoropatellar oluk, Fetus, Uyluk, Diz kapağı, Gestasyonel yaş

Introduction

The femoropatellar joint (FPJ) is formed between the trochlea of the femur and the articular surface of the patella [1]. The morphology of the patella and trochlea is of prime importance in providing a stable and smooth platform for patellar movement along the trochlea [2]. The femoropatellar groove (FPG) or trochlear groove helps to stabilize the patella. An abnormal shallow groove predisposes to its instability [3]. It is known that femoral obliquity is not genetically determined but is attained with biped walking [4].

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Femoropatellar (FP) articulation plays a major role in locomotion and other activities that involve knee flexion and extension. FP instability can be defined as movement of the patella out of its normal position, and can be divided into dislocation and subluxation [5]. The patella plays a major role in extensor mechanism by acting as a fulcrum [6].

The stability of the FPJ is achieved through a complex interaction of a range of factors including the articular geometry of the patella and femur, the magnitudes and lines of action of the quadriceps muscle forces, the stiffness of the retinacular structures and the relative alignment and internal–external rotation of tibial and femoral shafts. Abnormality of any of the above factors may cause patellar malalignment within the femoral groove and leads to instability disorders such as lateral patellar compression syndrome and recurrent patellar subluxation or dislocation [7].

The stability of the patella in the trochlear groove is a combination of bony, ligamentous and muscular restraints [8]. The fundamental knowledge of anatomy of the femoropatellar articulation leads to the better understanding of patellar stability [9]. The altitudes of the femoral condyle and the FP angulation are required during the evaluation of knee joint congruence and its abnormalities [10].

Studies have also suggested that the shape of the lower extremity of the femur is determined early in development, long before standing and walking [11-13]. However, literature lacks the data of the dimensions of FPG in Indian context. Therefore, the present study was aimed to describe the morphology of FPG and the altitude of the lower end of adult and fetal femora. The study was also aimed at correlating the pattern of growth of FPG and its angulation with the gestational age using the fetal femora which would add the reference values for the existing literature.

Material and Methods

The present cross sectional study was carried out using fetal and adult femora procured from the Department of Anatomy, Kasturba Medical College, India. Thirty-seven dry adult femora of unknown age and 24 fetal femora of known gestational age were included in the study. Clearance for the study was obtained from the Institutional Ethics Committee. Damaged femora and fetuses with any limb anomaly were excluded from the study. Fetal femora were dissected and were cleared from all the soft tissues.

End on view of the lower end of the femora were taken using Nikon digital camera and were stored in JPEG format. The maximum altitudes of the right and left femoral condyles were measured at the extreme ends of the FPG. The minimum altitude of the lower end of the femur was measured at the center of the FPG. The dimensions of the FPG and the angulation were calculated digitally using Image J software and the data were stored in excel format for statistical analysis. The measured dimensions are shown in Figure 1. The same parameters were measured in both adult as well as fetal femora.

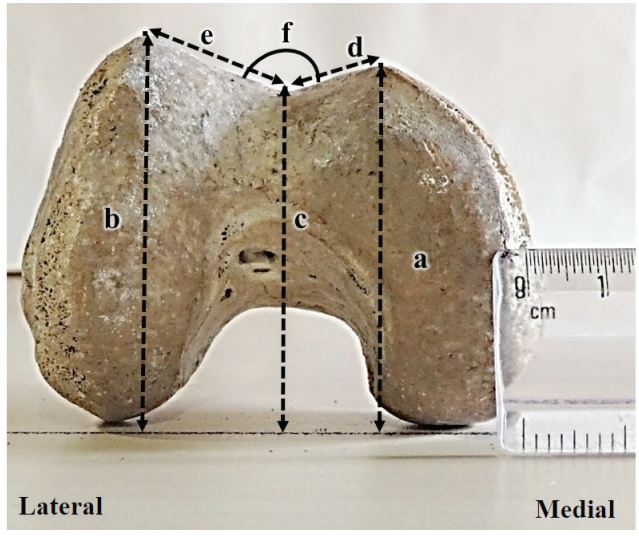

Figure 1. End on view of the lower end of right femur showing the parameters measured

a and b: Maximum altitude of the medial and lateral margins of the patellar groove
c: Minimum height of the lowest point on the patellar groove
d and e: Width of the medial and lateral sides of the patellar groove
f: Angle of patellar groove

Mean and standard deviations were calculated for all the parameters. All the fetal parameters were correlated with the gestational age for estimating the pattern of growth.

Results

The mean and standard deviations of the altitude of the lower end of femur and dimensions of FPG measured in adult femora are shown in Table I. The femoropatellar angulation ranged from 136.38° to 142.38° in adult femora. The dimensions of right and left femora were not compared statistically because they were not of the same individual.

The gestational age of the fetuses ranged from 16 to 36 weeks. The dimensions and angulation of the femoral condyles and FPG were correlated with the gestational age.

Table I. The mean and standard deviations of the parameters measured

Parameter measured in cm	Right	Left
Maximum altitude of the medial margin of the patellar groove	4.98±0.35	5.2±0.16
Maximum altitude of the lateral margin of the patellar groove	5.44±0.40	5.50±0.14
Minimum height of the lowest point on the patellar groove	4.89±0.21	4.94±0.04
Width of the medial side of the patellar groove	1.30±0.38	1.88±0.16
Width of the lateral side of the patellar groove	2.30±0.09	1.90±0.10
Angle of patellar groove	136.38±2.59°	142.38°

The dimensions of FPG and the altitude of lower end of the femur increased significantly with the gestational age ($P<0.05$).

