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HLA-B*51 POZİTİF BEHÇET HASTALARINDA HLA-B*51 ALLELLERİNİN ARAŞTIRILMASI

Sinem TOPCU AYAS[1,2], Aslı OZKIZILCIK KOCYIGIT[3], Tulay KILICASLAN AYNA[4,5*], Kiymet Handan KELEKCI[6], Mustafa SOYOZ[7,8], Ibrahim PIRIM[9,10]

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ABSTRACT

Aim: The initial identification of Behçet's disease (BD) occurred in 1937, credited to the Turkish dermatologist Prof. Dr. Hulusi Behçet. Symptoms included repeated oral aphthae, genital ulcers, and uveitis. Then, it was revealed that the illness involves the joints, blood vessels, intestines, lungs, and brain system. Age, gender, psychological factors, infectious agents, immune responses, and genetic predispositions affect illness progression. The most common genetic risk factor is HLA-B*51. This study aimed to examine the relationship between HLA-B*51 sub-alleles and illness etiology.

Materials and Method: We compared the prevalence of two HLA-B*51 sub-alleles (HLA-B*51:01 and HLA-B*51:08) in patients with BD versus healthy individuals. The samples of 24 HLA-B*51 positive individuals were typed by Polymerase Chain Reaction with Sequence-Specific Primers (PCR-SSP). In the control group, 73 healthy bone marrow donors were HLA-B*51 subtyped by DNA sequencing.

Results: The prevalence of HLA-B*51:01 and 51:08 sub-alleles in patients was 80% and 20%, respectively. The frequencies of HLA-B*51:01, 02, 05, 07, and 08 in the control group were 90.4%, 4.1%, 2.7%, 1.4%, and 1.4%, respectively. There was no significant difference in HLA-B*51:01 allele frequency between patient and control groups ($p>0.05$; $p=0.457$ $RR<1$). Statistically significant differences were seen for the HLA-B*51:08 allele ($p<0.05$; $p=0.003$ $RR=18.8$). No statistically significant correlation was found between HLA-B*51:01 and HLA-B*51:08 sub-alleles and clinical symptoms (p-value > 0.05).

Conclusion: HLA-B*51:08 sub-allele may be an important risk factor for BD development. Future investigations can further highlight the significance of its role in the pathophysiology of the disease.

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INVESTIGATION OF HLA-B*51 SUB-ALLELES IN HLA-B*51 POSITIVE BEHCET PATIENTS
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ÖZET

Amaç: 1937 yılında Türk Dermatolog Prof. Dr. Hulusi Behçet tarafından keşfedilen Behçet Hastalığının (BH) semptomları tekrar eden oral aft, genital ülserler ve üveyitti. Daha sonra bu hastalığın eklemleri, kan damarlarını, bağırsakları, akciğerleri ve beyin sistemini de kapsadığı bildirilmiştir. Hastalığın seyrini yaş, cinsiyet, fizyolojik faktörler, enfeksiyöz ajanlar, immün yanıt ve genetik geçişler etkiler. En yaygın görülen genetik risk faktörü İnsan Lökosit Antijeni (HLA)-B*51'dir. Bu çalışmada HLA-B*51 alt alleleri ile hastalık etyolojisi arasındaki ilişki irdelenmesi amaçlanmıştır.

Gereç ve Yöntem: BH hastaları ile kontrol grubu arasında HLA-B*51 alt allellerinin prevalanslarını karşılaştırdık. Sekans spesifik primer polimeraz zincir reaksiyonu (SSP-PZR) yöntemiyle HLA-B*51 pozitif olan 24 kişinin doku tiplemesi yapılmıştır. Kontrol grubunda ise kemik iliği donörü olan 73 sağlıklı bireyin HLA-B*51 alt allel tiplemesi DNA dizi analizi yöntemiyle belirlenmiştir.

Bulgular: Hasta grubunda HLA-B*51:01 ve 51:08 alt allellerinin prevalansı sırasıyla %80 ve %20 bulunmuştur. HLA-B*51:01, 02, 05, 07 ve 08 alt allellerinin kontrol grubundaki sıklıkları sırasıyla %90,4, %4,1, %2,7 %1,4 ve %1,4 olarak bulunmuştur. Hasta ve control grubu arasında HLA-B*51:01 alt allelinin sıklığı bakımından istatistiksel olarak anlamlı bir farklılık bulunmamıştır ($p>0.05$; $p=0.457$ RR<1). İstatistiksel olarak anlamlı sonuçlar HLA-B*51:08 alt alleli için bulunmuştur ($p<0.05$; $p=0.003$ RR=18.8). HLA-B*51:01 ve HLA-B*51:08 alt allelleri ile klinik semptomlar arasında anlamlı bir ilişki bulunmamıştır.

Sonuç: HLA-B*51:08 alt allelinin BH gelişiminde önemli bir faktör olabilir. Yapılacak çalışmalarla hastalığın patofizyolojisi açısından önemi gösterilebilir.

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Introduction

Prof. Dr. Hulusi Behçet, a famous Turkish dermatologist, discovered Behçet's Disease (BD) in 1937. Recurrent oral, vaginal, and uveitis are the most common BD symptoms. After that, the illness was linked to joint, blood vessel, gut, lung, and nervous system symptoms (1). BD is common worldwide, especially in Silk Road countries (2). The disease was most common in Turkey (3). Males are more likely to be diagnosed between 20 and 40. In teenage males, the disease's development is connected to poor clinical outcomes (4,5). For years, diagnostic criteria and classifications have been researched, but BD diagnosis has no definitive clinical finding. According to the 1990 I International Study Group for Behçet's Disease (ISGBD) diagnostic criteria, oral aphthous ulceration patients must have two other clinical symptoms: papulopustular lesions, erythema nodosum-like lesions, genital ulcers, superficial thrombophlebitis, eye involvement, and/or positive pathergy test.

Several studies have found that the HLA-B*51 allele is the most crucial genetic predisposition factor. Ohno et al. first linked BD to HLA-Bw51 in 1982 (6). Those with a genetic predisposition are known to get the disease through infections and environmental causes. Patients with vaginal and gastrointestinal ulcers have Herpes Simplex Virus Type I genomes in their saliva and peripheral lymphocytes. Due to their functional importance, infectious pathogens resemble human heat shock protein 65 (Hsp65). It is believed that Mycobacterium-derived Hsp56 activates T cells like human Hsp60. Identifying a BD pathogen or autoantigen is still difficult (7,8). The second hypothesis is that HLA-B*51 suppresses BD by binding to the Killer cell immunoglobulin-like receptor 3DL1 (KIR3DL1) receptor on natural killer (NK) cells. If HLA-B*51 expression on the cell surface stays normal, the observed cellular response protects cells from cytotoxicity (9). NK cells are suppressed by HLA-B*51 and KIR3DL1, although NKG2D (one of the NK cell activating receptors) and its ligand MHC class I polypeptide–related sequence A (MICA) counteract this. It has also been recommended that HLA-B*51 and KIR3DL1 lower allele combinations may contribute to this syndrome (10).

Cross-reactivity between HLA-B*51 and organ-specific antigens may play a major role in disease development (11). B alleles like B*51 and B*27 share amino acids with retinal soluble antigen peptides (12). Another possibility for the correlation between BD and genetics is this antigen's linkage disequilibrium (13). Inheritance of MICA*009, Tumor necrosis factor (TNF)-α, and HLA-B*51 genes may impact disease development (14). The sub-alleles HLA-B*51:01 and 51:08 are more common in BD (15,16). Asparagine at 63 and phenylalanine at 67 identify these compounds. However, amino acids at positions 67, 97, 116, and 152 may provide a significant risk of BD. Different amino acids may play different functions in antigen presentation (15).

The objective of this study was to conduct a comparative analysis of HLA-B*51 sub-alleles in both patients and healthy volunteers, to identify any potential link between certain sub-alleles and the progression of the disease. This will facilitate the diagnosis of BD. Furthermore, an investigation was conducted to examine the correlation between sub-alleles and the manifestation of organ involvement in individuals who tested positive for HLA-B*51.

Material and Methods

Study populations

This study included a total of 24 patients who tested positive for HLA-B*51. These patients were under the care of the Dermatology Department in two separate hospitals over the period from February to September 2017. The study comprised healthy patients who applied to the same laboratory as a donor for hematopoietic stem cell transplantation and underwent high-resolution HLA-B typing, serving as the control group. A statistical comparison was conducted

between a group of seventy-three healthy individuals who tested positive for the HLA-B*51 gene and the patients.

Signed Informed Consents were obtained from all patients. In compliance with the Declaration of Helsinki, our Institutional Non-Interventional Clinical Research Ethics Committee approved the study (Decision No: 17, 09.02.2017).

DNA isolation

The process of DNA isolation from whole blood was performed with the QiaAmp DNA Blood Mini Kit (Qiagen, USA) in accordance with the instructions provided by the manufacturer. Specifically, a 200µl blood sample was introduced into a 1.5 ml micro-centrifuge tube, and the pre-prepared kit was placed into the automated DNA Isolation device (QIAGEN Geno-M6, Alameda, CA). Ultimately, a DNA sample of 50 µl was obtained through the process of elution. The Nanodrop Spectrophotometer device (Thermo Scientific Nanodrop 2000, Wilmington, Delaware USA) was utilized to determine the purity and concentration of the samples. The samples that exhibited a concentration greater than 15 ng/µl and a purity range of 1.80-1.90 were deemed suitable for inclusion in the study.

High-resolution sequence-specific primer (PCR-SSP) assay

HLA-B*51 positive Behçet patients' sub-alleles were determined by this assay. Following the manufacturer's recommendations, SSP HLA-B*51 Kit (HLA-B51 Excl Taq Lifecodes, Stamford, USA) was used: A mix was created by adding 264 µl master mix, 176 µl DNA sample, 433 µl dH2O, and 7 µl Taq DNA polymerase (Lifecodes, USA). For each well, a 10 µl sample was added from the mix. PCR conditions included 1 cycle of denaturation at 94°C for 2 minutes, 10 cycles of denaturation, annealing, and extension at 94°C and 65°C for 10 and 60 seconds, respectively, 20 cycles at 94°C for 10 seconds, 61°C for 50 seconds, and 72°C for 30 seconds. Amplicons were kept at 4°C for analysis. Amplification was followed by 2% Agarose gel electrophoresis (0.5X tris-boric acid-EDTA). Electrophoresis was 20 minutes at 140V and 400A. Under the UV transilluminator, gel bands were seen. The findings were evaluated using Olerup SSP Start Score Version 5.00.41T/07 (Stockholm, Sweden).

Statistical analysis

The Statistical Package for Social Sciences for Windows Version 22.0 (SPSS 22.0 Inc, Chicago, USA) for Windows 7 Software Program was utilized to conduct the statistical analyses. The numerical parameters were compared using the Mann-Whitney U Test. The statistical tests of Pearson Chi-square and Fisher's Exact test were utilized to examine the association between qualitative variables. A significance level of $p<0.05$ was deemed as statistically significant. The assessment of the likelihood of developing BD with HLA-B*51 sub-alleles was conducted based on the Relative Risk (RR) associated with the disease (17).

Results

The frequency of the HLA-B*51 allele among BD patients admitted to our laboratory between 2014 and 2017 was 71.4%. The study found that 62.5% (n=15) of the patients were male, whereas 37.5% (n=9) were female. Among the patient population, a majority of 79.1% (n=19) exhibited the HLA-B*51:01 sub-allele, while a smaller proportion of 16.6% (n=4) displayed the HLA-B*51:08 sub-allele. Additionally, a minority of 4.1% (n=1) presented with both the HLA-B*51:01 and HLA-B*51:08 sub-alleles. Among the cohort of healthy participants, it was observed that 90.4% (n=66) carried the HLA-B*51:01 allele, while 4.1%

(n=3) had the HLA-B*51:02 allele. Additionally, 2.7% (n=2) of the participants exhibited the HLA-B*51:05 allele, while 1.4% (n=1) had the HLA-B*51:07 allele. Lastly, another 1.4% (n=1) of the healthy individuals carried the HLA-B*51:08 sub-allele. The frequencies of HLA-B*51 sub-alleles in patients with BD and the control group were presented in Figure 1 and Figure 2, respectively.

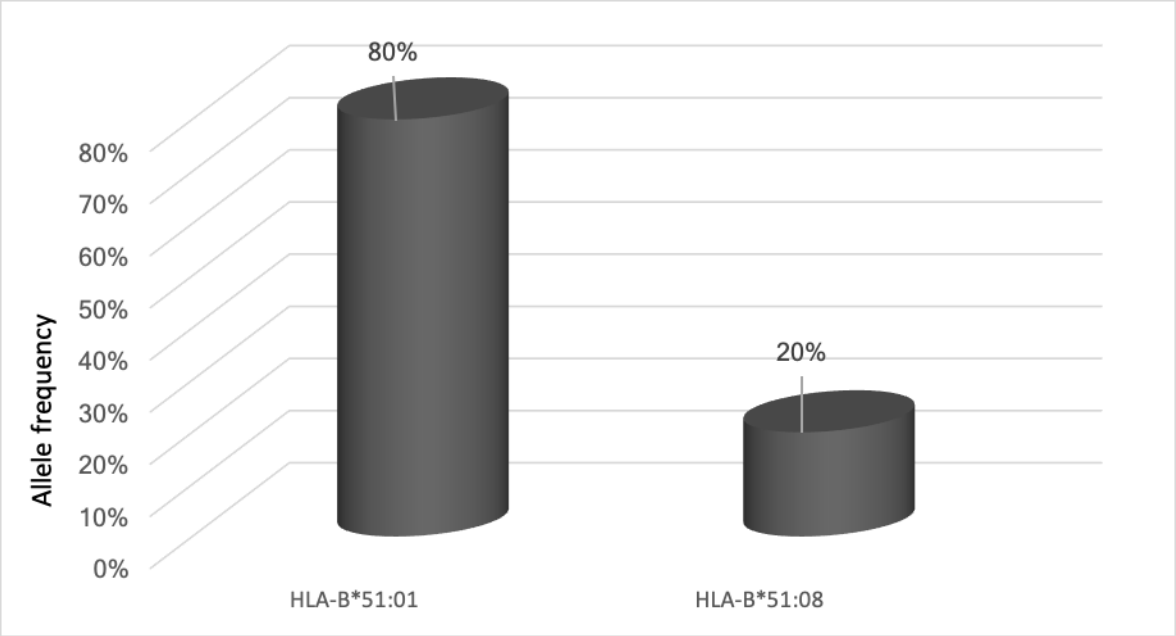

Figure 1. HLA-B*51 sub-allele frequencies of the patient group

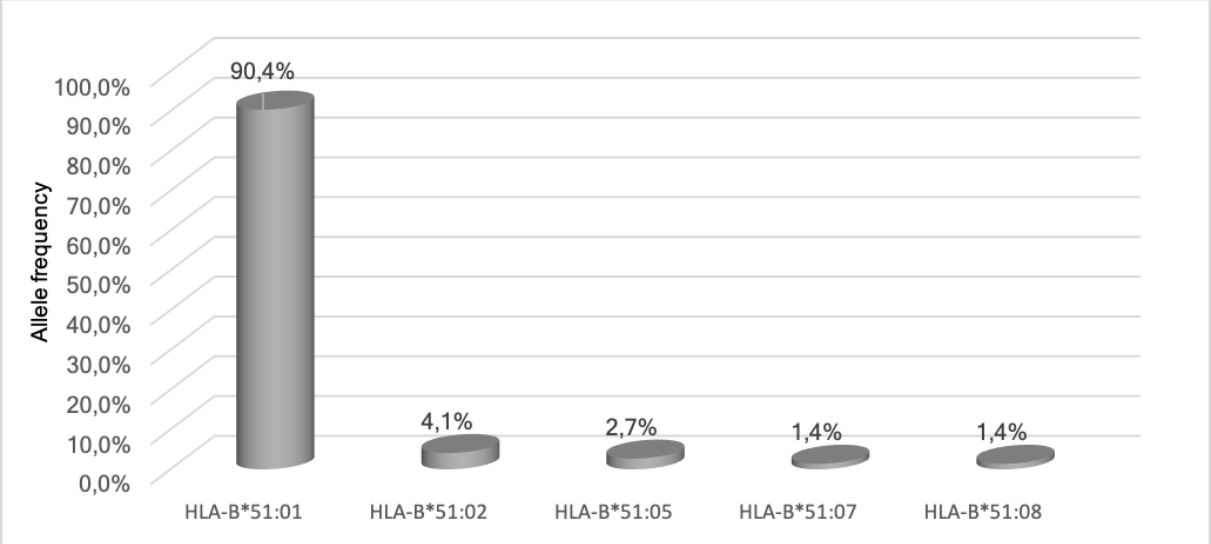

Figure 2. HLA-B*51 sub-allele frequencies of the control group

The clinical manifestations were categorized into two groups: major symptoms, which included oral aphthae, vaginal aphthae, dermatological complaints, and ophthalmic involvement, and minor findings, which encompassed neurological, joint, and vascular involvement. This classification was employed to investigate the potential correlation between HLA-B*51 and the clinical symptoms.

