ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Retrospective Analysis of Patients Admitted to Physical Medicine and Rehabilitation Outpatient Clinics with Osteoarticular Findings and Diagnosed with Brucellosis

Fiziksel Tıp ve Rehabilitasyon Polikliniklerine Osteoartiküler Bulgularla Başvurarak Bruselloz Tanısı Alan Hastaların Retrospektif Analizi

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ABSTRACT

Aim: *In endemic regions, we aimed to consider Brucella infection in the differential diagnosis of musculoskeletal manifestations and to emphasize the diversity of presentation.*

Material and Method: *Our study has a retrospective design. Between 01.01.2020 and 01.01.2024, patients who applied to the physical therapy and rehabilitation department of a second-stage public hospital located in a region where brucella infection is endemic and were diagnosed with brucellosis with osteoarticular findings were included in our study. Demographic data, complaints at presentation, musculoskeletal examination findings, Brucella serology tests, liver function tests, complete blood counts, sedimentation rate (ESR) and C-reactive protein (CRP) levels, and related musculoskeletal imaging data were recorded.*

Results: *47 patients were enrolled in the study. 68.1% (32/47) of the patients were male, while 31.9% (15/47) were female. The average age of the patients was 44.43±15.47 years. Joint pain and low back pain were the predominant symptoms observed in the majority of cases; the most common types of involvement were arthralgia (46.8%), sacroiliitis (19.1%), spondylodiscitis (14.9%) and monoarthritis (14.9%). We found elevated CRP in 48.93%, elevated ESR in 27.65%, leukocytosis in 14.89%, leukopenia in 8.51%, anemia in 31.91%, elevated ALT in 12.76% and elevated AST in 10.63%.*

Conclusion: *Brucellosis may present with various musculoskeletal findings. Considering Brucella infection in the differential diagnosis is crucial for preventing potential complications through prompt diagnosis and treatment in patients presenting with musculoskeletal symptoms, particularly in endemic areas.*

Key words: *arthritis; brucella; sacroiliitis; spondylodiscitis*

ÖZET

Amaç: *Brusella enfeksiyonunun endemik olduğu bölgelerde, osteoartiküler bulgular değerlendirilirken ayırıcı tanıda Brusella enfeksiyonunun da akılda tutulması gerekliliği ve prezentasyon çeşitliliğini vurgulamak amaçlandı.*

Materyal ve Metot: *Çalışmamız retrospektif bir tasarıma sahiptir. 01.01.2020 ile 01.01.2024 tarihleri arasında Brusella enfeksiyonunun endemik olduğu bir bölgede yer alan ikinci basamak bir devlet hastanesinin fizik tedavi ve rehabilitasyon bölümüne osteoartiküler bulgular ile başvurup bruselloz teşhisi alan hastalar çalışmamıza dâhil edildi. Olguların demografik verileri, başvuru şikâyetleri, kas-iskelet sistemi muayene bulguları, Brusella seroloji testleri, tam kan sayımları, sedimantasyon (ESH), C-reaktif protein (CRP) değerleri, karaciğer fonksiyon testleri ve ilgili kas-iskelet sistemi görüntüleme verileri kaydedildi.*

Bulgular: *Çalışmaya 47 bruselloz olgusu dâhil edildi. Hastaların %68,1'i (32/47) erkek, %31,9'u (15/47) kadındı. Hastaların yaş ortalaması 44,43±15,47 idi. En sık görülen semptomlar eklem ve bel ağrısı; en sık tutulum tipleri ise artralji (%46,8), sakroileit (%19,1), spondilodiskit (%14,9) ve monoartritti (%14,9). Hastaların %48,93'ünde CRP yüksekliği, %27,65'inde ESH yüksekliği, %14,89'unda lökositoz, %8,51'inde lökopeni, %31,91'inde anemi, %12,76'sında ALT yüksekliği, %10,63'ünde AST yüksekliği saptadık.*

Sonuç: *Bruselloz çeşitli kas-iskelet sistemi bulguları ile prezente olabilmektedir. Özellikle Brusella enfeksiyonunun sık görüldüğü bölgelerde kas-iskelet sistemine ait bulguları olan hastaları değerlendirirken ayırıcı tanıda brusellozun akılda tutulması erken teşhis ve tedavi ile olası komplikasyonları engelleyebilmek adına faydalı olacaktır.*