In fetal femora, the mean and standard deviations of the maximum altitude of the medial femoral condyle were 1.57±0.27 cm and 1.53±0.288 cm on the right and left sides respectively. The mean and standard deviations of the maximum altitude of the lateral femoral condyle were 1.64±0.31 cm and 1.67±0.33 cm on the right and left sides respectively. The mean and standard deviations of the minimum altitude of the lower end of the femur at the center of FPG were 1.5±0.31 cm and 1.49±0.32 cm on the right and left sides respectively.

In fetuses the femoropatellar angulation ranged from 138.72° to 157.75°. There was a significant negative correlation found between the gestational age and the femoropatellar angulation ($P<0.05$). The change in the femoropatellar angulation is depicted in Figure 2.

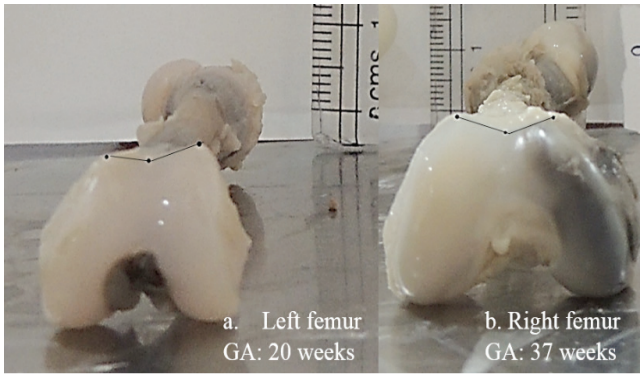

Figure 2. End on views of fetal femora indicating the change in the femoropatellar angulation

155° at 20th week of gestation (a) and 147° at 37 weeks of gestation (b) depicted in black line.
GA: Gestational age

Discussion

The literature mentions several studies concerning the FPG and femoropatellar pathology in children and in adults.

Doskocil in 1985 published the first series concerning the anatomy of the FPG in embryos of 4 to 10 weeks of gestational age. He stated that, the patellar groove was asymmetric, with a lateral lip bigger and wider than the medial one, but it was a subjective and visual observation, without any biometry or measurement [11]. Similar observations were noted in the present study.

Doskocil also pointed out that during development there is a distal migration of the patella to its final place, and this occurs within the third month of intrauterine life. This variation modifies the position of the patella in its femoral groove and could be responsible for mechanical remodeling of joint surfaces [11].

Biometric evaluation series of the patellar groove in adults was carried out by Wanner et al., which comprised 32 right femurs from the Colorado University. He pointed out that the lateral side of the FPG was more elevated than the medial one, and that the lateral side of the FPG was about twice as wide as the medial one. He also showed that these parameters were very variable, but the angulation had a remarkable stability [14]. An asymmetric patellar groove with a lateral side that sticks out, associated with an oblique femur, is a specific mark of biped walk for many authors [15, 16]. In the current study, there was a significant difference in the parameters of the medial and lateral margins of the FPG which were in agreement with Wanner's observations.

Nietosvaara carried out an ultrasonographic study on knees of 50 normal children aged from birth to 18 years to measure the angles of the bony intercondylar and the cartilaginous FPG. At all ages, the angle of the cartilaginous groove was 134 to 155 degrees, although the osseous angle was found to be inversely related to the child's age. The authors suggested that the configuration of the FPG is

already well developed at birth [17]. In the current study, the mean FP angulation observed was 138.72° to 157.75° on the right and left sides respectively in fetal femora. It was also observed that the femoropatellar angulation was inversely proportional to the gestational age.

Many clinical investigators have related the radiological appearances of the femoropatellar joint to femoropatellar pain, malalignment, chondromalacia of the patella, abnormal femoropatellar angulation, congruence, patellar subluxation and dislocation, dysplasia of the patella and of the femoral trochlea, patellar position and movement [18-21].

A study done by Glard et al., on fetuses of 13 to 38 weeks of gestation showed a positive correlation between the FP angulation and the dimensions of the lower end of the femur [4]. However, in the current study the authors observed a significant positive correlation for the parameters of lower end of femur and a negative correlation for the FP angulation.

Conclusion

This study provides a range of dimensions of the lower end of femur and the femoropatellar angulation which would be added to the existing database. The study also provides the pattern of growth of lower end of fetal femur. These findings are essential in determining the patellar stability during walking. The altitudes of the femoral condyles and the angulation are also required during the evaluation of knee joint congruence and its abnormalities.

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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Acute poisoning in children; Evaluation of cases admitted to Marmara University Hospital in 2015

Çocuklarda akut zehirlenme; 2015 yılında Marmara Üniversitesi Hastanesi'ne başvuran olguların değerlendirilmesi

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ABSTRACT

Objectives: According to Turkish Statistical Institute (TurkStat), 6477 children aged between 1 and 17 years, died in 2015 and 29.5% (n=1909) of these deaths were because of injuries due to external causes and poisoning. Our aim is to produce solutions to this problem by evaluating demographics, clinical features of patients and the causes and consequences of poisoning.

Materials and Methods: The hospital medical records of children who were admitted with acute intoxication to Pediatric Emergency Service at Marmara University Hospital in 2015, were evaluated retrospectively.

Results: In 2015, a total of 1110 patients applied to the hospital due to poisoning. Of these cases, 31.6% (n = 351) were children, about half of them were male (n = 173) and half were female (n = 178). The mean age of males was 6.24 years and mean age of females was 8.47 years. Sixty percent (n=213) of patients were in 0-6 age group, 8% (n=28) of patients were in 7-11 age group, 32 % (n=110) of patients were in 12-18 age group. Forty-six point one percent (n = 162) were poisoned with medications. Among the pharmaceuticals, paracetamol was the most commonly used agent (14.8%). In non-pharmaceuticals, caustic/corrosive substances (detergent, bleach, acetone etc.) were the most frequently used agents (54%).