The most common HLA-B*51 sub-allele in both groups was 51:01. HLA-B*51:08 was also common in patients (Table 1).

Table 1: Comparison of HLA-B*51 suballeles frequency of Behçet's patients and control group

HLA-B*51 suballeles	**Patients (*n*=24)**	**Control (*n*=73)**	***p***	**Relative risk (RR)**
HLA-B*51:01	20 (80%)	66 (90.4%)	0.457	0.88
HLA-B*51:02	0 (0%)	3 (4.1%)	-	
HLA-B*51:05	0 (0%)	2 (2.7%)	-	
HLA-B*51:07	0 (%0)	1 (%1.4)	-	
HLA-B*51:08	5 (%20)	1 (%1.4)	**0.003**	**18.8***

*95% Confidence Interval 18.8 (2.08-166)

There was no statistically significant difference observed in the prevalence of the HLA-B*51:01 sub-allele between patients diagnosed with BD and the control group (p=0.457, relative risk (RR)=0.88). Given that the RR is smaller than 1, there is a decreased likelihood of disease occurrence in individuals who carry the HLA-B*51:01 allele. There was a statistically significant difference in the frequency of HLA-B*51:08 between the sick group and the control group (p=0.003, RR=18.8). In this particular scenario, individuals who carry the HLA-B*51:08 allele exhibit a significantly elevated risk, approximately 18.8 times greater, of developing the condition in question.

The occurrence of significant clinical observations, such as oral aphthae, vaginal aphthae, and ocular involvement, was noted in a comparable sequence, as indicated in Table 2. There was no statistically significant association seen between HLA-B*51:01 and HLA-B*51:08 and organ involvement, as indicated by a p-value greater than 0.05. The occurrence rates of significant clinical observations, including dermatological, neurological, joint, and vascular involvement, exhibited comparable frequencies (see Figure 3).

Table 2: Relationship between HLA-B * 51 sub-alleles and clinical symptoms in BD patients

	HLA-B*51 sub-alleles (*n*=24)				χ^2	
	HLA-B*51:01 (*n*=20)		HLA-B*51:08 (*n*=5)		HLA-B*51:01 (*n*=20)	HLA-B*51:08 (*n*=5)
	Positive	Negative	Positive	Negative		
Major clinical findings						
Oral aphthae	90% (n=18)	10% (n=2)	100% (n=5)	0% (n=0)	0.461	0.461
Genital Aphthae	50% (n=10)	50% (n=10)	80% (n=4)	20% (n=1)	1	1
Eye involvement	40% (n=8)	60% (n=12)	60% (n=3)	40% (n=2)	0.341	0.341
Minor clinical findings (dermatological, neurological, joint and vascular involvement**)**	%55 (n=11)	%45 (n=9)	%40 (n=2)	%60 (n=3)	1	1

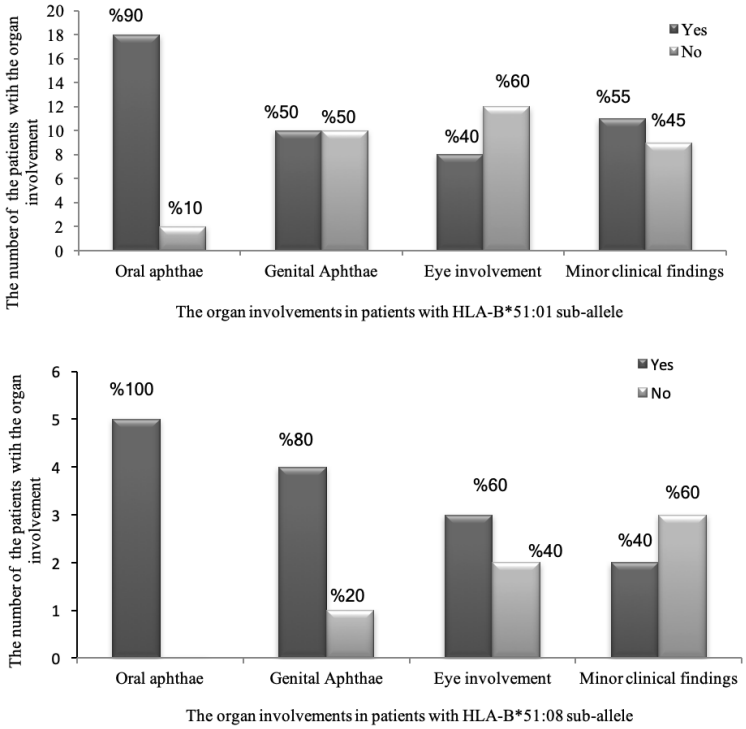

Figure 3. The comparison of organ involvement in Behçet's patients with HLA-B*51:01 and HLA-B*51:08 sub-alleles

Discussion

The human genome's most variable region is the 4 Mb HLA region (18). Over two hundred genes reside in the region, and twenty-two are linked to the immune system (19) and other illnesses (17). HLA-B5 and its variation, HLA-B*51, were documented by Ohno (20) in Japan and by Yazıcı (21), Soylu (22), (23), and Azizlerli (24) in Turkey. Zierhut et al. (25) helped Germans grasp this subgroup. Several methods linked HLA-B*51 polymorphism to BD. With the development of molecular technologies, HLA gene DNA analysis became possible. After the discovery of HLA-B*51 in BD, sub-alleles have garnered attention. Based on 2017 data, 280 HLA-B*51 sub-alleles were discovered. The findings linked BD to the HLA-B*51:01 and 51:08 sub-alleles (26).

Six Turkish research examined sub-alleles and HLA-B*51-positive BD. Balkan et al. found HLA-B*51:01 (97.5%) and HLA-B*51:09 (2.5%) sub-alleles in 2017 HLA-B*51 positive patients (27). Müller et al.'s 2005 study found that HLA-B*51:01 (87.5%) and HLA-B*51:08 (14.2%) were the most common sub-alleles (28). Pirim et al. (2004) found HLA-B*51 sub-alleles: HLA-B*51:01 (45.5%), HLA-B*51:08 (25%), HLA-B*51:05 (9.1%), HLA-B*51:11 (6.81%), and HLA-B*51:04 (4.54%) (29). Demirseren et al. (2014) found HLA-B*51:01 (68.6%), 51:02 (33.3%), 51:09 (21.5%), and 51:22 (17.6%) sub-alleles (30). Kötter et al. found HLA-B*51:01 (81%), HLA-B*51:08 (11%), and HLA-B*51:05 (2%) in 2001 (31). Atalay et al. (1998) found 94% of patients had HLA-B*51:01 and 6% had 51:08/09 (32).

The present investigation examined the prevalence of HLA-B*51 sub-alleles in patients who tested positive for HLA-B*51. The results revealed that HLA-B*51:01 was observed in 80% of the patients, whereas HLA-B*51:08 was found in 20% of the patients. The findings of this study were in line with previous research conducted on Turkish patients diagnosed with Behçet's disease. A higher prevalence of the condition was noted among males in both the Turkish population and Mediterranean countries (3). In the present investigation, a total of 24

patients were included, with 62.5% (n=15) being male and 37.5% (n=9) being female. Among the male patients, 75% exhibited the presence of HLA-B*51:01, whereas the remaining 25% displayed HLA-B*51:08. All female patients in the study had the presence of HLA-B51*01. The observation of a male patient possessing both alleles is noteworthy.

This study revealed a significant association between the presence of the HLA-B*51:08 sub-allele and an increased illness risk, with patients carrying this sub-allele exhibiting an 18.8-fold higher susceptibility compared to those with alternative sub-alleles. The study conducted by Belem et al. (2020) revealed that HLA-B*51:08 was only detected in patients, while other sub-alleles were observed in both patients and healthy individuals within the Brazilian community (33). A prior meta-analysis has additionally demonstrated a robust correlation between the susceptibility to the disease and the existence of HLA*B51. Nevertheless, the sub-alleles were not taken into account in the study (34).

Behçet's disease's key criteria, such as recurrent mucosal and skin symptoms, ocular findings, and pathergy skin test, vary by ethnicity. Clinical criteria are used to diagnose Behçet's illness since there is no pathognomonic characteristic. In 2005, Davatchi et al. found oral aphthae in 100%, genital in 88%, eye involvement in 29%, joint involvement in 16%, and neurological complaints in 2.2% of BD patients regardless of tissue type, but no dermatological complaints (35). Demirseren et al. showed that 100% of patients had oral aphthae, 82.4% had genital, 35.3% had ocular, 47.1% had joint, and 7.8% had neurological problems (30). We found oral aphthae in 23 patients (95%), genital in 14 (58.3%), eye involvement in 11 (45.8%), and dermatologic/neurological/joint/vascular symptoms in 13 (65%). HLA-B*51:01 patients had the same order of key clinical findings as previously reported (19). We found that HLA-B*51:08 sub-alleles increased organ involvement (oral, vaginal, and ocular). The tiny size of our cohort may have hampered our investigation.

Conclusion

In conclusion, while there have been previous investigations on the sub-alleles of HLA-B*51 in Turkish individuals with BD, we posit that the identification of sub-alleles among patients residing in the Izmir region will make a valuable contribution to the existing body of literature. This study identified the HLA-B*51:08 sub-allele as a significant factor in the chance of developing BD. The findings of this study indicate that the presence of the HLA-B*51:08 sub-allele, as opposed to the HLA-B*51:01 allele, may offer significant insights into the pathophysiology of the disease.

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RESULTS OF ORAL STEROID TREATMENT IN PATIENTS DIAGNOSED WITH IDIOPATHIC GRANULOMATOUS MASTITIS

İDİOPATİK GRANULOMATÖZ MASTİT TANILI HASTALARDA ORAL STEROİD TEDAVİ SONUÇLARI

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ABSTRACT

Introduction: Idiopathic granulomatous mastitis (IGM) is a benign, chronic disease characterized by granulomatous inflammation in the breast tissue. There is still no standard treatment model for the disease. Treatment methods range from medical treatments to wide excisions. This study aimed to retrospectively analyze high-dose steroid use and its results in patients diagnosed with IGM.

Materials and methods: In this retrospective study, 48 patients diagnosed with granulomatous mastitis were evaluated, and it was determined that 46 of these patients were diagnosed with IGM. Histopathological diagnosis was made by core biopsy. The patients' age, gender, pathological diagnosis, culture results, presence of abscess, treatment dose, treatment duration, treatment responses, and recurrence were evaluated.

Results: 48 patients diagnosed with granulomatous mastitis were evaluated. Two of these patients were excluded from the study because infectious agents were detected. 46 patients were included in the study. All patients were women. The average age of the patients was 36.32 years and the follow-up period was 28.52 months. The average PPD test results of the patients was found to be 5.58 mm. Patients were started on 0.8 mg/kg/day methylprednisolone tablets. After 3 weeks, the treatment was reduced by 0.1 mg/kg/day per week and completed after 10 weeks. Relapse was observed in 3 patients (6.52%). No surgical procedure was performed on the patients. Abscess formation was observed in 9 patients while receiving steroid treatment. Samples were taken from these patients by aspiration and sent for culture. Coagulase (-) staphylococcus grew in 3 patients (6.52%).

Conclusion: It was concluded that high-dose steroid treatment is effective in IGM cases, and good results can be achieved with low recurrence rates and minimal deformity without the need for surgical intervention.

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ÖZET

Giriş: İdiopatik granülomatöz (IGM) mastit meme dokusunda granülomatöz bir inflamasyon ile karakterize benign, kronik bir hastalıktır. Hastalığın halen standart bir tedavi modeli bulunmamaktadır. Medikal tedavilerden geniş eksizyonlara kadar uzanan tedavi yöntemlerine rastlanılmaktadır. Bu çalışmada IGM tanılı hastalarda yüksek doz steroid kullanımı ve sonuçlarının retrospektif analizi amaçlanmıştır.

Gereç ve yöntem: Bu retrospektif çalışmada 48 granülomatöz mastit tanılı hasta değerlendirildi, bu hastaların 46 tanesinin IGM tanısı aldığı belirlendi. Hastalara histopatolojik tanı core biyopsi ile konuldu. Hastaların yaşı, cinsiyeti, patolojik tanıları, kültür sonuçları, abse varlığı, tedavi dozu, tedavi süresi, tedavi cevapları ve nüks durumları değerlendirildi.

Bulgular: Granülomatöz mastit tanısı alan 48 hasta değerlendirildi. Bu hastalardan ikisisinde enfeksiyon ajanları tespit edildiği için çalışma dışı bırakıldı. 46 hasta çalışmaya dahil edildi. Hastaların tamamı kadın idi. Hastaların yaş ortalaması 36,32 yıl, takip süresi 28,52 ay olarak bulundu. Hastaların PPD test sonuçlarının ortalaması 5,58 mm olarak bulundu. Hastalara 0,8 mg/kg/gün metilprednizolon tablet başlandı. 3 hafta sonra haftada 0,1 mg/kg/gün azaltılarak 10 hafta sonra tedavi tamamlandı. 3 hastada (%6,52) nüks görüldü. Hastalara herhangi bir cerrahi işlem yapılmadı. Steroid tedavisi alırken 9 hastada apse formasyonu görüldü. Bu hastalardan aspirasyon ile örnek alınıp kültüre gönderildi. 3 hastada (%6,52) koagülaz (-) stafilokok üredi.

Sonuç: IGM olgularında yüksek doz steroid tedavisinin etkin, cerrahi müdahaleye gerek kalmadan düşük nüks oranları ve minimal deformite ile iyi sonuçlar ortaya koyabileceği sonucuna varılmıştır.

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Introduction

Idiopathic granulomatous mastitis (IGM) is a rare chronic granulomatous inflammation of the breast (1). The etiology of granulomatous mastitis includes diseases characterized by granuloma formation such as tuberculosis, sarcoidosis, and cat scratch disease. The term idiopathic granulomatous mastitis is used when no specific cause of granuloma formation can be identified. IGM is a benign breast pathology (2). IGM can present with clinical and radiological features similar to breast cancer (3). There is no standard approach to the treatment of IGM, and various treatment modalities ranging from medical treatments to wide excisions have been reported (1,4). IGM is a pathology based on a chronic disease that can have recurrences. Surgical procedures performed in patients diagnosed with IGM can result in volume loss and deformities in the breast. Therefore, medical treatments that preserve breast integrity and result in less deformation are more widely accepted nowadays.
This study aimed to retrospectively evaluate the outcomes of high-dose oral steroid treatment without any surgical intervention in patients diagnosed with IGM.

Materials and Methods

Patients who presented to the same general surgeon diagnosed with granulomatous mastitis based on biopsy results between January 2015 and July 2020 were retrospectively evaluated. A total of 48 patients diagnosed with granulomatous mastitis were identified, and their data were reviewed retrospectively through the hospital record system. Age, gender, histopathological and microbiological data, treatment methods applied, presence of abscess, treatment dose, treatment duration, treatment response, and recurrence status were recorded for all patients. This study was conducted retrospectively using data obtained from the hospital database. Hospital retrospective study permission was obtained for the study (2020-13626).

Results

A total of 48 patients diagnosed with granulomatous mastitis were retrospectively screened. It was determined that all patients were diagnosed through histopathological examination by performing a core biopsy under ultrasound guidance.
Out of the 48 patients diagnosed with granulomatous mastitis, one was male (2.08%) and 47 were female (97.92%).