Anahtar kelimeler: *artrit; brusella; sakroileit; spondilodiskit*

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Introduction

Brucellosis is a zoonotic disease caused by gram-negative coccobacilli bacteria of the genus Brucella. Humans can contract it through inhalation, skin contact, or by consuming unpasteurized dairy products[1,2]. Brucellosis commonly affects the young and middle-aged population, with less frequency observed in children and geriatric patients[3]. Brucellosis is endemic in our country[4]. According to the analyses of the Public Health General Directorate of the Ministry of Health of the Republic of Türkiye, the incidence of brucellosis in the province of Yozgat, where our hospital is located, is above the national average in Türkiye[5].

Brucellosis can affect various systems with diverse and nonspecific clinical manifestations. The most common symptoms are fever, weakness, fatigue, loss of appetite, muscle-joint pain, headache, lymphadenopathy, digestive system symptoms, weight loss and night sweats[6]. This wide-ranging clinical presentation poses diagnostic challenges; some studies suggest that the initial diagnosis is incorrect in one-third of patients[7]. It is reported that the musculoskeletal system is involved in brucellosis, with a frequency between 10 and 85%. The most commonly affected musculoskeletal areas are the sacroiliac, spinal and peripheral joints. Osteomyelitis, discitis, bursitis and tenosynovitis are less common types of involvement. Musculoskeletal involvement can be seen in patients with acute, subacute or chronic brucellosis[8,9].

Brucellosis may present with a wide variety of musculoskeletal system findings. Physical medicine and rehabilitation (PMR) outpatient clinics are among the most common referral points for patients with musculoskeletal complaints. With this study, we emphasize that brucellosis infection should be considered in the differential diagnosis when evaluating musculoskeletal system findings in regions where brucellosis is endemic and to highlight the diversity of presentations.

Material and Method

Our study has a retrospective design. Patients who applied to Yozgat City Hospital PMR outpatient clinics between 01.01.2020 and 01.01.2024 and were diagnosed with brucellosis with osteoarticular findings were included in the study. The diagnosis of Brucella infection was based on clinical findings and a Brucella Coombs test titer above 1/160. The age, gender, presenting complaints, musculoskeletal system examination findings, Brucella serology tests, liver function tests, complete blood counts, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and relevant musculoskeletal imaging data were recorded for the cases included in our study. Erythrocyte sedimentation rate >20 mm/hour was considered elevated ESR; CRP >0.8 mg/dl was considered elevated CRP; aspartate aminotransferase (AST) and alanine aminotransferase (ALT) values above 40 IU/ml were considered elevated. Hemoglobin levels below 12 g/dl were considered anemia in women and below 13 g/dl in men; a leukocyte count below 4000/mm^3 was leukopenia; a leukocytosis above 10000/mm^3 was leukocytosis; a platelet count <150000/mm^3 was thrombocytopenia, and a platelet count >450000/mm^3 was thrombocytosis.

The Ankara Bilkent City Hospital Ethics Committee approved our study (date: 10.01.2024, number: E2-24-6082).

Statistical Analysis

Data were analyzed using the IBM Statistical Package for Social Sciences (SPSS) program version 25.0 (IBM Inc., Armonk, NY, USA). The normality of numerical data distribution was examined using the Shapiro-Wilk test. Continuous variables with normal distribution were presented as mean and standard deviation, and those without normal distribution were presented as median and interquartile range (IQR; 25 th-75th percentiles), while qualitative data were expressed as frequency and percentages. Binary logistic regression analysis was performed to investigate possible variables that may be associated with the presence of arthritis and sacroiliitis/spondylitis. The confidence interval is 95%, and the accepted margin of error is 5%. The p-value is considered significant at $p<0.05$.