Conclusion: In this study, 80.3% of the cases were preventable accidental poisoning. Regulations on child-resistant packaging should come into force as soon as possible.

Keywords: Forensic origin, Child, Intoxication

ÖZ

Amaç: Türkiye İstatistik Kurumu 2015 verilerine göre; 1-17 yaş grubunda 6477 çocuğun öldüğü, bu ölümlerin %29,5'inin (n=1909) dış sebeplere bağlı yaralanmalar ve zehirlenmeler nedeniyle olduğu belirtilmiştir. Amacımız, çocukların demografik bilgilerini, klinik özelliklerini, zehirlenmenin sebep ve sonuçlarını değerlendirerek bu soruna çözüm üretmektir.

Gereç ve Yöntem: Marmara Üniversitesi Hastanesi Çocuk Acil Servisi'ne 2015 yılı buyunca akut zehirlenme ile başvuran çocukların hastane kayıtları retrospektif olarak değerlendirilmiştir.

Bulgular: 2015 yılında zehirlenme nedeniyle toplam 1110 olgu başvurmuştur. Bunların %31,6 (n=351) çocuktur, bu çocukların yaklaşık yarısı erkek (n= 173) yarısı da kızdır (n= 178). Erkeklerin yaş ortalaması 6,24 yıl, kızların ise 8,47 yıldır. Hastaların %60'ı (n=213) 0-6 yaş aralığında, %8'i (n=28) 7-11 yaş aralığında, %32'si (n=110) 12-18 yaş aralığındadır. %46.1'i (n=162) ilaçla zehirlenmiştir. İlaçlarda parasetamol %14,8'i ile en sık kullanılan etkendir. İlaç dışı etkenlerde ise kostik/koroziv maddeler (deterjan, çamaşır suyu, aseton vb) %54 ile en sık kullanılan etkendir.

Sonuç: Bu çalışmadaki olguların %80,3'ünü (tüm olgulardaki kazaya bağlı zehirlenme oranı) gerekli düzenleme ve tedbirlerle önlenebilir nitelikte olan zehirlenmeler oluşturmaktadır. Çocuğa dirençli paketleme ile ilgili düzenlemeler bir an önce yürürlüğe konmalıdır.

Anahtar kelimeler: Adli orijin, Çocuk, Zehirlenme

Introduction

In the last century with rapid industrialization, toxic chemical products have spread rapidly all over the world. The sale of these products without adequate control poses a great risk for children to be exposed to these products [1]. As a reflection of this situation, acute poisoning has been one of the most important causes of hospitalization indications in children and this situation causes serious symptoms or even death in children. In the National Toxicology Consultation Center's 2008 Study Report, it was stated that a total of 77.988 people applied to the center and 46.894 (60.13%)

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of them were children [2]. Moreover, according to data from the Turkey Statistical Institute in our country in 2015, 6477 children between the ages of 1 and 17 died and the cause of death in 1909 (29.5%) of them was "injuries due to external causes and poisoning". No prevalence study has been done in our country until this time. Current studies are not enough to explain the frequency and causes of poisoning in our country.

In this study, it was aimed to produce a solution proposal to prevent acute poisoning problems in children by evaluating the demographic, clinical features, causes, and consequences of poisoning of children admitted to our hospital with a forensic perspective.

Materials and Methods

The forensic and clinical records of children admitted to Marmara University Hospital Pediatric Emergency Service between 01.01.2015 and 31.12.2015 for acute poisoning were evaluated retrospectively. From the hospital data; the gender and age of children, the cause of poisoning, the origin of the poisoning, the blood values, the date of the application were obtained. Patients were divided into 3 age groups according to the period of childhood development; 0-6 years (preschool period), 7-11 years (school period), 12-18 years (adolescence period). The obtained data were analyzed statistically with SPSS version 21.0. Chi-square and Student's t test were used for statistical analysis. A P value of less than 0.05 was considered statistically significant.

Results

In 2015, a total of 1110 people applied to Marmara University Hospital for poisoning. 351 of these (31.6%) were children. 173 of the children were boys and 178 were girls. The average age of boys was 6.24 years and that of girls was 8.47 years. 60% (n = 209) were between 0-6 years of age, 8% (n = 28) between 7-11 years of age and 32% (n = 114) between 12-18 years of age. The distributions of cases by age and gender are shown in Figure 1.

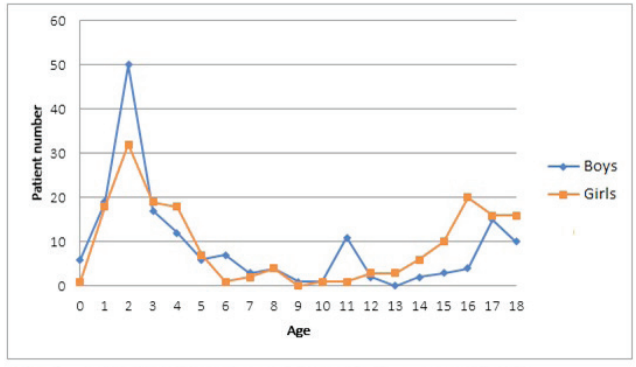

Figure 1. Distribution of poisoning cases by age and gender.