In 2 out of the 48 patients with a diagnosis of granulomatous mastitis, specific causes of granulomatous inflammation were identified. One of these patients had a positive mycobacterium tuberculosis PCR result and mycobacterium tuberculosis growth in the Löwenstein Jensen medium. This patient was started on anti-tuberculosis treatment by the Department of Pulmonary Diseases and followed up. The other patient had an infection with the causative agent Bartonella henselae, confirmed by culture, and was treated with azithromycin by the infectious diseases department. The PPD result of the patient diagnosed with tuberculosis was 22 mm, and the PPD result of the patient with cat scratch was 11 mm. These two patients were excluded from the study as specific causes of granulomatous mastitis were identified. In the remaining 46 patients, no specific cause of granulomatous inflammation was identified, and these 46 patients were diagnosed with "Idiopathic Granulomatous Mastitis". All 46 patients diagnosed with IGM were female. The mean age was 36.32 years, and the mean follow-up duration was 28.52 months. It was determined that 4 of these patients (8.7%) were postmenopausal. When the microbiology culture results obtained during the diagnosis stage were examined, no growth was observed in any of the patients. The average PPD test result was found to be 5.58 mm.

After giving the patients 0.8 mg/kg/day methylprednisolone tablets (Prednol®, Mustafa Nevzat, Istanbul, Turkey) for 3 weeks, the dosage was gradually reduced over the following weeks: 0.7 mg/kg/day in the 4th week, 0.6 mg/kg/day in the 5th week, 0.5 mg/kg/day in the 6th

week, 0.4 mg/kg/day in the 7th week, 0.3 mg/kg/day in the 8th week, 0.2 mg/kg/day in the 9th week, and 0.1 mg/kg/day in the 10th week. To prevent the gastric side effects of methylprednisolone, all patients were given 30 mg/day of lansoprazole.

Aspiration was performed in 9 patients (19.56%) during the follow-up period due to accompanying abscess, and empirical antibiotic therapy was initiated. Coagulase-negative staphylococcus was detected in the culture of 3 patients (6.52%), while no growth was observed in the cultures of the remaining 6 patients.

No open drainage or surgical excision was performed in any of the patients during the treatment and follow-up period. One patient with a lesion located in the inner quadrant of the breast showed improvement with deformity after treatment (Picture 1). Recurrence was observed in 3 patients (6.52%) at the 4th, 7th, and 11th months. During the treatment period, patients were called for follow-up every 3 weeks.

Picture 1. A case of IGM that healed with deformity after treatment.

Discussion

IGM is a benign disease that is a chronic inflammatory pathology requiring long-term treatment. IGM is histopathologically described as chronic granulomatous lobulitis. Granulomas containing caseous necrosis are observed in tuberculosis mastitis, granulomas accompanied by vasculitis are observed in Wegener's granulomatosis, and diffuse granulomas are observed in sarcoidosis (5). In this study, tuberculosis was detected in one patient diagnosed with granulomatous mastitis, and cat scratch disease was detected in another patient, so they were not included in the IGM cases.

IGM generally affects women in premenopausal (1,4). In this study, 42 of our patients (91.3%) were premenopausal women, which confirms the literature data.

A PPD test result of 10 mm or higher is considered positive (6). In evaluating 48 cases of granulomatous mastitis in this study, PPD test results of 10 mm or higher were detected in 7 cases (22.92%) and considered positive. The PPD result of the patient who was excluded from the IGM cases due to tuberculosis diagnosis was 22 mm. No evidence supporting tuberculosis was found in the evaluation of the other 6 patients. Performing a PPD test for all patients before diagnosing IGM is important in distinguishing tuberculosis patients.

In their study, Tan et al. stated that they administered 20 mg/day oral methylprednisolone treatment for an average of 45 days to 88 patients diagnosed with IGM and achieved a good response rate of 80.7% (7). Another literature study reported that treatment started with 0.5 mg/kg/day methylprednisolone, the dose was reduced and discontinued after 2 weeks, and a complete response was obtained in 63% of the patients (8). Montazer et al. compared high and low-dose oral steroid use in IGM and stated that high-dose oral steroid use yielded better results and no relapses were observed (9). In this study, 0.8 mg/kg/day (high dose) methylprednisolone was administered for 3 weeks and the dose was reduced by 0.1 mg/kg/day starting from the 4th week, and the treatment was completed in a total of 10 weeks. A good response was obtained in 84.78% of the patients (Picture 2-3). The relapse rates in the literature are reported to be between 0% and 33.3% (6, 9, 10). In this study, the relapse rate was found to be 6.52%. Relapses were observed in the 4th, 7th, and 11th months in 3 out of 46 patients diagnosed with IGM. In addition to mastitis symptoms, cavitary lesions that fistulized to the skin were detected clinically and ultrasonographically in 2 of the relapsed patients. The third patient had symptoms of erythema, edema, tension, and tenderness in the mastitis. The same dose and duration of treatment as the initial treatment were repeated for these 3 patients. Complete response was achieved in the patients who experienced a relapse in the 7th and 11th months. However, no response was obtained in the patient who experienced a relapse in the 4th month. Since erythematous lesions also appeared on the patient's legs and were evaluated by dermatology, a diagnosis of erythema nodosum was made and confirmed by biopsy. Systemic methotrexate treatment was started for this patient. Remission was observed in this patient after treatment. The coexistence of IGM and erythema nodosum is rarely seen in the literature (11).

Picture 2. Pre-treatment appearance of the patient diagnosed with IGM.

Picture 3. Image of a patient diagnosed with IGM 6 months after oral steroid treatment.

There are studies in the literature that have used methylprednisolone treatment for 11 months (11, 12). This situation is associated with the prevalence of the disease, treatment response, and relapse.

The development of suppurative infection during steroid treatment of patients is a possible condition (12). When abscess formation is encountered, aspiration should be performed under ultrasound guidance and the abscess material should be sent for microbiological examination. If there is growth in culture, treatment should be given according to the appropriate antibiogram result.

In 3 out of 46 patients with no infectious agents in the culture results obtained at the beginning of treatment, coagulase-negative staphylococcus was detected in the collections that

developed during steroid treatment (6.52%). These patients were given treatment according to the antibiogram result.

Conclusion

With this study, it was concluded that high-dose oral steroid administration may be an effective treatment option for patients diagnosed with IGM, and good results with low relapse rates and minimal deformity can be achieved without the need for surgery.

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ÖZOFAGUS ATREZİSİ-TRAKEOÖZOFAGEAL FİSTÜL OLGULARINDA ANASTOMOZ KAÇAĞINI ÖNGÖREN RİSK FAKTÖRLERİ

RISK FACTORS PREDICTING POSTOPERATIVE ANASTOMOTIC LEAK IN ESOPHAGEAL ATRESIA- TRACHEOESOPHAGEAL FISTULA PATIENTS

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ÖZET

Amaç: Özofagus atrezisi/trakeoözofageal fistülün (EA/TÖF) olgularında primer onarımı sonrası anastomoz kaçağı insidansı %16,7 olarak bildirilmiştir. Ancak klinik olarak anlamlı büyük kaçaklar bunların yalnızca %5'ini oluşturmaktadır. Bu çalışmanın amacı, ÖA/TÖF olgularında primer onarım sonrası anastomoz kaçağı gelişimi için risk faktörlerinin değerlendirilmesidir.

Gereç ve Yöntem: 2000-2020 yılları arasında kliniğimizde özofagus atrezisi/trakeoözofageal fistül nedeniyle ameliyat edilen ve takip edilen toplam 152 hasta retrospektif olarak incelendi. Hastalar demografik bilgiler ve temel klinik veriler, hastalık özellikleri ve operasyon hakkında bilgiler, postoperatif dönem açısından analiz edildi. Anastomoz kaçağı gelişimini etkileyebilecek faktörler Student-T testi ve Ki kare testi ile değerlendirildi.

Bulgular: Hastaların %52'si erkek, %48'i kız idi. Ortalama doğum ağırlığı 2509 ± 653 gr idi. Hastaların tamamı torakotomi ile opere edildi. ÖA/TÖF operasyonundan sonra anastomoz kaçağı %21 oranında görüldü. Hastaların %24,6'sında uzun aralıklı atrezi (≥2cm) vardı. Prematüre varlığı ve preoperatif mekanik ventilasyon uygulanmış olması istatistiksel olarak anlamlı risk faktörleri olarak bulundu($p<0,05$). Bunun aksine majör doğumsal kalp hastalığı varlığı, özofagus uçları arası mesafe uzunluğu, doğum ağırlığı, eşlik eden sendromlar istatistiksel olarak anlamlı risk faktörleri olarak saptanmadı ($p>0,05$).

Sonuç: Prematürite ve preoperatif mekanik ventilasyon ihtiyacı, ÖA/TÖF nedeni ile opere edilen hastalarda primer onarımından sonra anastomoz kaçağını öngörmede anlamlı risk faktörleri olarak bulunmuştur. Bu risk faktörlerine sahip hastalarda anastomoz kaçağı kontrolü ve postoperatif takip planlaması açısından gerekli izlem planlarının erken dönemde yapılması önemlidir.

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ÖZOFAGUS ATREZİSİ-TRAKEOÖZOFAGEAL FİSTÜL OLGULARINDA ANASTOMOZ KAÇAĞINI ÖNGÖREN RİSK FAKTÖRLERİ

RISK FACTORS PREDICTING POSTOPERATIVE ANASTOMOTIC LEAK IN ESOPHAGEAL ATRESIA- TRACHEOESOPHAGEAL FISTULA PATIENTS

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ABSTRACT

Aim: Overall incidence of anastomotic leak after primary repair of esophageal atresia/tracheoesophageal fistula (EA/TEF) is 16,7%. However, major leaks only comprise 5% of them. The study aims to evaluate predicting risk factor indicators for anastomotic leaks in EA/TEF patients.

Material and Methods:A total of 152 patients operated on and followed in our clinic between 2000-2020 with esophageal atresia/tracheoesophageal fistula (EA/TEF) were retrospectively reviewed. Patients were analyzed for demographic information and basic clinical data, information about disease characteristics and operation, and the postoperative period. Factors that may affect the development of anastomotic leak were evaluated by Student's T test and Chi-square test..

Results: 52% of patients were male and 48% of them were female. The mean birth weight was 2509 ± 653 grams. All the patients were operated via thoracotomy. The incidence of anastomotic leak after EA/TEF operation was 21%. 24,6% of patients had a long gap atresia (≥2cm). The presence of prematurity and preoperative mechanical ventilation were found to be statistically significant risk factors ($p<0,05$). On the contrary, major congenital heart disease, esophageal gap length, birth weight, and concomitant syndromes are not significant risk factors ($p>0,05$).

Conclusion: Prematurity and the need for preoperative mechanical ventilation are predictors of anastomotic leak after primer repair of EA/TEF. For patients with these risk factors, postoperative follow-up is important in terms of anastomotic leak control and follow-up planning.

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Giriş

Özofageal atrezi (ÖA), özofagusun bütünlüğünün olmadığı doğumsal bir anormalidir ve ortalama olarak 2500-4000 canlı doğumda bir görülür(1). En yaygın tip (%85-88); proksimal ÖA ve distal trakeoözofageal fistül (TÖF)'dür(2). ÖA/TÖF vakalarının %30-60'ında vertebral, anorektal, renal ve ekstremite anormallikleri eşlik eder, en sık olarak ise kardiyak anomaliler (%35) görülmektedir. Major kardiyak anomali: operasyon gerektiren siyanotik kalp hastalığı veya kalp yetmezliğine yol açan siyanotik olmayan hastalık, patent duktus arteriyozus ligasyonu olarak tanımlanmaktadır(3). Eşlik eden anomalilerin/sendromların varlığı ve şiddeti, bu hastalarda mortalite ve morbiditeyi etkileyen önemli faktörlerdendir(4).
Anastomoz kaçağı, ÖA primer onarımından sonra doku iyileşmesindeki yetersizlik sonucu anastomoz sütür hattının bütünlüğünün bozulması olarak tanımlanmaktadır. Anastomoz tipinden bağımsız olarak anastomoz kaçağı görülme sıklığı ortalaması %16,7 'dir(5). Ancak majör kaçaklar bunların çok az bir kısmını oluşturduğundan insidansı genel olarak %5 civarında kabul edilir(6). Sıklıkla postoperatif 3.- 6. günler arası görülmektedir. Minör kaçaklar genellikle konservatif izlem ile gerileyebilmektedir. Majör kaçaklarda prognoz daha kötü seyreder. Primer ÖA/TÖF onarımı sonrası en sık görülen erken komplikasyonlardan olmakla beraber hem kısa hem de uzun dönem morbiditeyi etkileyen önemli bir sorundur(7).
Bu çalışmada, ÖA/TÖF olgularında anastomoz kaçağı gelişiminde rol oynayan risk faktörlerinin ortaya konması amaçlanmıştır.

Gereç&Yöntem

Hastanemiz etik kurul onayı alındıktan sonra, 2000-2020 yılları arasında çocuk cerrahisi kliniğinde opere ve takip edilen 210 olgunun verileri retrospektif olarak incelenmiştir. Opere olmadan ölen, dosyalarına tam eksiksiz ulaşılmayan, ameliyat sonrası takiplerine dış merkezde devam eden olgular çalışmaya dahil edilmemiştir. Totalde çalışmaya dahil edilen 152 olgu; demografik bilgiler ve temel klinik veriler (yaş, cinsiyet, gestasyonel doğum hastası, doğum kilosu prematürite varlığı, eşlik eden anomali/sendrom varlığı) , hastalık özellikleri ve operasyon hakkında bilgiler (preoperatif mekanik ventilasyon ihtiyacı, Gross sınıflamasına göre ÖA tipi operasyon tipi) , postoperatif dönem (anastomoz kaçağı, hastanede kalış süresi, mortalite, gastrointestinal ve solunumsal morbiditeler) açısından hastane dosya ve veri tabanında incelendi.
Sayısal değişkenlerin normallik testi *Kolmogorov Smirnov*ve *Shapiro-Wilk* testi ile kontrol edildi. Bağımsız iki grup karşılaştırılmalarında, sayısal değişkenlerin normal dağılım gösterdiği durumlarda *Independent Samples t test*, normal dağılım göstermediği durumlarda ise *Mann Whitney U* testi kullanıldı. İstatistiksel analizler ve figürler"Jamovi project (2020), Jamovi (Version 1.6.3) [Computer Software] (Retrieved from https://www.jamovi.org) ve JASP (Version 0.13.1)(Retrieved fromhttps://jasp-stats.org)programı ile yapılmış olup ve istatistik analizlerde anlamlılık düzeyi 0.05 (p-value) olarak dikkate alındı.

Bulgular

Çalışmaya 79/152 (%52)erkek ve 73/152 (%48) kız olgu dahil edildi. Hastaların ortalama doğum kilosu 2509,7 ± 653,2 gr ve ortalama doğum zamanı 37 ± 2,7 hafta idi. Prematürite oranı %23,7 idi. Olguların %57,2'sinde eşlik eden bir sendrom (%85,1 VACTERL) mevcuttu. Olguların 139/152'sinde (%91,4) kardiyak anomali varlığı tespit edildi. Kardiyak anomalilerin 93/139' ü (%66,9) minör kardiyak anomali idi. Mortalite oranı %25 olarak bulundu (Tablo-1). En sık Tip C (%90,1) ÖA/TÖF mevcuttu. %24,6 hastada uzun aralıklı ÖA mevcuttu. 33 olguda preoperatif mekanik ventilasyon ihtiyacı mevcuttu. Hastaların primer

onarımı torakotomi ile yapıldı. Tüm hastalara definitif operasyon öncesi bronkoskopi uygulandı (Tablo-2).

Tablo-1. Demografik ve temel klinik veriler

Cinsiyet	Erkek	79 (%52)
	Kız	73 (%48)
Doğum Kilosu (gr)		2509,7 ± 653,2
Doğum haftası		37 ± 2,7
Prematürite varlığı		36 (%23,7)
Kardiak anomali varlığı	Majör	59 (%33,1)
	Minör	93 (%66,9)
Hastada eşlik eden anomali/sendrom varlığı		87 (%57,2)
Hastada eşlik eden sendrom türü	VACTERL	74 (%85,1)
	VACTERL olmayan	13 (%14,9)
Mortalite		38 (%25)

Tablo-2. Hastalık ve operasyon verileri

ÖA tiplendirme (Gross sınıflandırılması)	
A	9 (%6,0)
C	**136 (%90,1)**
E	6 (%4,0)
Cerrahi teknik	
Servikal özofagostomi	3 (%2,0)
Servikal özofagostomi + Torakotomi	2 (%1,3)
Torakotomi	146 (%96,7)
Cerrahi yaklaşım	
Ekstraplevral	131 (%88,5)
İntraplevral	17 (%11,5)
Özofagus uçları arası mesafe	
Kısa	98 (%75,4)
Uzun(>2cm)	**32 (%24,6)**
Özofagus uçları arasındaki defekt uzunluğu (cm)	1.5 [min0.0 – max7.0]
Preoperatif mekanik ventilasyon ihtiyacı	33 (%21,7)
Bronkoskopi	152 (%100)

32 hastada (%27,1) anastomoz kaçağı görüldü. Hastaların preoperatif mekanik ventilasyon süresi ortalama 6 gün idi. İzlemde gelişen morbiditeler incelendiğinde; 64 olguda (%57,7) respiratuar sorunları olduğu; 59 olguda semptomatik anastomoz darlığı, 58 olguda gastroözofageal reflü, 38 olguda ise disfaji olmak üzere gastrointestinal morbiditeler olduğu gözlendi. Hastaların ortalama hastanede yatış süresi 22 gün idi. Çalışmaya katılan olguların ortalama izlem süresi 5 yıl olarak bulundu (Tablo-3).

Prematürite varlığı ve preoperatif mekanik ventilasyon ihtiyacı olması anastomoz kaçağı gelişen olgularda istatistiksel olarak anlamlı risk faktörleri olarak bulundu ($p<0,05$).Diğer değişkenler açısından gruplar arasında istatistiksel olarak anlamlı fark bulunmadı ($p>0,05$) (Tablo-4).

Tablo-3. Postoperatif dönem verileri

Preoperatif mekanik ventilasyon süresi (gün)	6.0 [min0.0 –max21.0]
Anastomoz kaçağı	32 (%27,1)
Solunumsal sorunlar	64 (%57,7)
Semptomatik anastomoz darlığı gelişmesi	59 (%52,7)
Disfaji varlığı	38 (%35,8)
Gastroözofageal reflü varlığı	58 (%52,3)
Hastanede kalış süresi	22.0 [min3.0 –max270.0]
Total izlem süresi (yıl)	5.0 [min0.3 –max17.0]

Tablo-4. İstatistiksel analiz sonuçları

	Anastomoz kaçağı yok	Anastomoz kaçağı var	P değeri
Cinsiyet			
-Kız	59 (49,2)	14 (43,8)	0,586
-Erkek	61 (50,8)	18 (56,3)	
Kardiak anomali	111 (92,5)	28 (87,5)	0,474
Prematürite	33 (27,5)	3 (9,4)	***0,032***
Hastada eşlik eden sendrom varlığı	68 (56,7)	19 (59,4)	0,783
Preoperatif mekanik ventilasyon ihtiyacı	3 (9,4)	30 (25)	**0,047**
Doğum Kilosu(gr)	2460,51±645,49	2694,22±658,98	0,072
Özofagus uçları arası mesafe (cm)	1,75±1,35	1,68±1,17	0,880
Özofagus uçları arası mesafe/doğum kilosu oranı (cm/kg)	0,81± 0,76	0,70± 0,63	0.45

(Univariate) lojistik regresyon analizi uygulandığında ise sadece prematürite varlığı anastomoz kaçağı gelişimi için risk faktörü olarak devamlılık gösterdi. (Tablo-5)

Tablo-5.(Univariate) Lojistik regresyon analizi sonuçları

	B	P	Exp(B)	95% C.I.	
Cinsiyet	-0,218	0,586	0,804	0,367	1,763
Kardiak Anomali	-0,566	0,374	0,568	0,163	1,978
Prematürite varlığı	-1,299	***0,042***	0,273	0,078	0,956
Hastada eşlik eden sendrom varlığı	0,111	0,783	1,118	0,506	2,469
Preoperatif mekanik ventilasyon ihtiyacı	-1,170	0,068	0,310	0,088	1,092
Operasyon yaşı (postnatal gün)	-0,004	0,807	0,996	0,966	1,028
Doğum Kilosu	0,001	0,074	1,001	1,000	1,001
Özofagus uçları arası mesafe(cm)	-0,038	0,806	0,963	0,710	1,305

Tartışma

Özofagus atrezisi/trakeoözofageal fistül hayatı tehdit eden bir konjenital anomalidir. Bu olguların yönetiminde mevcut gelişmeler ile genel sonuçlarda iyileşmeler görülmektedir. Preoperatif olarak yenidoğan yoğun bakımındaki gelişmeler, operasyon yöntemlerindeki iyileştirmeler ve teknik yenilikler, postoperatif dönemde ise multidisipliner izlem ile bu olguların sağkalım ve yaşam kalitesinde artışlar gözlenmektedir. Hastaların özellikle respiratuar ve gastrointestinal morbiditelerin gelişmesinde önemli rol oynayan etkenlerden biri de erken dönem komplikasyonu olan anastomoz kaçağıdır. Literatürde klinik anlamlı anastomoz kaçağı insidansı yaklaşık %5 olarak, genel olarak ise %16,7 olarak tanımlanmıştır(5, 6). Çalışmamızda anastomoz kaçağı literatürden yüksek olarak %27,6 olarak bulunmuştur. Hastaların anastomoz kaçağı görülme sıklığının çalışmamızda yüksek çıkması ve literatürde insidansın farklılıklar göstermesi bu durumu öngörebilen risk faktörlerini araştırmaya sebep vermiştir.

İlişkilendirilebilecek olası faktörler arasında anastomoz tekniği, sütur materyali, iki/tek katlı anastomoz, özofagus uçları arası mesafenin uzun olması, kan transfüzyonu, gergin anastomoz gösterilmiştir(8).

Morbidite gelişmesindeki risk faktörleri ise erkek cinsiyet, prenatal tanı, preoperatif mekanik ventilasyon ve prematürite olarak gösterilmiştir(3).

Çalışmamızda anastomoz kaçağı gelişen olgular ile kaçak olmayan olgular karşılaştırıldığında; her iki grup arasında doğum kilosu, kardiyak anomali varlığı, eşlik eden sendrom ve her iki özofagus uçları arasındaki mesafe arasında anlamlı istatistiksel bir fark saptanmamıştır ($p>0,05$).

Yapılan bir çalışmada hastalarda anastomoz kaçağı gelişmesinde düşük doğum ağırlığı ile özofagus uçları arası mesafenin uzun olması anlamlı risk faktörleri bulunarak özofagus uçları arası mesafe/ doğum kilosu oranı ile prediktif bir parametre önerilmiştir (9). Ancak özofagus uçları arası mesafe/doğum kilosu oranı çalışmamızda istatistiksel olarak anlamlı bir parametre olarak sonuçlanmadı($p>0,05$).

ÖA/TÖF olgularında yaklaşık olarak %50 oranında ek bir anomali eşlik etmektedir(10). ÖA/TÖF olgularında prematürite görülme sıklığı çeşitli çalışmalarda %39,5 , %43,1 olarak sunulmuştur (sırasıyla (3, 4)). Çalışmamızdaki hastaların temel klinik verileri incelendiğinde eşlik eden sendrom varlığının yüksek (%57,2), prematüritenin (%23,7) ise literatüre göre daha düşük oranda olduğu görülmüştür.

Çalışmamızdaki kısıtlılıklardan birincisi, uzun dönem retrospektif bir çalışma olmasıdır. Tıbbi ve cerrahi yaklaşımlardaki değişiklikler nedeni ile çalışma popülasyonu homojen değildi. İkinci olarak, çalışma dosya kayıtlarından elde edilen verilere dayanmaktadır. Opere edilen tüm olguların takiplerini kliniğimizde devam ettirmediği görüldü. Bu nedende ortalama takip süreleri gözetilerek olguların iki yıllık izlemlerinin sonuçları değerlendirmeye alınmıştır.

Sonuç

Prematürite ve preoperatif mekanik ventilasyon ihtiyacı, ÖA/TÖF nedeni ile opere edilen hastalarda primer onarımdan sonra anastomoz kaçağını öngörmede anlamlı risk faktörleri olarak bulunmuştur. Bu risk faktörlerine sahip hastalarda anastomoz kaçağı kontrolü ve postoperatif takip planlaması açısından gerekli izlem planlarının erken dönemde yapılması uzun dönemde gelişebilecek respiratuar ve gastrointestinal morbiditeler açısından önemlidir.

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THE DETERMINATION OF LEFT VENTRICULAR WALL MOTION ABNORMALITY BY EMERGENCY MEDICINE RESIDENTS USING A BRIEF TRAINING MODULE

KISA BİR EĞİTİM MODÜLÜ KULLANILARAK ACİL TIP ASİSTANLARI TARAFINDAN SOL VENTRİKÜL DUVAR HAREKET ANORMALLİKLERİNİN BELİRLENMESİ

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ABSTRACT

Introduction: Evaluation of wall motion abnormalities by emergency physicians (EP) is a new subject and has not yet been included in emergency ultrasound guidelines. This study aims to evaluate the contribution of a short training module (STM) to the ability of EPs to recognize wall motion abnormalities.

Material and Methods: This prospective experimental study was conducted in the emergency department of a tertiary training and research hospital. EPs who were included in the 1-3-year postgraduate education program were included in the study. For the study, a short video-supported STM containing the thirty-minute wall motion error abnormality was created. A thirty-question test, including normal and wall motion defects, was prepared. The residents were subjected to three tests before the training (pre-test), immediately after the training (post-test), and one month after (final test). ANOVA was used to compare the tests. In post-hoc analyses, the Bonferroni test was used to calculate the statistical significance value (0.05/3=0.016), a value of 0.016 was considered statistically significant.

Results: 23 EMRs were included in the study. The residents answered an average of 50±12 of 90 questions correctly in the pre-tests before the training, 70±12 questions in the post-test, and 63±12 questions one month later. The short training model had a statistically significant effect on residents' recognition of wall motion defects ($p<0.001$). There was a significant difference between pre-test and post-test scores in post-hoc analysis ($p<0.001$).

Conclusion: The short 30-minute training model, which includes all wall motion defects and normal wall motion, was found to be an effective training method for EPs to visually recognize wall motion abnormalities

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THE DETERMINATION OF LEFT VENTRICULAR WALL MOTION ABNORMALITY BY EMERGENCY MEDICINE RESIDENTS USING A BRIEF TRAINING MODULE

KISA BİR EĞİTİM MODÜLÜ KULLANILARAK ACİL TIP ASİSTANLARI TARAFINDAN SOL VENTRIKÜL DUVAR HAREKET ANORMALLİKLERİNİN BELİRLENMESİ

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Bedside ultrasound, education, emergency medicine, focused cardiac ultrasound, myocardial infarction

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ÖZET

Giriş: Duvar hareket anormalliklerinin acil servis hekimleri (ASH) tarafından değerlendirilmesi yeni bir konudur ve henüz acil ultrason kılavuzlarına dahil edilmemiştir. Bu çalışmanın amacı, kısa bir eğitim modülünün (STM) ASH'lerin duvar hareketi anormalliklerini tanıma becerisine katkısını değerlendirmektir.

Gereç ve Yöntemler: Bu prospektif deneysel çalışma üçüncü basamak bir eğitim ve araştırma hastanesinin acil servisinde yürütülmüştür. Çalışmaya 1-3 yıllık mezuniyet sonrası eğitim programına dahil olan ASH'leri dahil edildi. Çalışma için otuz dakikalık duvar hareket hatası anormalliğini içeren video destekli kısa bir STM oluşturuldu. Normal ve duvar hareket kusuru patolojilerini içeren otuz soruluk bir test hazırlandı. Asistanlar eğitimden önce (ön test), eğitimden hemen sonra (son test) ve bir ay sonra (son test) olmak üzere üç teste tabi tutuldu ve testleri karşılaştırmak için ANOVA kullanıldı. Post-hoc analizlerde, istatistiksel anlamlılık değerini hesaplamak için Bonferroni testi kullanılmıştır (0.05/3=0.016), 0.016 değeri istatistiksel olarak anlamlı kabul edilmiştir.

Bulgular: Çalışmaya 23 ASH dahil edilmiştir. Asistanlar eğitim öncesi ön testlerde 90 sorudan ortalama 50±12'sini, son testte 70±12'sini ve bir ay sonra 63±12'sini doğru yanıtlamıştır. Kısa eğitim modelinin asistanların duvar hareket kusurlarını tanıması üzerinde istatistiksel olarak anlamlı bir etkisi vardı ($p<0.001$). Post-hoc analizinde ön-test ve son-test puanları arasında anlamlı bir fark vardı($p<0.001$).

Sonuç: Tüm duvar hareket kusurlarını ve normal duvar hareketini içeren 30 dakikalık kısa eğitim modeli, ASH'lerin duvar hareket anormalliklerini görsel olarak tanımaları için etkili bir eğitim yöntemi olarak bulundu.

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Introduction

Bedside ultrasound (B-USG) has become an indispensable component of critical patient management in the emergency department. B-USG was first described as a practicable tool for emergency physicians in 1994 (1). In subsequent years, it came to be used in several fields in the emergency department, such as pulmonary embolism diagnosis (2), volume status evaluation (3), and the differential diagnosis of dyspneic patients (4). The American College of Emergency Physicians (ACEP) added non-cardiac themes that had not previously been included, such as bowel ultrasound and airway ultrasound, to its latest emergency ultrasound guideline published in 2016. (5) Pericardial effusion, tamponade, evaluation of cardiac activity, global systolic function assessment, and volume status evaluation remain included in the guideline among the cardiac themes (5). However, bedside evaluation of wall motion abnormality by emergency physicians is still not included in the B-USG guidelines, and studies on the subject are limited (6). New studies concerning the evaluation of wall motion abnormality by emergency physicians using B-USG are therefore needed.

Echocardiography is one of the first diagnostic tools recommended in the evaluation of both acute coronary syndromes and the complications thereof in patients presenting with chest pain (7). Bedside echocardiography is a valuable tool in the detection of pathologies at differential diagnosis of chest pains, such as pericardial tamponade, pulmonary embolism, and free wall rupture (8). However, echocardiography has been reported to have much higher sensitivity (91%) in predicting cardiac events in patients with probable cardiac ischemia than electrocardiography (40%), which is widely employed to determine cardiac ischemia (9). Several studies have shown that wall motion abnormality is an effective tool in assessing myocardial ischemia in the evaluation of patients with suspected acute coronary syndrome (10, 11). The addition of wall motion abnormality to the B-USG parameters for emergency physicians can contribute to the early assessment and identification of these patients (9, 8).
However, the evaluation of wall motion abnormality by emergency physicians with limited experience on the subject requires specific training and experience.

The purpose of this study was to develop a short training module to improve the abilities of emergency physicians to identify wall motion abnormalities and to investigate the effectiveness of that module.

Method

Study design and setting

This prospective experimental study was conducted in the emergency medicine clinic of a tertiary training and research hospital in Turkey with a 1200-bed capacity and receiving approximately 200.000 patient visits a year. The study began following the approval from the hospital ethical committee under protocol number 265.

Study population

Our team included emergency medicine 1st to 3rd-year residents, working in the emergency medicine clinic, and with no previous training regarding wall motion abnormality in the study. Consent was obtained from all participants regarding voluntary participation in the study. The residents included in the study had previously completed B-USG courses and had a mastery of basic cardiac window images. Residents who had not yet completed their six months of training and with no practical experience or education on basic cardiac windows, and residents in their fourth year with experience of wall motion abnormality were excluded from the study.

Study protocol and data collection

The study was carried out with emergency department residents in two sessions in the emergency department teaching room. The emergency department residents taking part in the study were administered a pre-test measuring their wall motion abnormality testing skills and involving 30 pre-prepared pathological and non-pathological video clips. Following the pre-test, a brief, 30-minute training module was applied containing normal and abnormal wall motions. The teaching session was then followed by a post-test. Pre-test and post-test results were assessed using a pre-prepared answer key, and the data obtained were recorded. To test the permanence of the instruction, the same test questions from the brief training module were re-administered after one month to the same residents, although in a different order. No resident received any other instruction regarding wall motion abnormality during that one month, and the residents were also unaware that they would subsequently be subjected to a final test after one month. The emergency department residents were also unaware of what proportions of the test would consist of pathological and non-pathological images.