When poisoning cases were evaluated according to the judicial origin, 80.3% were accidents, 19.4% were suicides, 0.3% were homicides. Since, the data obtained according to age groups showed a significant difference, data were divided into age groups. Table I shows the distribution of cases according to age groups, the poisoning effect, and gender.

Table I. Distribution of the Cases According to Age Groups, Poisoning Agent and Gender.

Age				Used Agents		Total	Gender	
				Medications	Non-Medication Agents		Boys	Girls
0-6 years	**Origin**	**Accident**	n (%)	93 (44.5%)	116 (55.5%)	209 (100%)	116 (55.5%)	93 (44.5%)
7-11 years	**Origin**	**Accident**	n (%)	2 (7.4%)	25 (92.6%)	27 (96,4%)	20 (74.1%)	7 (25.9%)
		Suicide	n (%)	0 (0%)	1 (100%)	1 (3.6%)	0 (0%)	1 (100%)
12-18 years	**Origin**	**Accident**	n (%)	8 (17.4%)	38 (82.6%)	46 (40.3%)	26 (56.5%)	20 (43.5%)
		Suicide	n (%)	58 (86.6%)	9 (13.4%)	67 (58.8%)	10 (14.9%)	57 (85.1%)
		Homicide	n (%)	0 (0%)	1 (100%)	1 (0.9%)	1 (100%)	0 (0%)

In terms of age groups, among the 0-12 age groups the accident covered almost all cases (99.6%) but in the 12-18 age group, suicide (58.8%) was more prominent. This change was statistically significant (P <0.00001). There was no statistically significant difference between pharmaceutical and non-pharmaceutical factors in terms of poisoning effect in 0-6 age group (P> 0.05). Apart from the 0-6 age group, in other age groups, 86.3% of the accidental poisonings were due to non-pharmaceutical factors. 85.3% of suicide cases were composed of girls and this difference between genders was statistically significant (P <0.00001). 85.3% of suicide cases were attempted suicide by using medication. Of the 58 patients who committed suicide, 25 used multiple medications and 14 used medications that affected the central nervous system. In addition, 161 (45.8%) children were poisoned due to medications and 190 (54.2%) children were poisoned due to non – medication factors. Paracetamol (n = 26, 16%) was the most frequently used among the medications and among the non-pharmaceutical agents caustic and corrosive fluids were the most frequently used agents (n = 103, 54.5%). Table II shows the distribution of poisonous substances.

Particularly, in the 12-18 age group addictive substances were used. The distribution of non-pharmaceutical intoxication agents is shown in Table III.

There were 27 cases of poisoning due to the use of addictive substances, only 5 (18.5%) of them were girls and this difference between genders was statistically significant (P <0.00001). Two of the 351 patients died. When it came to the causes of death, one case aspired thinner and in the other, synthetic marijuana called "bonsai" caused death. In addition, no statistically significant differences were found when the results of routine blood and urine analysis (complete blood count, biochemistry, arterial blood gas) were compared.

Table II. Distribution of medication-induced and non-medication poisoning agents

Medication Related Poisoning Agents	Number	Percentage	Non-Medication Poisoning Agents	Number	Percentage
Multi-medication use	34	21%	Caustic and corrosive substances	103	54%
Central nervous system	34	21%	Addictive substances	27	14%
Nonsteroidal antiinflammatory	30	19%	Food	18	9%
Hormones	16	9%	Carbon monoxide	14	7%
Vitamins	8	5%	Thinner	10	5%
Antihistamines	8	5%	Mouse poison	6	3%
Antibiotics	7	4%	Solvents	3	2%
Cardiovascular system	8	5%	Idiopathic	3	2%
Herbal medicines	5	3%	Paint	3	2%
Gastrointestinal system	5	3%	Hydrocarbon	2	1%
Antitussive	1	1%	Disinfectant	1	1%
Anticholinergic	1	1%	Total	190	100%
Antiseptic	2	1%			
Decongestant	1	1%			
Unknown	1	1%			
Total	161	100%			

Table III. Percentage distributions of the poisoning agents of non-medication poisoned cases in 12-18 age group

12-18 Age Group Non-Medication poisoning agents	Number	Percentage
Addictive substances	27	56%
Caustic and corrosive substances	7	15%
CO (Carbon monoxide)	6	13%
Food	3	6%
Idiopathic	2	4%
Solvents	1	2%
Hydrocarbon	1	2%
Disinfectant	1	2%
Total	48	100%

Discussion

Poisoning is one of the most important causes of mortality and morbidity in childhood. Approximately one-third (31.6%) of the poisoning cases admitted to the emergency department of our hospital were children. The majority of children with acute poisoning cases in our study were grouped in two age groups (0-6 (60%) and 12-18 (32%) age groups, respectively) in accordance with the literature [3-8]. According to the age distribution of genders, males in 0-6 years and females in 12-18 years were more prominent. Many of the similar studies have reached the same conclusion [9-11].