Brief Training Module and Test Processing

The test module comprised 30 videos, 22 involving abnormal wall motions and eight involving normal motions. The video clips lasted 5-10 sec each and were retrieved from the hospital archive and individual archives. The video clips involving both pathological and non-pathological images were taken from the parasternal long and short axis and apical four-chamber views. Video clips showing normal wall movements from all three windows were present. The pathological videos were prepared to include at least one example of both hypokinesia and akinesia pathologies on all walls evaluated from all three windows. In addition, two videos showing apical dyskinesia, one from the parasternal long axis and one from the apical four-chamber windows, were included. Each video was numbered before the test. Participants were asked to respond to each video in three stages. In the first step, they were asked to assess whether pathology was present. In the second step, they were asked to locate the pathology, if applicable. In the third step, they were asked to determine the type of pathology, if applicable (hypokinesia, akinesia, or dyskinesia). No time restriction was imposed on the test steps. A score of one was given for each step in class assessment. The highest total possible score for each of the 30 three-step videos was 90.

The brief training module was applied following the pre-test. The module first described all cardiac wall images capable of evaluation from the parasternal long axis, parasternal short axis, apical four-chamber, and subcostal windows. Videos containing at least one example of normal wall motion, hypokinesia, akinesia, and dyskinesia for each wall were shown. This training was completed in 30 min, after which the post-test consisting of 30 videos in three steps was applied. The same videos as shown in the pre-test were used in the post-test but in a different order. The brief training module was prepared by an experienced emergency medicine physician who had been an instructor in the Turkish Emergency Physicians Association ultrasound section for five years and by a specialist cardiologist.

Outcome measurement

The primary outcome measurements were the pre- and most-training test scores. The aim was to compare the initial training levels of the brief training module applied to emergency medicine residents with the post-training levels. The secondary outcome measurement was the final test results one month after training. This test aimed to test the permanency of the knowledge imparted by the brief training module on the subject of wall motion abnormality.

Primary data analysis

Percentage distributions and pie charts were used to evaluate categorical variables at descriptive analyses, while central distribution and prevalence criteria were employed to examine continuous variables. The t-test was used to check for confounding at two-way independent variable analysis, and ANOVA for three-way analysis variables. Since the continuous variables to be analyzed at repeated measurements were found to be normally distributed, ANOVA was used for repeated measurements and the independent samples t test at post-hoc analyses. The Bonferroni test was employed to calculate the statistical significance value at post-hoc analyses, a value of (0.05/3=0.016) 0.016 being determined significant.

Results

Thirty-three residents, 20 of whom were men (60%), were included in the study. Sixteen (26.1%) were in their first year after graduation, nine (39.1%) in their second year, and eight (34.8%) in their third. The residents answered a mean of 50 ± 12 questions correctly at pre-tests before training, 70 ± 12 questions at the post-test, and 63 ± 12 after one month. A comparison of the test scores at repeated measurements revealed that the residents' mean scores altered significantly between the tests (p<0.001) (Table 1). Bonferroni-corrected post-hoc analysis performed to identify the source of the difference between two measurements detected at repeated measurements revealed a highly significant difference between mean pre-test and post-test scores (p<0.001). No significant difference was determined between mean post-test and final-test scores (p=0.018). A significant difference was also determined between mean pre-test and final-test scores (p=0.004) (Table 1).

Table 1: A comparison of mean pre-test, post-test and final-test scores

*: p value of repeated measures ANOVA (p<0.05 statistically significant)

	Mean± SD	Median	Interquartile percentile (25%-75%)	P**
Pre-test	50 ± 12	51	38 - 59	**P****
Post-test	70 ± 12	71	62 - 77	**<0.001** 0.018
Final-test	63 ± 12	65	55 - 74	
P*	**P <0.001**			

**: p value of Bonferroni correction post-Hoc analysis (p< 0.016 statistically significant)

Test scores were also compared according to gender and number of years spent as a resident to check confounding factors. Mean pre-test values were 44 ± 8 for women and 53 ±13 for men (p=0.068), mean post-test values were 66 ± 10 for women and 72 ± 14 for men (p= 0.212), and final-test values were 67 ±10 for women and 60 ± 13 for men (p= 0.251). A comparison of resident physicians' mean scores in terms of gender and years spent as a resident is shown in Table 2. Gender and years spent as residents did not emerge as confounding factors for analyses.

Table 2: A comparison of pre-test, post-test, and final test scores by gender and years of residency

		PRE-TEST (mean±SD)	POST-TEST (mean±SD)	LAST-TEST (mean±SD)
Gender	**Male n:20**	53±13	72±14	60±13
	Female n: 13	44 ±8	66±10	67±10
	P*	0.068	0.212	0.251
Post graduate year	**I First postgraduate year n:16**	48 ±7	69±7	67±10
	Second postgraduate year n:9	48±13	68±7	59±12
	Third postgraduate year n:8	53±15	72±19	66±12
	P**	0.599	0.820	0.372

***:** p value of Student's t-test for comparison of normally distributed continuous variables in independent groups ($p<0.05$ regarded as statistically significant)
****:** p value of repeated measures ANOVA ($p<0.05$ regarded as statistically significant)

Discussion

B-USG has been effectively employed in several different areas, especially in the last two decades, such as in the evaluation of cardiac functions (12), volume status (13), and major vascular pathologies (14), and in the management of cardiopulmonary resuscitation (15). The areas of use of B-USG in the emergency department are also increasing as users acquire experience (5, 6). Echocardiography is an important diagnostic tool in determining wall motion abnormalities showing cardiac ischemia or infarction in patients with chest pain and for the differential diagnosis of chest pain. Since echocardiography is known to be successfully used in showing cardiac ischemia (16), attention in the last decade has focused on the use of bedside echocardiography in the evaluation of cardiac ischemia in the emergency department (6). Wall motion abnormality is still a new subject for emergency departments, and has still not been included in the ACEP ultrasound guideline (5). However, studies investigating the recognition of wall motion abnormality by emergency physicians have commenced (6), and this should be included in the emergency curriculum in the near future.

Physicians should be properly trained in both wall motion defects and other areas of use that have just entered the scope of B-USG, which is already widely employed in the emergency department. The requisite training modules must therefore be established for each of these areas. The content of the education provided for emergency physicians should therefore be defined for fields newly entering into use. Training standards to permit emergency physicians with no experience in this subject to be capable of identifying wall motion defects must therefore be established. The present research is one of the rare studies proposing an effective training module for wall motion defects (6). The 30-minute brief training module applied in the

present study was found to increase residents' abilities to visually identify wall motion defects, irrespective of gender or years of residency, for at least one month.

The participants in this study correctly answered 50 (56%) of the 90 questions involved at the pre-test, but 70 (78%) at the post-test. Chris et al. used a 30-minute brief training module, as in the present study, and reported a correct pre-test response rate of 67% and a correct post-test response rate of 87% (6). However, the questions in that study were multiple-choice questions consisting of only two options, 'wall motion defect present' or 'no wall motion defect.' In the present study, however, one-third of the questions were in 'pathology present-absent' form, another third involved the site of the pathology, and a third involved describing the pathology as hypokinesia, akinesia, or dyskinesia. Our test module and training required more detailed knowledge and pathology identification. Initial and post-test result success was therefore lower than that reported by Chris et al. However, identification of the pathology in this way may be more useful as a training model. Bearing this difference in mind, we observed that the location and type of wall motion abnormality pathology can be learned utilizing a 30-minute video-supported training model, and that it produces visual memory with permanency of at least one month.

Wall motion defect was not part of the education curriculum in our clinic, and no resident had received any previous training on the subject. There was no difference in pre-test correct response rates between the one-year residents at 53%, the two-year residents at 53%, and the three-year residents at 59% (p=0.599). This also applied to the post-test and final-test results, showing that the success of the training module was independent of the years of residency. The gender-based analysis also revealed no difference in the establishment of visual perception with brief 30-minute training between men and women. These results show that the success of the brief training module produced was similar in all participants regardless of years of residency and gender.

Limitations

The principal limitation of this study is that the model developed targeted only visual perception. Echocardiography training sessions should be conducted in the form of two-stage training. The first stage should involve the visual identification of normal structures and pathological images, while the second concerns the user's ability to obtain appropriate axes and improvement of the user's manual skills. The present study involved only the first stage and was intended to provide the training required for users to detect wall motion abnormality on a visual basis. Future studies after the present research should concentrate on training models aimed at also increasing users' manual skills.

Wall motion defect does not only occur in acute ischemia. A large proportion of observed wall motion abnormalities are chronic and sequelae of previous events. The physician evaluating the wall motion abnormality should therefore interpret the wall motion information obtained from echocardiography together with such factors as the patient's history, medical history, and examination findings.

Conclusions

The 30-minute brief training model developed in this study can be sufficient for the visual identification of wall motion abnormality. The visual perception formed in the training model can persist for at least one month, irrespective of the years of residency.

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EVALUATION OF THE ATTITUDES OF CLINICAL MEDICAL FACULTY STUDENTS TOWARD SCABIES PATIENTS
KLİNİK DÖNEM TIP FAKÜLTESİ ÖĞRENCİLERİNİN UYUZ HASTALARINAYÖNELİK TUTUMLARININ DEĞERLENDİRİLMESİ

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ÖZET

Amaç: Bu çalışma, tıp öğrencilerinin klinik eğitim deneyimlerine odaklanarak uyuz hastalığına yönelik tutumlarını ve endişelerini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntemler: Kesitsel nitelikteki bu çalışma, 2 Ocak 2023 - 28 Şubat 2023 tarihleri arasında çeşitli üniversitelerin tıp fakültelerinde eğitim gören tıp öğrencileri ile yürütülmüştür. Veriler, demografik bilgileri, uyuz hastalığına yönelik tutumları, endişeleri ve bilgileri kapsayan 29 maddelik bir anket yolu ile toplanmıştır.

Bulgular: Tıp öğrencileri, uyuz hastalığına yönelik orta düzeyde bir tutum seviyesi sergilemiş (ortanca puan: 17 üzerinden 10,00) ve hasta yaklaşımlarında endişelerini ifade etmiştir (ortanca puan: 70 üzerinden 33,00). Daha genç yaş grubundaki öğrenciler daha yüksek endişe puanları göstermiştir. Tutum ve endişe puanları arasında negatif bir korelasyon bulunmuştur ($p < 0.001$).

Sonuç: Uyuz hastalığına yönelik endişeler, daha genç tıp öğrencileri arasında daha yüksekken, bilgi arttıkça azalmaktadır. Mezuniyet öncesi eğitimi sırasında hastalığın bulaşma yolları ve önleyici tedbirleri ele alan eğitim müdahaleleri önerilmektedir.

ABSTRACT

Objective: This study aims to evaluate medical students' attitudes and concerns towards scabies by focusing on their clinical training experiences.

Material and Methods: This cross-sectional study was conducted with medical students studying at medical faculties of various universities between January 2, 2023, and February 28, 2023. Data were collected through a 29-item survey covering demographic information, attitudes, concerns, and knowledge about scabies.

Results: Medical students demonstrated a moderate level of knowledge about scabies (median score: 10.00 out of 17) and expressed concerns (median score: 33.00 out of 70) during the patient approach. Younger students displayed higher concern scores. There was a negative correlation between attitude and concern scores ($p < 0.001$).

Conclusion: Concerns about scabies transmission were higher among younger medical students, decreasing with increased knowledge. Educational interventions addressing transmission modes and preventive measures are recommended during pre-graduation training.

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Introduction

The causative agent of scabies, Sarcoptes scabiei var. hominis, is a microscopic mite from the arthropod class and is an ectoparasite that can affect individuals of all ages, genders, geographical locations, and cultures. It is primarily transmitted from person to person through skin-to-skin contact or by contact with items such as clothing and sheets (1-3).

On Earth, scabies affect an estimated 200 to 300 million people annually (4). It ranks among the most prevalent skin diseases worldwide (5) and is particularly endemic in developing regions (6). In children from developing countries, the average prevalence is estimated to range from 5% to 10% (4). Unlike institutional outbreaks, scabies is not a mandatory disease to be reported in Western countries; consequently, the epidemiology and actual prevalence of scabies remain unclear (7). In Turkey, scabies continues to pose a significant health challenge (3). According to a study conducted in Turkey, 0.77% of patients who sought care at the dermatology outpatient clinic between 2017 and 2019 received a diagnosis of scabies (8).

The scabies parasite is typically transmitted through prolonged and direct skin contact, although there are rare instances of transmission via fomites, where it can survive for up to 8 days (9). While scabies can be transmitted through any form of direct skin contact, it is most spread through close and extended interactions between individuals (10). The transmission of the disease through direct skin contact can occur with the presence of a single adult female mite or several larvae. Given the slow movement of mites in the external environment, transmission typically requires repeated or continuous skin contact, lasting approximately 20-30 minutes (11,12).

People who have close contact with these patients, including family members and healthcare providers, can be at risk of transmission, even after brief contact. Transmission may even occur from contact with the scales shed by these patients (11). Consequently, scabies with crusted lesions can trigger nosocomial outbreaks (13). Contrary to common misconceptions, scabies is not linked to poor hygiene. It can be found in individuals from all social strata and age groups, including families with young children, students living in shared accommodations, and people in various living situations (10, 14). Mites that become separated from their human host can survive for up to 48 hours at 21°C in the outdoor environment with a humidity range of 40-80%. However, they cannot endure temperatures exceeding 50°C for more than 10 minutes. Their survival time increases at lower temperatures and higher humidity levels (15).
To prevent mite penetration into the skin, it is essential to wash hands after examining scabies patients; however, this does not reduce the number of mites, so wearing gloves during patient examinations is necessary (9).

In daily medical practice, scabies is a relatively common condition among inpatients. The disease can also elicit anxiety among medical students who encounter scabies patients, as it is primarily transmitted through direct person-to-person contact or by sharing living spaces (16).
As far as our literature review indicates, there is a noticeable gap in studies examining medical students' attitudes, concerns, fears, and knowledge about scabies. Therefore, the primary objective of this study is to assess the level of concern and explore potential factors influencing medical students' approach to patients with scabies during their clinical training. This research will focus on clinical-term students from various medical schools, providing valuable insights into the clinical field's perspectives and experiences.

Method

This study is a cross-sectional descriptive study and is designed as a survey application. Data collection for the study took place from January 2, 2023, to February 28, 2023. The questionnaire was administered face-to-face to students at Izmir Katip Celebi University, while

students from other universities participated through an online survey. The survey typically required approximately 30 minutes to complete.

Participants

The study included participants who were 4th, 5th, and 6th-year students at İzmir Katip Çelebi University and students from several other medical faculties, including Adıyaman University, Akdeniz University, Ankara Yıldırım Beyazit University, Çukurova University, Dicle University, Dokuz Eylül University, Kahramanmaraş Sütçü İmam University, Maltepe University, Manisa Celal Bayar University, Mersin University, Muğla Sıtkı Koçman University, Tekirdağ Namık Kemal University, Van Yeni Yüzyıl University, Yeditepe University, and Zonguldak Bülent Ecevit University.

Data collection tool

For this study, a 29-item questionnaire was developed based on a review of the existing literature (17-30) and considering practical training issues within the medical faculties' training programs. Prior to participating in the online survey, participants were presented with consent information, and access to the questionnaire was granted only upon providing consent.

The initial four items gathered demographic information, including age, gender, university affiliation, and class. Other questions included medical students' attitudes and concerns during contact with scabies patients and their perceptions about the self-care of scabies patients.

Assessment of Medical Students' Attitude:

The survey assessed participants' attitudes about the modes of transmission when approaching a scabies patient using 17 statements (response options: I agree, disagree, no opinion). "In items 5, 7, and 8, 'I agree' was considered the correct response, while 'I disagree' was the correct response for the other items. The Physician Approach to Scabies Patient Information Score was calculated on a scale of 0-17 points, with 1 point awarded for each correct response to the 17 statements and 0 points for incorrect responses."

Assessment of Medical Students' Concerns:

To assess concern in the medical students' approach to a scabies patient, participants responded to 7 statements, each rated on a scale from 1 to 10, where 1 indicated "I am not worried at all," and 10 indicated "I am very worried." For items 15-17 and 24, the direction of concern was correct, while for the remaining items, it was reversed.
For the reversed items, scores were assigned as follows: a score of 10 was given for "1" answers, and 1 point was awarded for "10" answers. The concern score was evaluated on a scale ranging from 7 to 70."

Assessment of Perception of Patients' Self-Care:

Item 29 of the survey asked participants to rate their perception of the self-care behavior of scabies patients compared to other patients. Agreement with this proposition was assessed on a scale from 1 to 10, where 1 signified disagreement and 10 signified agreement.

Sample size

The "Snowball sampling method" was utilized to select the sample group for this study. Sample size calculations were performed using the Calculator.Net program. Since no similar studies had been conducted previously, it was assumed that the proportion of anxious individuals and those who were not would be equal (50%). To achieve a power of 95% and

maintain a type 1 error level of 5%, it was determined that a minimum of 385 participants would be required.

Statistical analysis

Age was categorized into three groups: 20-22, 23, and 24 and above.

Quantitative data were analyzed using IBM SPSS Statistics Standard Concurrent User Version 25 (IBM Corp., Armonk, New York, USA). Descriptive statistics were presented as counts (n), percentages (%), median (M), first quartile (Q1), and third quartile (Q3).

To assess the normal distribution of numerical variables, the Shapiro-Wilk normality test, Q-Q plots, box plots, histograms, and skewness-kurtosis coefficients were employed. Non-parametric data were analyzed using the Mann-Whitney U and Kruskal-Wallis tests. Correlation analysis was conducted using the Spearman Correlation Test. A significance level of $p < 0.05$ was considered statistically significant.

Ethical approval

For this study, approval (No. 510) was obtained from the Izmir Katip Celebi University Non-Interventional Clinical Research Ethics Committee on November 24, 2022.

Results

A total of 445 students participated in this study, with 51.0% being male, and 41.1% falling into the 20-22 age group. Furthermore, 354 students (79.6%) were enrolled at Izmir Katip Celebi University, and 45.8% of the students were in their 5th year of study. Table 1 provides an overview of the study group's distribution based on various sociodemographic characteristics.

Table 1: Distribution of the study group according to some sociodemographic characteristics

Variables	**n (%)**
Gender, *n* (%)	
Woman	215 (48,3)
Male	227 (51,0)
No information	3 (0,7)
Age group (year), *n* (%)	
20-22	183 (41,1)
23	159 (35,7)
24	103 (23,1)
School (University), *n* (%)	
İzmir Katip Çelebi	354 (79,6)
Other	91 (20,4)
Class, *n* (%)	
4th	116 (26,1)
5th	204 (45,8)
6th	125 (28,1)
Total	445 (100,0)

Medical students' attitude

The distribution of responses to propositions questioning the level of participants' knowledge about the modes of transmission of Scabies is presented in Table 2. The median score of the attitudes of participants was calculated as 10.00 (min 7.00- max 12.00).

Table 2. Distribution of responses to propositions questioning the level of attitude for medical students' approach to scabies patient

N: 445 The number of propositions in the questionnaire		**Agree (%)**	**Disagree (%)**	**I have no idea (%)**
Propositions where the correct answer is "**I agree**"				
5	Scabies can be transmitted with a short contact of 1-2 minutes.			
		38,0	44,5	17,5
7	Joint use of personal items such as bedding, clothes, and towels facilitates the transmission and spread of scabies.			
		97,8	0,7	1,5
8	The sick person can also transmit scabies during the period when he does not show signs of scabies.			
		68,8	9,9	21,3
Propositions with the correct answer **being "Disagree"**				
6	If there is transmission after contact with the scabies patient, it gives symptoms in a short time (1-3) days.			
		37,8	**38,0**	24,3
9	The itching caused by scabies does not change during the day, it always remains at the same intensity.			
		2,7	**85,4**	11,9
10	If scabies patients are hospitalized, they should be isolated in separate rooms.			
		72,6	**18,4**	9,0
11	Patients with scabies should be isolated in a separate ward in the hospital.			
		42,9	**45,2**	11,9
12	The materials used in scabies patients (portrait, pliers, pliers, etc.) should be sterilized by a special method other than the sterilization methods normally applied.			
		35,5	**47,0**	17,5
13	Hospital items used by scabies patients (sheets, pillows, pillowcases, beds, etc.) cannot be used in other patients even if they are cleaned according to the standard procedure.			
		34,8	**43,1**	22,0
14	In the treatment of scabies, it is enough to treat only the person who shows symptoms of scabies, people living in the same house do not need to be treated.			
		5,4	**86,7**	7,9
18	I don't want to be in the same room as the scabies patient.			
		58,4	**36,6**	4,9
19	I do not want to examine the patient for scabies.			
		33,7	**60,2**	6,1
20	I do not want to use my stethoscope when examining a patient with scabies.			
		64,0	**29,2**	6,7
21	I do not want to dress the scabies patient.			
		34,8	**59,3**	5,8
22	I do not want to perform an interventional procedure on a scabies patient.			
		29,4	**64,5**	6,1
23	I do not want to do Cardiopulmonary resuscitation on a patient with scabies.			
		18,7	**75,7**	5,6
28	If the syringe I use in a scabies patient sinks into my hand, scabies can infect me.			
		22,0	**49,0**	29,0

Medical students' concern

The concern score of participants when approaching scabies patients was determined as 33.00 (min 27.00 - max 40.00) and the median scores of responses are given in Table 3.

Table 3. Distribution of answers to suggestions/questions questioning the level of concern for the medical students' approach to scabies patient

N: 445 Anketteki önerme no'su	**Proposition/Question**	**Score (Median (25%-75%)) Maximum achievable score (10.00)**
Suggestions/questions where a high score indicates concern		
15	How worried do you worry about approaching a patient who does not have a known infectious disease? I don't worry at all 1... I'd be too worried 10	5,00 (2,00-7,00)
16	How worried do you worry about approaching a scabies patient? I don't worry at all 1... I'd be too worried 10	8,00 (6,00-10,00)
17	How worried do you get when approaching a scabies patient with adequate protective equipment (gloves, gowns, visors, masks, etc.)? I don't worry at all 1... I'd be too worried 10	4,00 (2,00-6,00)
24	I am worried that there is a scabies patient in the ward where I work. I don't worry at all 1... I'd be too worried 10	5,00 (2,00-7,00)
Suggestions/questions where a low score indicates concern (Results presented with reverse scoring)		
25	After intervening with scabies, washing my hands with soap and water many times relieves me. **Never relieves 1**... Very relaxing 10	3,00 (1,00-6,00)
26	Wearing gloves when intervening with a scabies patient relaxes me. **Never relieves 1**... Very relaxing 10	3,00 (1,00-4,00)
27	Wearing an apron when intervening with a scabies patient relaxes me **Never relieves 1**... Very relaxing 10	3,00 (1,00-6,00)

In the analysis performed by excluding three participants who did not specify gender, the concern score did not show a statistically significant difference according to gender (Mann-Whitney: 25.895; p: 0.266) but there was a significant difference according to age groups. Accordingly, the concern score was higher in the 20-22 age group (35.00 (28.00-42.00)) than in the other two groups (score in the 23-age group: 31.00 (25.00-38.00)) and (in the 24-age group: 32.00 (26.00-38.00)), (Kruskal Wallis: 11.705; p: 0.003).

There was no statistically significant difference between the students of İzmir Katip Çelebi University and the students of other faculties in terms of concern score (Mann-Whitney U: 17.446.5; p: 0.204) and there was no statistically significant difference according to the classes studied (Kruskal Wallis: 5,912; p: 0.052).

A statistically significant and negative correlation was found between the attitude score and the concern score (Spearman: -0.418; p<0.001).

Perception of Patients' Self-Care

For the proposition 'I think the self-care of scabies patients is lower than other patients,' the agreement score ranged from 2.00 to 7.00, with a median score of 5.00.

Discussion

This study, encompassing 445 medical faculty students, assessed the medical students' i) attitudes, ii) concerns about scabies, and iii) perception about the self-care of scabies patients. The findings reveal that younger students exhibit higher anxiety, which decreases with an increase in knowledge about scabies. Moreover, the outcomes indicate that the study

participants generally maintained a moderate viewpoint concerning the potential stigmatization of scabies patients.

Scabies is currently endemic in developing third-world countries, and tropical and subtropical regions. In 2013, the World Health Organization (WHO) recognized the significance of this disease by including it in the list of 'Neglected Tropical Diseases and Other Neglected Diseases.' Accurate diagnosis and treatment of scabies are crucial due to its status as a worldwide public health concern (17). As a part of our study, we conducted a comprehensive assessment of the attitudes of medical students during the approach to scabies patients through a total of 17 statements. Notably, no similar study has been conducted in our country.

When we examine similar studies conducted in countries other than Turkey, we find that the assessment of medical students' knowledge in approaching scabies patients tends to be more superficial and comprises fewer questions. One study that aligns closely with our research was conducted by Alshehri et al. (22) in the Kingdom of Saudi Arabia in 2018, involving 445 medical students. Their findings indicated that the level of knowledge among medical students in Saudi Arabia regarding scabies and their preventive measures was deemed 'adequate', with an 85.8% proficiency rate. Furthermore, most participants were aware that scabies could be diagnosed through skin scraping, rather than through blood culture or stool analysis. In the same study, medical students' attitudes towards interacting with scabies patients in a clinical setting were assessed through specific items, including not taking the patient to a private room, restricting visitors until the treatment regimen is completed, and emphasizing the importance of preventing scabies through good personal hygiene. These attitudes were further evaluated in terms of 'Ensuring rapid treatment of scabies cases,' and the findings indicated that medical students displayed highly appropriate attitudes in these aspects. In 2019, Alsaidan et al. (23) conducted a study in Saudi Arabia involving 216 primary care physicians to assess their knowledge regarding the diagnosis and management of scabies, as well as the factors influencing this knowledge. The study identified that the highest level of knowledge was related to age sensitivity, clinical findings and diagnosis, mode of transmission, the causative pathogen, and the incubation period, with management being the lowest-scoring category. The results of the logistic model analysis revealed a correlation between a high level of knowledge about scabies and factors such as recent information review, older age, and more experience. However, despite these findings, Alsaidan et al. (23) concluded that the participating primary care physicians generally exhibited 'insufficient' knowledge regarding scabies. As can be seen, in one of two recent studies from Saudi Arabia, the knowledge level of medical students about scabies was reported to be sufficient, while the knowledge level of primary care physicians was reported to be insufficient.

In 2019, Alharthi et al. (24) conducted a study in Saudi Arabia targeting the general population, with a total of 3,778 participants aged between 15 and 30. The study aimed to assess the level of knowledge about scabies using a 12-question questionnaire. The findings revealed that approximately 93.3% of the participants exhibited a good level of knowledge about scabies. Notably, individuals with a higher level of knowledge were predominantly women, residents of urban areas, those who had previously heard about scabies, younger individuals, those with higher levels of education, and those employed in fields such as the medical and education sectors.

In 2001, Rathi et al. (25) conducted a study in Karachi, Pakistan, focusing on 200 General Practitioners (GPs) who had graduated within the past decade. The study aimed to assess their awareness of scabies. Surprisingly, only 36% of the participating physicians reported having a satisfactory level of awareness regarding scabies. Notably, the study did not find any significant impact of increased age or years of experience on the level of awareness.
A study conducted by Birjandi et al. (26) in Accra, Ghana, aimed to determine the prevalence of scabies and assess health literacy among 2,766 high school students across 22 high schools.

The study revealed that 53.4% of the students exhibited a good level of knowledge about scabies, while 44.1% had a medium level of knowledge. Remarkably, approximately 91.3% of the students displayed a positive attitude toward scabies prevention. These findings are notably high for high school students.

When considering studies conducted in Europe, Lapeere et al. (27) conducted research focusing on general practitioners and dermatologists in the Ghent region of Belgium. The study assessed knowledge levels about scabies through a knowledge test, and the results showed acceptable scores for both general practitioners and dermatologists, with median scores of 59% and 79%, respectively. Given that scabies falls within the domain of dermatology, it's not surprising that dermatologists exhibited a higher level of knowledge compared to general practitioners. Additionally, the study found that the duration of experience in scabies treatment (in years) and a higher annual estimated number of scabies cases were factors associated with an increased level of knowledge.

In our study, we found that 38% of participants incorrectly believed in the false proposition that 'Scabies can be transmitted through short contact of 1-2 minutes,' and the same percentage of participants also accepted the false proposition that 'If the infection occurs after contact with a scabies patient, symptoms will appear in a short time (1-3) days.' (Table 2). It's important to note that symptoms of scabies typically take 2-6 weeks to manifest in a person who has it for the first time (1,19). These findings highlight a lack of knowledge within the study group regarding the mode of transmission and the incubation period of scabies.

In our study, the lowest knowledge rate, at 18%, was observed for the proposition 'If scabies patients are hospitalized, they should be isolated in separate rooms.' It's worth noting that while some doctors may have the misconception that scabies patients should be isolated, such information is not supported by the literature.

In addition to these findings, misconceptions and knowledge gaps related to approaching scabies patients due to fear of contamination were evident. For instance, 29.2% of participants expressed that they would not want to use their stethoscope when examining a scabies patient, and 36.6% indicated that they would not want to be in the same room with a scabies patient (Table 2). These findings underscore the importance of addressing these issues in scabies patient approach guidelines and physician training programs.

In our study, the median score for the attitudes of medical students while approaching scabies patients was 10.00 out of a maximum possible score of 17. This score falls within the 'medium' knowledge level range, especially considering that medical students have recently received clinical training. It suggests that there may be perceived deficiencies in approaching scabies patients among this group. As such, it is advisable to plan post-graduate training programs to bridge this knowledge gap.

When examining the results of studies conducted in various countries, comparing the level of knowledge about scabies becomes challenging due to variations in questionnaire design, scales, and different study populations, including the general population, physician groups, medical students, and high school students. It can be concluded that new studies addressing this gap and contributing to the literature about scabies are needed, as there appear to be insufficient publications in the existing literature.

In a study conducted by Alharthi et al. (24) in Saudi Arabia, the "Fear of Scabies Scale-10" was employed to assess the degree of apprehension regarding scabies within the general population. This scale, ranging from 10 to 40 points, with a higher score denoting greater fear, yielded an average score of 33±4.46, indicating that 58.3% of participants harbored heightened fear. Given that our investigation targeted medical students rather than the general population, a reduced level of concern regarding scabies might have been anticipated. However, our study found that the medical students' approach to scabies patient concern score was 33.00 (27.00-40.00). This score, assessed against a maximum of 70 points, categorizes the level of concern

as "medium". In comparison to the findings of Alharthi et al. (24), it appears that the level of concern about scabies is relatively lower in our study. It is crucial to note that our study employed a researcher-developed questionnaire, whereas the Fear of Scabies Scale-10 was utilized in Alharthi's study.

In this study, it was found that gender, the university where medical education is received, and the class level do not significantly differ in physicians' approach to anxiety toward scabies patients. However, in the younger age group of 20-22, the anxiety score was higher. The elevated anxiety score among younger participants may be attributed to these students being newcomers to clinical practice in the medical faculty. When examining the questions assessing anxiety in approaching scabies patients, although the median score was obtained as "8" in the evaluation on a scale of 10 for the question "How worried are you about approaching a scabies patient?", it is observed that anxiety decreases to a median score of "4" when approaching a scabies patient with adequate protective equipment (gloves, gown, face shield, mask, etc.). Moreover, washing hands repeatedly with soap and water after intervening with scabies patients and wearing gloves and a gown while dealing with them were found to reduce anxiety (Table 3).

In the study by Alharthi et al. (24), although the level of knowledge was deemed good, the concern level regarding scabies was found to be high, and a positive correlation was reported between the attitude level and the concern level. In our study, an inverse relationship was observed: as the medical students' attitude score towards scabies increased, the concern score decreased, indicating a negative correlation between the two ($p<0.001$). Despite these seemingly contradictory findings, it's essential to consider that Alharti et al.'s study was conducted in the general population with a focus on understanding scabies disease, whereas our study specifically delves into medical students' perspectives on scabies. As students' knowledge about the disease increases, their inclination to take preventive measures and educate patients may contribute to reduced concerns.