In our study, more than half of the poisonings were observed in the 0-6 age group (60%). It is known that children in this age group are more fragile and vulnerable to accident-related intoxication because of their curiosity, tendency to explore their environment or inexperience with harmful substances [12]. In addition, it had been reported that labeling of containers with warning labels did not have any deterrent effect on children under 6 years of age, and may even attract them [13]. In another study, it was reported that pills with a good taste and candylike appearance caused deaths in 90's [14]. When studies that seek solutions to children poisoning are reviewed; In a study on children aged 5 years and younger, conducted by Ramos et al., it was found that hiding poisonous substances under 150 cm increased the poisoning rate by 17 times when compared to the control group, and also prevention of this condition reduced the poisonings in this age group by 19%. As a precautionary measure, special packaging for children under 5 years that make opening and obtaining their contents difficult, came into force in many developed countries [1,15,16]. In England, the rate of death due to poisoning in children under 10 years of age was 151 in 100.000 in 1968, with this arrangement, this ratio had dropped to 23 in 100.000 until 2000 [16]. In the United States, this regulation was put into effect in 1970, and from that time on significant reductions in the frequency of poisoning due to accidental digestion of substances have been observed [1]. Following after some prevention measures taken between 1960 and 1968 in Finland, deaths due to poisoning decreased rapidly in children under 5 years of age, and this trend of decline continued between 1969 and 2003, and was even zeroized at a certain time. In this time interval, there was no obvious decrease in deaths due to suicide and substance abuse in adolescents [8]. The above-mentioned studies and the World Health Organization report have shown that accident-related poisoning can be avoided [1,8].

In our study, we found that 58.8% of self-poisoning cases were suicide-related in the 12-18 age group. 85.3% of suicide cases were girls. 81.5% of the poisonings due to addictive substance use in the 12-18 age group composed of boys. This is consistent with other studies in adolescents. They found that girls had higher rates of suicides and boys had higher rates of substance abuse [5,7,8,17,18].

When we consider the poisoning factors, these factors vary according to socioeconomic and cultural conditions, laws controlling these factors, climate, local industry or agricultural activity. Medication, cosmetic, household cleaning products and alcohol poisoning are common in developed countries and in developing countries, especially in economies based on agriculture, in addition to medication poisoning, poisoning by insecticides and toxic animal bites are also common [1,19]. For example, in a study conducted in India, pesticides predominantly organophosphates were found to be the most frequent poisoning agent (53.3%) and secondly chemical home products (33.7%) [20]. In a study conducted in Finland, terbutaline was the most frequently seen poisoning medication in children under 6 years of age [21]. Most studies conducted in our country and abroad found that the most frequent poisoning agent in children was medication [3,7,15,22-24] but in our study, it was found that the most common poisoning agent was non-pharmaceutical substances (54%). There are studies that reached similar results [25-27]. In our study, paracetamol was found to be the most frequently used agent in medication-induced poisonings and there are studies that show similar findings [2,22-24]. In addition, paracetamol is considered to be the most frequently poisoning medication because it is an over the counter medication and easy to access, moreover, a box of paracetamol can be lethal [28]. The most frequent etiologic factor among the non-pharmaceutical factors is caustic and corrosive fluids as well as in many studies [2,3,7,21,23,25,26,29]. The most common forensic origin of poisoning in our study was accident with 100% in 0-6 age group according to hospital records and in the 12-18 age group it was suicide with 58.8%. Despite there are similar results [5,7] in studies conducted both in our country and in the world, Yin's study found that an average of 510 children under the age of seven intentionally poisoned in the USA between 2000-2008 [30,31]. It is also suggested that intentional intoxications had a much higher mortality, morbidity, and duration of exposure than accident-related

intoxications [32,33]. In our study, according to medical records, all children under the age of seven were poisoned accidentally. In the hospital records which our study was based on, there was no data entry that these cases were assessed due to abuse and negligence, and due to the legal requirement. They were reported to law enforcement officers as only poisoning. In cases where the person who is responsible for taking care of a child does not provide a safe environment and does not look after a child adequately, in these situations the child's poisoning should be considered as negligence [32]. Poisoning the child intentionally by giving him substance with different intentions such as psychopathology of the caregiver (Münchausen syndrome by proxy etc.), sexual abuse or facilitation the assault, killing, training, behavior changing and distraction should be considered as abuse [32]. The literature data suggest that some of the cases which were considered as accidents may have been exposed to neglect or abuse. According to Hines, the first and most important key point to diagnose poisoning-related child abuse and neglect is to doubt [33]. For this reason, in order to protect children from abuse and neglect, it is necessary to examine the suspected cases in more detail and after the notification is made, follow-up should be done by relevant institutions of the state which primary duty is to protect the child.

Our study has several limitations; only the patients who applied to the emergency department of our hospital were included in the study. Due to the presence of other private and public hospitals in the vicinity, the data cannot fully represent the population of the region. Secondly, toxicological screening or concentration determination was not performed for most of the active substances. Active substances were recorded on the basis of anamnesis from the patient or patient's relatives and clinical findings. On the other hand, we were unable to follow the judicial process in cases that judicial notification was made. This caused us not to be able to determine whether the cases entered as "an accident" to medical records were assessed by the authorities as abuse or neglect.

Conclusion

In children, the poisoning-related clinical picture may be easily misdiagnosed or undiagnosed. For this reason, it may delay the treatment and cause severe damage to the child. Therefore, the best fight against poisoning is the prevention studies [34]. Eighty percent point three of the cases in our study (rate of poisoning due to accidents in all cases) can be prevented by necessary regulations and measures. Wide range of groups and sectors must work together in order to prevent poisoning of children effectively. In addition to the health sector, parents and caregivers, education sector, Ministry of Justice, trade and industry institutions, consumer associations, non-governmental organizations related to child safety, manufacturers and sellers of pharmaceuticals, agricultural chemicals and other toxic substances, industrial establishments using toxic substances in which children are employed need to be involved for the successful prevention of incidental poisoning of children. And in order to prevent child poisoning the first thing that needs to be done in our country is the regulations on child-resistant packaging [35], which have been considered to be the most effective method up to now, should be put into effect as soon as possible.