In our investigation, we explored medical students' perspectives on whether they perceived the self-care of scabies patients as lower than that of other patients. The obtained median score was 5 out of 10 points. This outcome suggests that the study participants held a moderate viewpoint regarding the potential stigmatization of scabies patients. It is noteworthy that scabies disease is not directly associated with personal hygiene.

Conclusion

In this study, it was found that concern is higher among younger medical students regarding scabies patients, and as the level of knowledge about scabies increases, the concern decreases. It is recommended to address concerns about the transmission of scabies to physicians who intervene in the approach to scabies patients through educational interventions on the mode of transmission and preventive measures of the disease during pre-graduation training in medical faculties.

Limitations

This study is constrained by its cross-sectional design and the absence of a scale with established validity and reliability for calculating both the concern and attitude scores. Nevertheless, a notable strength of this study is its pioneering nature, as no other study has explored the concern in the approach to scabies patients among medical students in Turkey.

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MYOCARDIAL INFARCTION DUE TO COCAINE BODY PACKER SYNDROME – A CASE REPORT

KOKAİN BODY PACKER SENDROMUNA BAĞLI MIYOKARD ENFARKTÜSÜ - BIR OLGU SUNUMU

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MAKALE BİLGİLERİ
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ABSTRACT

Introduction: "Body packing" refers to an act of ingesting large numbers of illicit drug-filled packets for smuggling purposes. Due to the fact that Istanbul, Turkey is considered to be one of the main air traffic hubs connecting many international airlines, it is potentially on the routes of body packing smugglers. This case report presents a case of myocardial infarction (MI) due to cocaine Body Packer Syndrome.

Case Presentation: A 43-year-old woman of Venezuelan nationality was brought to the Emergency Department on suspicion of seizure and deterioration during her flight and diagnosed with MI due to cocaine Body Packer Syndrome.

Conclusion: Body packers may have intoxication due to the leakage or rupture of the cocaine packets. One of the consequences is MI related to cocaine intoxication.

ÖZET

Giriş: Body packing, çok miktarda yasadışı maddenin kaçakçılık amacıyla kişinin vücudu içinde gizlenmesini tarif etmektedir. İstanbul, Türkiye birçok havayolunun bağlandığı ana hava trafiği aktarma merkezlerinden biri olması nedeniyle, body packing kaçakçılarının rotaları üzerinde olma potansiyelindedir. Bu olgu sunumunda, kokain body packer sendromuna bağlı bir miyokard enfarktüsü (MI) vakası sunulmuştur.

Olgu Sunumu: 43 yaşındaki Venezuela uyruklu kadın, uçuş sırasında nöbet geçirme şüphesi ve kötüleşme nedeniyle Acil Servis'e getirildi ve kokain Body Packer Sendromuna bağlı MI tanısı aldı.

Sonuç: Kokain paketlerinin sızması veya yırtılması nedeniyle body packerlarda intoksikasyon görülebilir. Bunun olası sonuçlarından biri, kokain intoksikasyonuna bağlı MI'dır.

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Introduction

Body packing is defined as ingesting large numbers of illicit drug-filled packets with the aim of international drug smuggling. “Body packers” usually conceal the packets either by swallowing or by inserting them into the rectum or vagina. The three most frequently smuggled drugs in this method are cocaine, heroin, and cannabis.

Different types of cocaine packets used by body packers were defined in the literature (1,2). There seems to be a new trend of using liquid cocaine packets, and due to their radiotransparent nature, it is harder to diagnose them correctly (3).

Detecting a body packer usually rests on clinical presentation and appropriate medical history. A body packer can classically be diagnosed with an abdominal radiograph and computed tomography (CT).

In some cases, the packets filled with illicit drugs can leak or rupture, and may have consequences due to acute drug intoxication, which is appropriately named “Body Packer Syndrome”. These cases need emergency surgical procedures to prevent mortality(4).

Cocaine is one of the most consumed stimulants. It causes a local anesthetic effect by inhibiting voltage-gated sodium channels, and it also affects neurotransmission by inhibiting the reuptake of dopamine and other monoamines from the synaptic cleft(5). It can be consumed through various routes and can be quickly absorbed transmucosally. Even the rupture of one cocaine packet may be lethal(2). Cocaine toxicity may present with tachycardia, hypertension, hyperthermia, diaphoresis, mydriasis, and agitation. Patients often die due to neurological and cardiovascular side effects (2,5).

Cocaine, with its complex effects on the body, has severe cardiac side effects ranging from atypical chest pain to unstable angina pectoris and acute MI. Management of these cases has some differences from Acute Coronary Syndrome (ACS) cases.

Case Presentation

A 43-year-old woman of Venezuelan nationality was brought to the Emergency Department with an ambulance, on suspicion of seizure and deterioration during the last minutes of her flight between Buenos Aires and Istanbul.

The patient’s vital signs were stable at admission to the Emergency Department (ED), with a blood pressure of 130/75 mm-Hg, pulse rate of 105 beats/min, respiratory rate of 17/min, sPO2 of 99%, and temperature of 36.5 0C. The patient was alert and oriented. A full physical examination showed no pathological findings other than conjunctival hyperemia and mild dilation of the pupils.

In the detailed medical history, it is learned that the patient felt chest pressure and became unwell but did not lose consciousness, and has no known history of illnesses. She explained that she was flying from Buenos Aires to İstanbul as a transit passenger. The airplane landed in İstanbul at 11 p.m., and she had a flight to Bucharest/Romania at 6:45 p.m. the next day. Accompanying airline personnel remarked that this was an unusual flight pattern for a transit passenger, and the airport police suspected she was a possible drug smuggler.

An electrocardiogram (ECG) test is obtained and interpreted as normal. Arterial blood gas, hemogram, cardiac marker enzymes (troponin T and creatine kinase), coagulopathy, urinalysis, B-HCG, and blood and urine drug tests were measured. Arterial blood gas test showed respiratory alkalosis. Posteroanterior chest-x-ray and abdominal x-ray of the patient were taken, and interpreted as normal (Figure 1).

Figure 1. Abdominal x-ray of the patient. Foreign bodies are not apparent.

Troponin level was 6800 pg/mL, creatine kinase (CK) level was 661 U/L, CK-MB level was 27,9 ng/mL, and echocardiography (Figure 1) showed possible anterior wall motion abnormality. With these results, the cardiologist diagnosed the patient with MI, and emergency coronary angiography (CAG) was performed. It resulted as normal with no significant coronary lesions.

3rd-hour control Troponin level was 5967 pg/ml, CK: 551 U/L, CK-MB: 21,8 ng/mL (7th-hour Troponin level: 7526 pg/mL).

Drug test results were only positive for cocaine (>900 ng/mL), and a non-contrast abdominal CT scan was performed for detailed evaluation of the abdomen. CT Scan showed some air-fluid levels, and hyperdense findings in the stomach and bowels consistent with foreign bodies (Figure 2). With these results, the patient underwent emergency laparotomy with the diagnosis of “Body Packer Syndrome”. A total of 43 mostly perforated packets filled with liquid cocaine were found scattered along the stomach and the bowels, and successfully recovered (Figure 3).

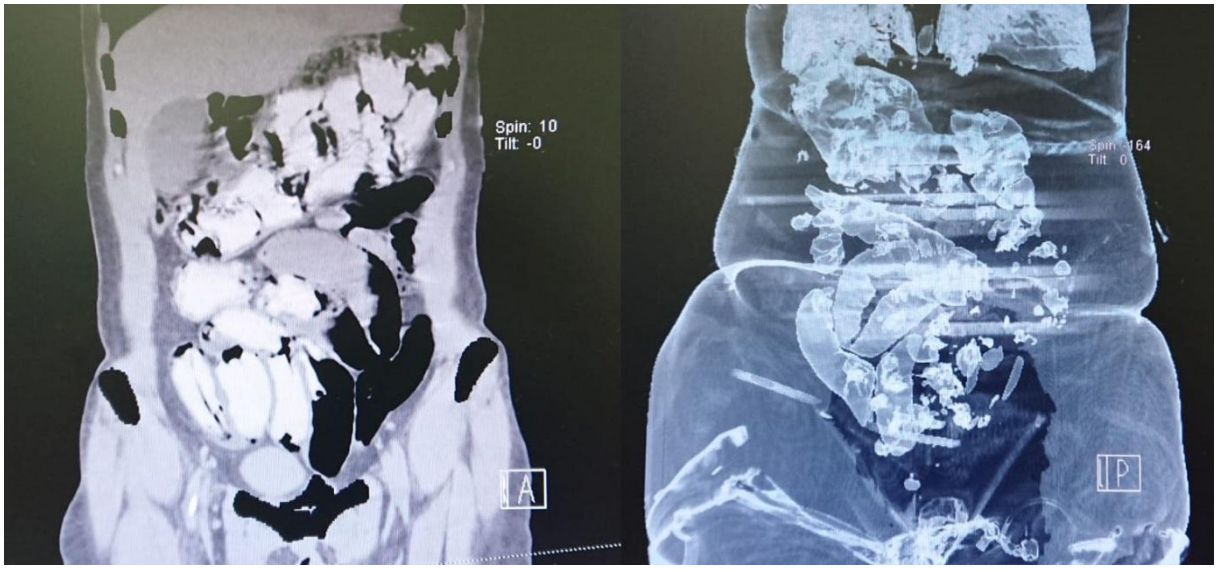

Figure 2. Hyperdense findings consistent with foreign bodies in Coronal non-contrast abdominal CT (left) and, 3-Dimensional reconstruction of it (right).

Figure 3. Recovered packets filled with liquid cocaine.

After the operation, the patient was admitted to the Intensive Care Unit (ICU). No complications occurred within the first 5 days following the operation where the patient was in the ICU, and the patient was admitted to the General Surgery Department for further observation. After 5 more days without complications, the patient was discharged and handed over to the law forces.

Discussion

Smugglers carrying illicit drugs in their body cavities are named “Body Packers” in the literature, and often present to health facilities with three presentations: 1) Drug toxicity, 2) Bowel obstruction, and 3) Asymptomatic body packers who are detected by the police forces and brought to health facilities for medical evaluation.

Because of the legal aspects, the medical history of the patients is typically misleading. Also, in some cases with drug toxicity, the patient's consciousness may deteriorate, and be unsuitable to obtain an accurate history.

Abdominal X-ray has been reported to have 40-100% sensitivity in the diagnosis of body packing. Cocaine packets are usually seen as radio-opaque objects (6).

Apart from 4 classic packet types (2), packets filled with liquid cocaine have been reported lately. With their homogeneous hyperdense fillings, these packets are typically hard to diagnose (6). That was indeed correct for the present case's X-ray images too, which the packets could not be successfully distinguished. In contrast, hyperdense findings consistent with foreign bodies can easily be distinguished in non-contrast abdominal CT images (Figure 2).

Literature search for "body packer (-ing)", "body stuffer (-ing)", "intracorporeal drug concealment", "drug courier", and "cocaine mule" expressions in PubMed is summed up in Table 1. We have found only one cocaine body packer case ended with mortality due to cardiotoxicity in the literature (7). Also, except for the present case, there is only one case reported with MI due to cocaine Body Packer Syndrome (8).

Table 1. PubMed search results of Cocaine Body Packer cases with cardiotoxicity.

Source	Number of Total Cases	Cardiac Toxicity	Description	Mortality
Marcovigi et al. (1995)(9)	1	1	Severe dysrhythmias occurred, and a pacemaker was applied.	No
De Prost et al. (2005)	581	3	One cardiac arrest, One MI, One VF	1 case
Alfa-Wali et al. (2016)	120	1	High Troponin and nonspecific ECG changes were seen and observed in the CICU	No
Pramanik et al. (2016)	1	1	Cardiac arrest shortly after chest pain. Packets filled with cocaine have been found in the autopsy.	Yes
Present Case	*1*	*1*	*Emergency CAG was performed with the diagnosis of MI*	*No*

Abbreviations: ECG; Electrocardiography, MI; Myocardial infarction, VF; Ventricular Fibrillation, CICU; Coronary Intensive Care Unit, CAG; coronary angiography.

Cocaine has several cardiotoxic effects that include stimulation of the sympathetic nervous system, blockade of sodium and potassium channels, promotion of thrombosis, vasoconstriction, oxidative stress, and mitochondrial damage that lead to ischemia. It also leads to myocardial damage with its effects on myocardial contraction, increasing myocardial oxygen demand while simultaneously decreasing oxygen supply (9,10). 10% of MI patients under 50 years old have a history of cocaine and/or cannabis use, and their mortality due to cardiac causes (and all-cause mortality) is higher. They conclude that drug testing should be performed to define the cause of young MI patients (11). 6% of the patients present to the ER with chest pain associated with cocaine have been diagnosed with MI (12). Current guidelines suggest approaching chest pain associated with cocaine, like other ACS cases. However, there is a debate over the high number of negative CAGs arising from this approach (13). Gitter et al.'s study showed that none of the chest pain associated with cocaine patients had MI (14). Another retrospective analysis conducted lately in the USA showed that 6.7% of these patients had CAG, but the Type 1 MI rate was a mere 0.69%. Researchers stated that these patients had low mortality rates (15).

MI cases related to cocaine use may have no ECG findings. However, there may be Q waves on anterior and inferior leads, and an ECG finding in presentation is related to higher mortality (16). CAGs of these patients show 1-2 vessel disease in 31-66%, 3 vessel disease in

13-15%, normal coronary arteries in 18-45%, and thrombosis in 24% (12). There was no definitive ECG finding in our case, and the CAG resulted as normal. No additional cardiac pathology has been found in the observation period.

Conclusion

Body packers may have consequences of intoxication due to the leakage or rupture of the cocaine packets. One of these consequences is MI. In these patient groups, ending exposure by emergency laparotomy, and using a standard ACS approach, is the treatment choice. It should be noted that Body Packer Syndrome is an easy-to-miss life-threatening diagnosis, especially if it's not suspected, and one of the consequences is MI due to cocaine intoxication.

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MANAGEMENT OF ACUTE CERVICAL FRACTURES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

ANKİLOZAN SPONDİLİTLİ HASTALARDA GELİŞEN AKUT SERVİKAL KIRIKLARIN YÖNETİMİ

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ABSTRACT

Ankylosing spondylitis (AS) is a type of arthropathy that mainly affects the sacroiliac region and spine. In AS, patients are four times more likely to experience spinal fractures compared to the general population. In this specific group, these fractures often lead to a high incidence of neurological complications. In individuals with AS, spinal fractures are often caused by simple traumas, such as falling from the same level. The ossification of the ligaments and the annulus alters the biomechanics of the spine, acting like a long bone, and reduces its ability to absorb even minor impacts. This article aims to highlight the distinctions in acute cervical fractures among patients with AS compared to fractures in the general population by discussing three different case examples and drawing insights from existing literature.

ÖZET

Ankilozan spondilit primer olarak sakroiliak eklemleri ve omurgayı etkileyen seronegatif bir artropatidir. Spinal kırıklar, ankilozan spondilitli hastalarda genel popülasyona göre dört kat daha sıktır. Bu popülasyondaki kırıklar, yüksek nörolojik komplikasyon oranına sahiptir. Ankilozan spondilit hastalarında spinal kırıklar sıklıkla aynı seviyeden düşme gibi düşük enerjili bir mekanizmadan kaynaklanır. Bu hastalarda spinal ligamanların ossifikasyonu ve anulus fibrozisin kalsifikasyonu, ufak darbeleri bile absorbe etme yeteneğini sınırlayan uzun bir kemik gibi davranarak omurganın biyomekaniğini değiştirir. Bu yazıda, ankilozan spondilitli hastalarda gelişen akut servikal kırıkların normal popülasyondaki kırıklara göre farklılıklarını üç farklı olgu örneği ile literatür eşliğinde tartışarak sunmayı amaçladık.

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Introduction

Ankylosing spondylitis (AS) is a disease affecting the sacroiliac joints and spine (1). Patients with AS face a fourfold higher risk of spinal fractures (SFs) compared to the general population (2). Low-energy traumas frequently cause SFs in these individuals. The ossification of the ligaments and annulus alters the biomechanics and limits the ability to absorb even small impacts (3). This article intends to delineate the unique characteristics of acute cervical fractures in patients with AS compared to the fractures in the general population by discussing three different case examples in light of the literature.

Cases

Case-1

A 43-year-old male with AS presented complaining of diffuse muscle weakness after being punched in the face. Physical examination revealed quadriplegia below C6 and absence of anal sphincter tone. Fractures of calcified longitudinal and posterior ligaments are seen in CT and MR in combination with hyperlordosis and gap formation between C6-C7 (Figure 1). After medical preparations, the patient was operated on the 3rd day of the trauma. Pedicle screws were inserted in C6-C7-T1 on the right and C6&T1 on the left. After connecting the rods, hyperlordosis was somewhat reduced. Then the patient turned into the supine position, and the PEEK-cage was inserted into the gap between C6&C7. Plate-screw fixation of C5-C6-C7 was performed using a midline cervical plate. Anterior plate-screw instrumentation fixed the residual kyphosis (Figure 2). The patient was admitted to the rehabilitation clinic postoperatively.

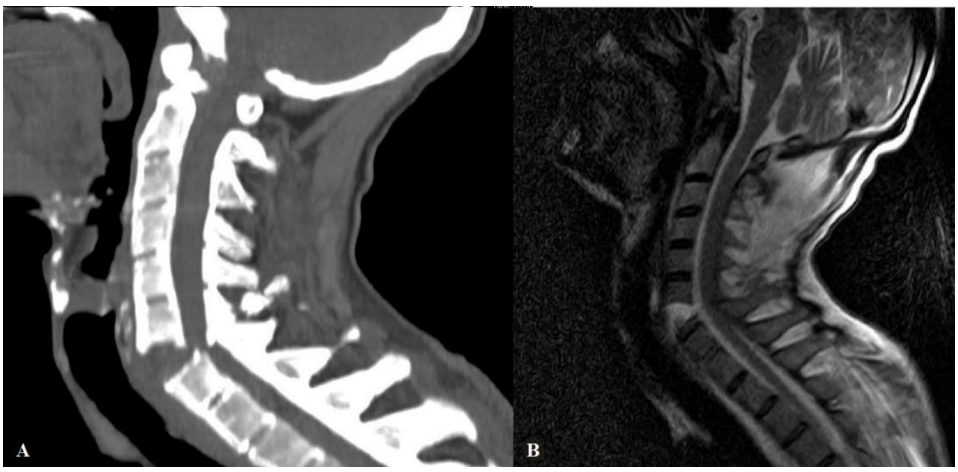

Figure-1: The first case. **A.** The breakage of calcified anterior-posterior longitudinal ligaments and ligamentum flavum, on the level of C6-C7 at preoperative CT mid-sagittal reconstruction; hyperlordosis formation with ligamentum flavum fracture as the pivot and C6-C7 vertebral vertebrae are seen to diverge. **B.** preoperative sagittal T2 weighted MRI is showing posterior spinal cord compression due to hyperlordosis.

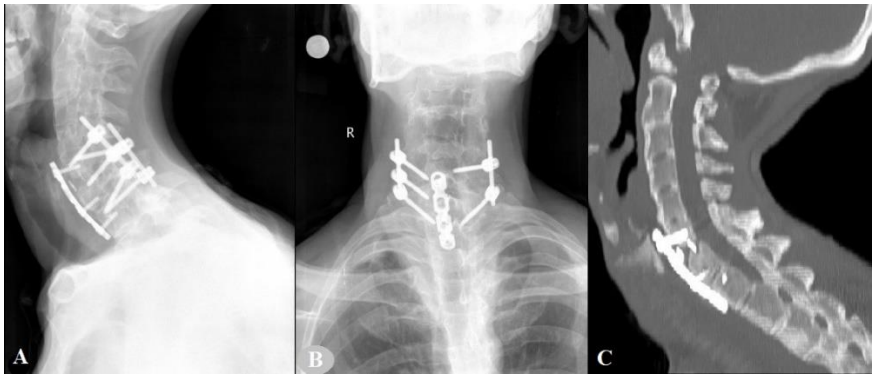

Figure-2: The first case. **A. B.** At postoperative lateral and AP direct cervical radiography, right C6-C7-T1, left C6-T1 pedicle screws, and anterior midline plate screw fixation are seen **C.** At postoperative CT mid-sagittal reconstruction, it is seen that hyperlordosis is fixed, and vertebral alignment has been brought top re-traumatic position with a cervical plate and PEEK cage between C6-C7 vertebrae.

Case-2

A 56-year-old male presented complaining of neck pain and paresthesia in his hands, after hitting his head against the wall and falling from the same level. There was no motor deficit, sphincter tone was present. Although there is no information in his medical history, bilateral facet joint fusions, and calcified anterior and posterior ligaments, which are compatible with the "bamboo spine" appearance typical of AS, were seen in CT. The cervical vertebrae were fractured at the C5-C6 level and dislocated to the anterior (Figure 3). After medical preparations, the patient was operated on the 14th day of the trauma, and dislocation was reduced and stabilized with C5-C6 pedicle screws (Figure-4). The patient was discharged with a recommendation for rheumatological evaluation on the postoperative 2nd day.

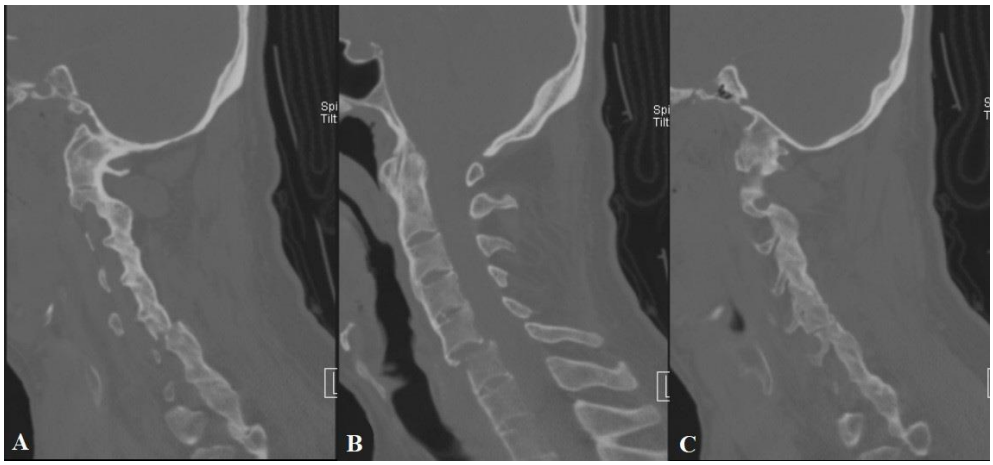

Figure-3: The second case. **A.** CT parasagittal reconstruction passing right cervical facet joint **B.** CT mid-sagittal reconstruction **c.** "Bamboo spine" image at CT parasagittal reconstructions passing left cervical facet joints; fracture line and anterior dislocation are seen on the level of C5-C6

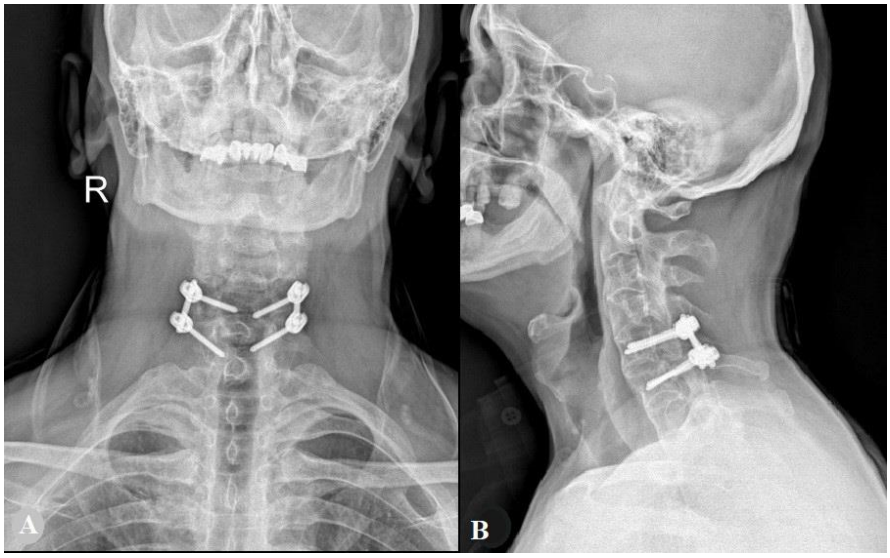

Figure-4: The second case. **A.** AP and **B.** C5-C6 pedicle screw stabilization is seen at lateral postoperative early cervical direct radiographs.

Case-3

Sixty-six-year-old male was resuscitated from cardiac arrest after falling from the same level. He was admitted to the neurology intensive care unit with a preliminary diagnosis of cerebrovascular accident. His medical history (obtained from his relatives) included chronic obstructive pulmonary disease and AS. He had undergone cervical posterior decompression and stabilization some years ago. In the intensive care unit, the patient regained consciousness, and a physical examination revealed left hemiplegia. While there was no evidence in favor of ischemia in the brain MR, it was seen that the odontoid process was fractured and C1-C2 dislocated posteriorly, creating hyperlordosis on CT. In addition to the "bamboo spine" appearance, calcified anterior/posterior longitudinal ligaments between the C6-C7 corpus were broken, as a result of which the C6&C7 separated (Figure-5). In the follow-up, quadriplegia developed, and the patient died 25 days after trauma, without being operated on.

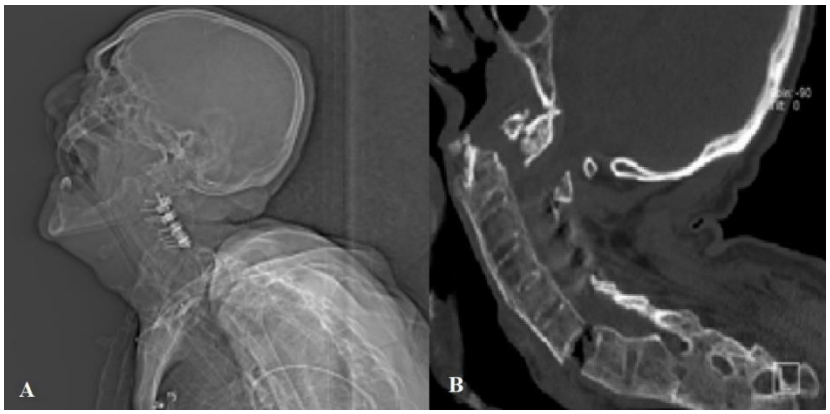

Figure-5: The third case. **A.** Lateral CT "scout" image shows previous C3-C6 lateral mass screw stabilization. **B.** CT mid-sagittal reconstruction shows a "bamboo spine" appearance on the cervical region. The odontoid process has been fractured and posteriorly dislocated. A small part of the fractured atlas can also be seen in front of the C2 corpus. Severe hyperlordosis has occurred in the atlantoaxial joint. Moreover, C6-C7 calcified anterior and posterior longitudinal ligaments

fractured, and C6-C7 vertebrae have been separated. C3-C4-C5 posterior elements appear to have been removed in the previous surgery.

Discussion

AS is a progressive inflammatory condition that mainly affects the skeletal system (1). In the early stage, inflammatory sacroiliitis caused by cartilage destruction and bone erosion is observed, followed by rising vertebral inflammation that develops in apophysis and epiphysis (4). In late-stage AS, erosions in the sacroiliac joint and spine appear to be repaired by ossifying over time. Unlike rheumatoid arthritis, where inflammation causes bone erosion, AS leads to the formation of bones to enthesophytes and syndesmophytes. Ossification of the longitudinal ligament results in the classic "bamboo spine" appearance (5). This rigid spine acts as a long bone and plays a crucial role in the susceptibility of AS patients to SFs.

Patients with AS are at a higher risk of spinal traumas than in the general population since these patients are unable to perform sudden movements, such as turning their heads. Also, they have higher rates of neurological complications. 2/3 of these patients have spinal cord damage when they first present to the emergency room (2). In addition, AS patients with traumatic SFs have a significantly increased risk of death (18-32%) due to their morbidity compared to patients with traumatic SFs but without AS (3). One of our three patients developed quadriplegia below the C6 level, and another patient died. Our other patient had no neurological deficit.

Most of the acute SFs in the AS population occur in the cervical spine (81.2%), especially in the C5-C6 and C6-C7 levels (2). Facet joints in the cervical region make an angle of 45 degrees with the horizontal plane, 60 degrees in the thoracic, and 80-90 degrees in the lumbar region. Accordingly, while the cervical region has greater mobility, movements in the lumbar region are quite limited. It is particularly prone to injuries due to the oblique facet joint angle of the cervical region and the junction in the transition from a more mobile head and neck to a more stable thoracic region. In our patients, fractures were observed at these levels (6).

Approximately 75% of these fractures have a hyperextension mechanism (3), which is primarily due to pre-existing kyphotic deformity. Due to the reduced elasticity of the disc and calcification of the annulus, the fracture can occur at the disc level besides the vertebral corpus (7). In our 3 cases, fractures were passing through the disc levels.

The purpose of the treatment is to restore the patient's pre-injury position and remove the neural compression (8). One of the features that should be considered is that the pre-injury postures of these patients are kyphotic. Extended segmental instrumentation is recommended (9, 10). We performed anterior and posterior stabilization in one of our patients and short segment stabilization in the patient with almost no deformity.

Conclusion

It should be kept in mind that in patients with AS, unstable SFs can develop even with low-energy traumas, can be misdiagnosed easily with plain radiographs, and the fracture line can pass through the disc level. The risk of neurological deficit and mortality is higher than in the general population.

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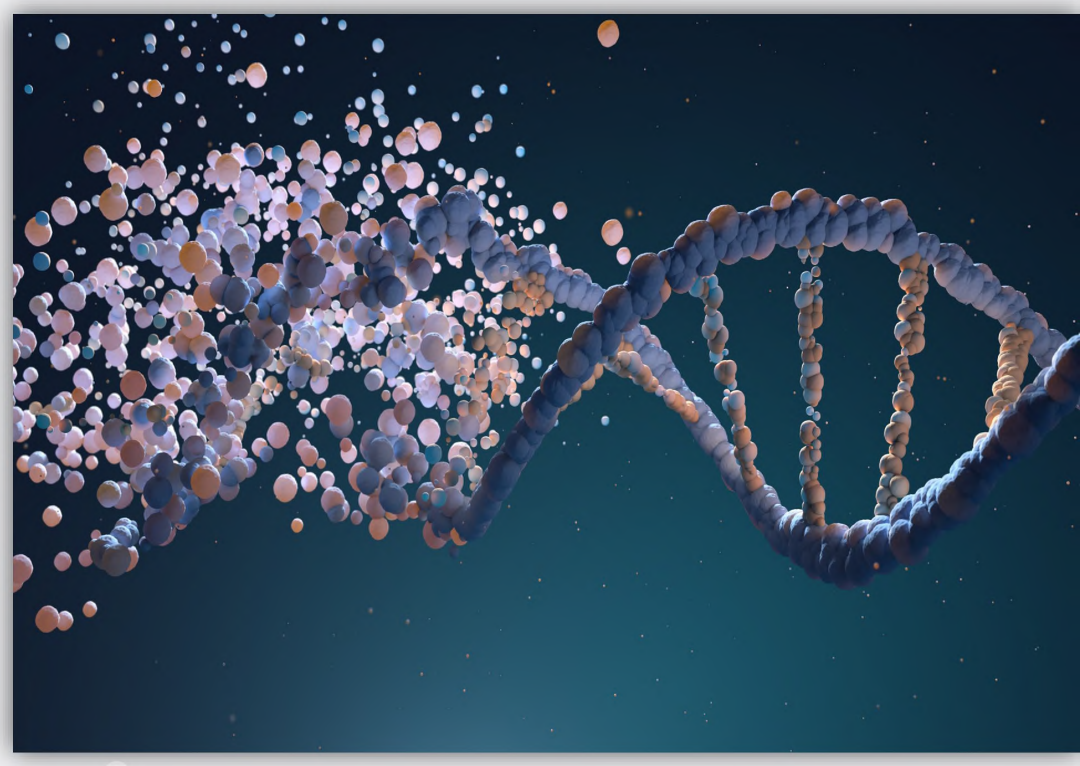

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