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CASE REPORT / OLGU SUNUMU

Ultrasound and MRI features of lipomatosis of the median nerve: A case study

Median sinir lipomatozisinin ultrason ve MR görüntüleme özellikleri

Cemal Aydin GUNDOGMUS, Onur BUGDAYCI, Mustafa Erkin ARIBAL

ABSTRACT

We present a case of a 10 year-old girl with slowly enlarging, painless mass at the volar aspect of her left hand. The lesion had been present since infancy. Diagnosis was lipomatosis of the median nerve which is a very rare, benign tumor involving peripheral nerves. Magnetic resonance imaging (MRI) and ultrasound (US) features of this lesion are discussed.

Keywords: Median nerve lipomatosis, Fibrolipomatous hamartoma, Congenital tumor, Peripheral nerve

ÖZ

Bu vaka bildiriminde, sol el volar yüzde, infant döneminden beri olan, yavaş büyüyen, ağrısız şişlik şikayeti olan 10 yaşında bir kız çocuğu sunulmaktadır. Tanı, periferik sinirleri tutan çok nadir, benign bir tümör olan median sinirin lipomatozisi idi. Yazıda median sinir lipomatozisinin magnetik rezonans görüntü (MRG) ve ultrason (US) özellikleri tartışıldı.

Anahtar kelimeler: Median sinir lipomatozisi, Fibrolipomatöz hamartom, Konjenital tümör, Periferik sinir

Introduction

Lipomatosis of the peripheral nerves are very rare congenital lesions. The median nerve is the most commonly affected nerve, mostly at the level of the wrist. Magnetic resonance imaging (MRI) is diagnostic for this entity and most of the case reports (less than 100 so far) put emphasis on its MRI features [1]. Ultrasound (US), as well, provides very valuable information. In this report, we discussed US imaging features of lipomatosis of the median nerve with MRI correlation.

Case Report

A 10-year-old girl admitted to our orthopedics clinic with complaints of swelling at the volar aspect of her left (non-dominant) hand. Her history revealed that it had been present since infancy and had grown slowly. She did not have complaints of pain, sensorial loss or muscle weakness. There were no signs of carpal tunnel syndrome.

Physical examination revealed an elastic, soft, non-tender, 4x3 cm mass at the central region of her left proximal palmar region. The mass was not extending to the wrist. Macrodactyly was not present. No thenar atrophy was noticed. Sensorial alteration was not noted. Both Phalen's and Tinel's signs were negative.

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Results of baseline laboratory tests were in normal ranges. Intravenous (IV) contrast enhanced MRI of her left hand was requested.

The MRI examination revealed a 57x32 mm lesion, originating from median nerve at the volar aspect of the left hand. The lesion was isointense to fat on all sequences and surrounding nerve fibers (the so called "co-axial cable like" or "spaghetti like" appearance) (Figure 1a,b,c). The lesion did not enhance with IV contrast (Figure 2a,b). We performed US examination to determine its proximal extent.

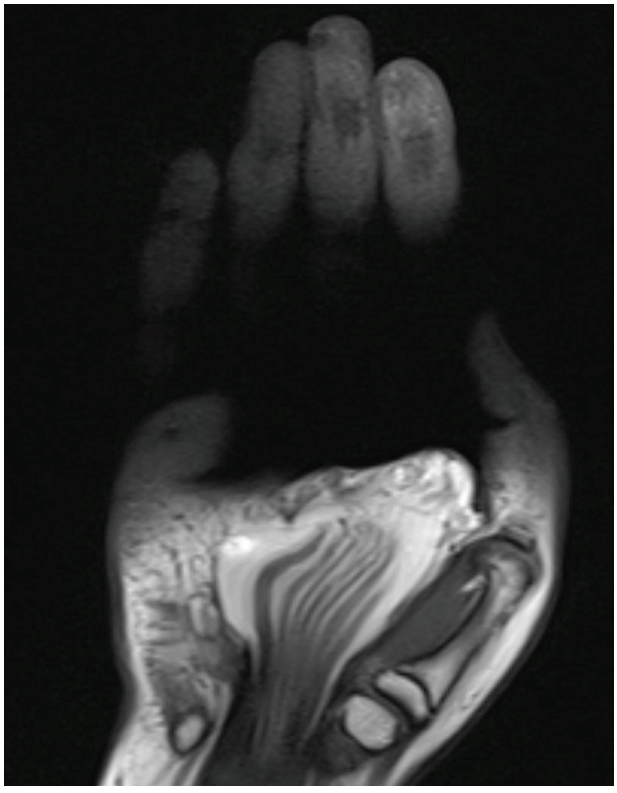

Figure 1a. T1 TSE coronal images show spaghetti like and co-axial cable like appearences.

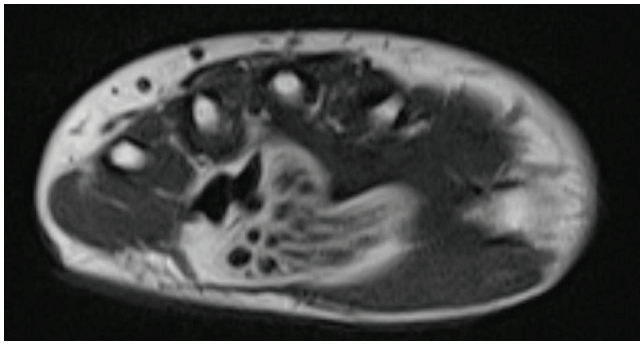

Figure 1b. T1 TSE axial images show spaghetti like and co-axial cable like appearences.

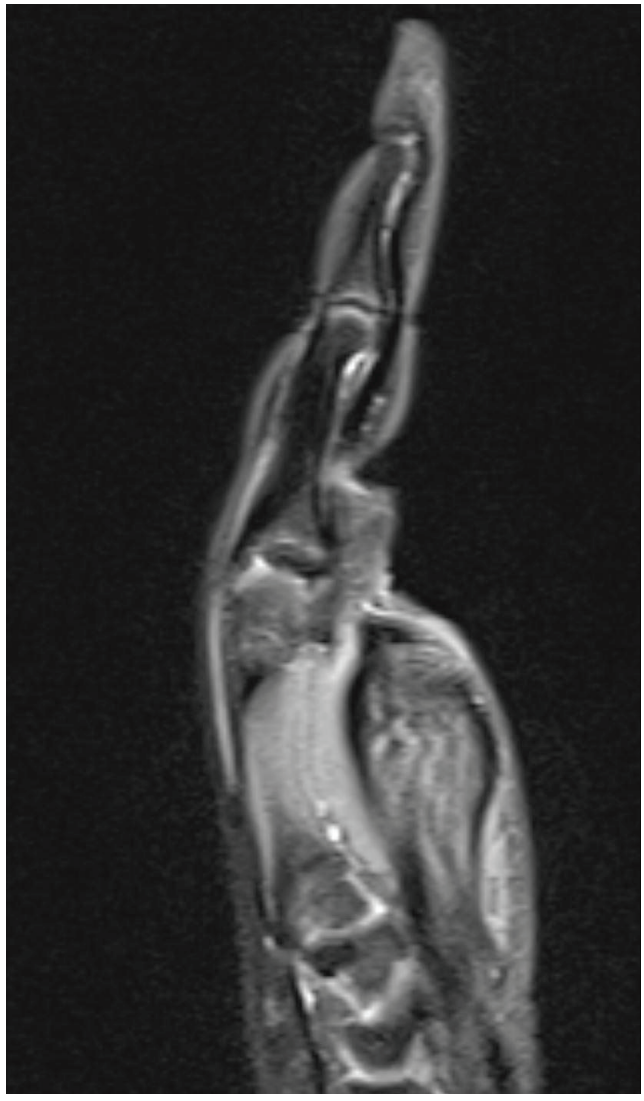

Figure 1c. Pd TSE fat saturated sagittal image shows hyperintense nerve bundles surrounded by hypointense fibrofatty tissue.

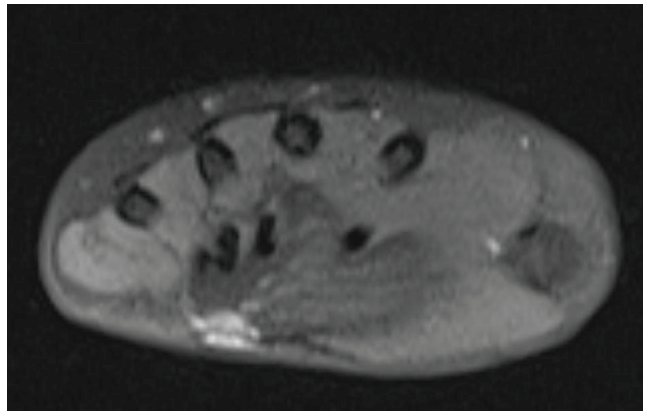

Figure 2a. T1 TSE axial fat saturated pre-contrast image.

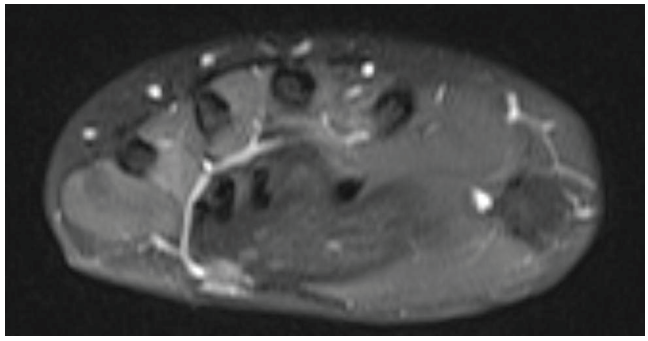

Figure 2b. T1 TSE fat saturated post-contrast image reveals that the lesion shows no enhancement.

US examination showed a 75x35 mm lesion composed of echogenic fat tissue and hypoechoic, thickened nerve fibers. The lesion extended to the distal forearm. Nerve fibers had the classical "co-axial cable like appearance" on axial US images, as well. On Doppler examination the lesion was hypovascular and there was only minimal intralesional blood flow (Figure 3a,b,c).

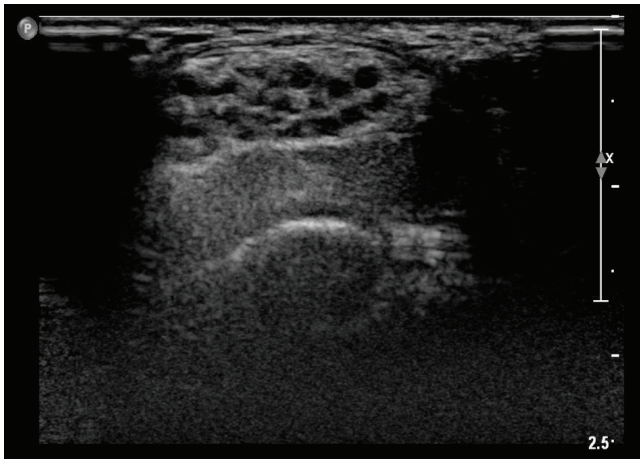

Figure 3a. Axial US images reveal round hypoechoic nerve bundles surrounded by hyperechoic fat.

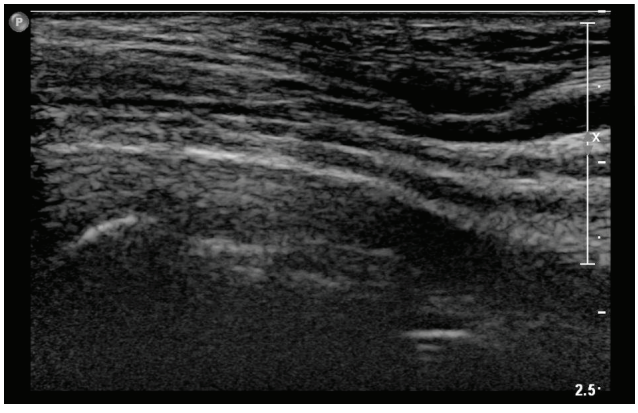

Figure 3b. Longitudinal US image reveals round hypoechoic nerve bundles surrounded by hyperechoic fat and extension to distal forearm.

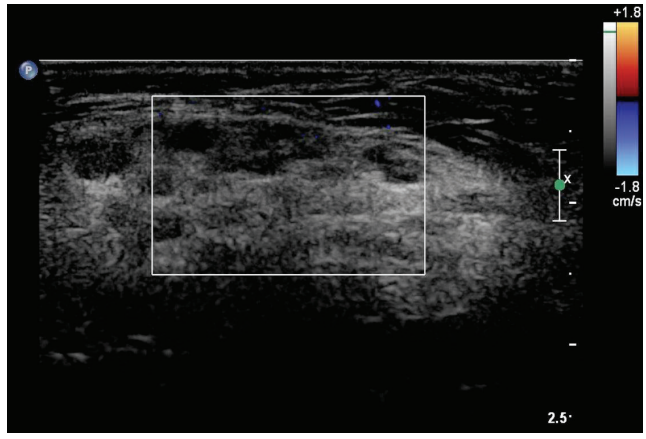

Figure 3c. Doppler US shows no evident blood flow.

Diagnosis was made with MRI and US findings, biopsy was not performed. Since it is a benian condition and patient did not have median nerve compression findings or macrodactyly, surgery was not performed in our case.

Discussion

Two percent of all upper extremity tumors are nerve tumors. Schwannoma is probably the most common diagnosis. Usually, diagnosis of nerve tumors is based on histopathologic findings. In contrast, lipomatosis of nerve has characteristic MRI findings [1].

Lipomatosis of nerve was first described by Mason in 1953 [2]. Johnson and Bonfigilo introduced the term lipofibromatous hamartoma [3]. In 2002, the World Health Organization adopted the term lipomatosis of nerve [4]. To date, there are several terms used to describe this condition including fibrolipomatous hamartoma, intraneural hamartoma, neural fibrolipomatosis and neural fibrolipoma [5].

Lipomatosis of the nerve is a rare, congenital, benign tumor consisting fibrofatty proliferation within peripheral nerves with unknown etiology. Hypertrophy of fat and fibroblasts in the epineurium results in enlargement of the involved nerve. The median nerve is the one most commonly affected, followed by the ulnar and radial nerves, the brachial plexus and cranial nerves [6].

Most common presentation of lipomatosis of nerve is a swelling or mass on the volar aspect of the wrist or distal forearm. Patients present mostly during childhood and the chief complaint is a painless mass. The mass usually appears years before neurologic symptoms since it grows slowly. Associated clinical symptoms are pain, numbness,

motor and sensory deficits in the median nerve distribution caused by compression of median nerve in the carpal tunnel [7]. Guthikonda et al., classified lipid-containing neural masses according to relation with parent nerve. Soft tissue lipoma, lipomatosis of nerve, intraneural lipoma and macrodystrophia lipomatosis are included to this classification. Soft tissue lipomas are easily differentiated as they are located outside the nerve and does not contain any neural proliferation. Intraneural lipomas are focal lipid masses which are separate from nerve bundles [8]. Macrodactyly is seen in %27-67 patients and has been referred to as macrodystrophia lipomatosa [9-11]. Other causes of macrodactyly are neurofibromatosis type 1, Proteus syndrome and Klippel-Trenaunay-Weber syndrome.

US and MRI examination of these lesions are pathognomonic and usually diagnosis can be made without a biopsy. US examination reveals round hypoechoic nerve bundles surrounded by hyperechoic fat. Long axis examination shows the "spaghetti like" appearance and on the axial plane a "co-axial cable like" appearance is seen. Color Doppler US shows no evident blood flow within the lesion. MRI reveals fusiform enlargement of the nerve containing thickened axonal bundles encased in epineural fibrous tissue giving again the "co-axial cable like" appearance on axial images and "spaghetti like" appearance on coronal images [12]. The lesions do not enhance with IV contrast material.

US revealed hypoechoic nerve bundles surrounded by fat tissue without evident blood flow in our case. The extension of the lesion to the forearm was also assessed with US imaging. MRI showed spaghetti like and co-axial cable like appearences and in proton density fat-saturated sequences showed hyperintense nerve bundles surrounded by hypointense fibrofatty tissue. All of the imaging findings in this case were consistent with the literature.

Histopathologic examination reveals fatty infiltration separating nerve bundles.

Treatment is mostly conservative. Surgery may be performed in symptomatic patients for decompression and amputation may sometimes be necessary for macrodactyly.

Acknowledgements

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