Results

Our study included 47 patients diagnosed with brucellosis with osteoarticular findings. Of the patients, 68.1% (32/47) were male, and 31.9% (15/47) were female. The mean age of the patients was 44.43±15.47 years. The mean age was 48.7±17.0 and 42.4±14.5 in females and males, respectively; no significant difference was found between females and males (p=0.194). The most common symptoms were joint and lower back pain; the most common types of involvement were arthralgia, sacroileitis, monoarthritis and spondylodiscitis. Of the patients with sacroileitis, 5 had unilateral, and 4 had bilateral involvement. Among the patients with monoarthritis, 4 had knee arthritis, 2 had ankle arthritis, and 1 had hip arthritis. Hip arthritis was detected in a 10-year-old girl, the only

Table 1. *Analysis of patients according to age, gender, symptoms and musculoskeletal system involvement type*

	N/%	Mean ± SD
Age		44.43±15.47
Female		48.7±17.0
Male		42.4±14.5
Gender		
Female	15 (31.9)	
Male	32 (68.1)	
Symptoms		
Joint pain	33 (70.2)	
Back pain	10 (21.3)	
Chest pain	1 (2.1)	
Weakness/Tiredness	1 (2.1)	
Neck pain	1 (2.1)	
Joint swelling	1 (2.1)	
Musculoskeletal involvement		
Polyarthralgia	12 (25.5)	
Monoarthralgia	10 (21.3)	
Sacroiliitis	9 (19.1)	
Monoarthritis	7 (14.9)	
Spondylodiscitis	7 (14.9)	
Polyarthritis	1 (2.1)	
Synovitis	1 (2.1)	

SD: Standard deviation

Table 2. *Analysis of patients' biochemical data*

	Median (IQR; 25%-%75)	N (%)
Brucella Coombs titer	640.00 (2240.00)	
Sedimentation (mm/hour)	18.00 (27.00)	
• Elevated sedimentation		13 (27.65)
C-Reactive Protein (mg/dl)	1.28 (3.04)	
• Elevated C-Reactive Protein		23 (48.93)
Leukocyte count (mm^3)	7400 (2400)	
• Leukocytosis		7 (14.89)
• Leukopenia		4 (8.51)
Neutrophil count (mm^3)	4400 (2150)	
Lymphocyte count (mm^3)	2100 (1200)	
Platelet count (mm^3)	256000 (95500)	
• Thrombocytopenia		1 (2.12)
• Thrombocytosis		-
Hemoglobin (mg/dl)	13.6 (1.75)	
• Anemia		15 (31.91)
ALT (IU/ml)	20 (15)	
• Elevated ALT		6 (12.76)
AST (IU/ml)	21 (9.5)	
• Elevated AST		5 (10.63)

IQR: interquartile range; ALT: alanine aminotransferase; AST: aspartate aminotransferase

child in the patient group. There was no accompanying osteomyelitis in the arthritis cases. Of the patients with spondylodiscitis, 5 had lumbar involvement, and 2 had thoracic involvement; there were no patients with cervical involvement. There were no accompanying abscesses or neurologic complications in cases of spondylodiscitis. Table 1 summarizes the age, gender, predominant symptoms, and musculoskeletal involvement types of the patients. We found elevated CRP in 48.93%, elevated ESR in 27.65%, leukocytosis in 14.89%, leukopenia in 8.51%, anemia in 31.91%, elevated ALT in 12.76% and elevated AST in 10.63%. Biochemical analyzes of the patients are presented in Table 2.

In binary logistic regression analysis, no significant correlation was found between age, gender, laboratory parameters, and the presence of arthritis and sacroiliitis/spondylodiscitis.

Discussion

The Central Anatolia region, where our hospital and our study population are located, has a high incidence of brucellosis[10]. Brucellosis can present with multisystem involvement and various nonspecific clinical findings. The musculoskeletal system is one of the systems that is frequently affected and should be kept in mind[8]. Therefore, brucellosis patients with musculoskeletal symptoms often visit PMR outpatient clinics.

Our patient group mainly consisted of male and young adult patients, which is in line with other studies[11,12]. The predominance of male patients may be related to the fact that men engaged in animal husbandry are more exposed to this infection. The most common involvement in our patient group was nonspecific arthralgia; however, radiologically, sacroileitis, spondylodiscitis and arthritis were prominent. In the study of Geyik et al.[12] where they evaluated osteoarticular involvement in brucellosis patients, sacroiliitis, peripheral joint involvement and spondylodiscitis were the most common involvement types, respectively. In another study conducted in our country, the types of involvement are as follows: sacroiliitis, peripheral joint involvement, synovitis and spondylodiscitis[11]. The results of these studies are in line with our data. Brucella sacroileitis is mostly seen in adults and may be unilateral or bilateral. Patients may present with severe pain in the sacral region. It is asymptomatic in 24% of patients. Sacroiliitis may be accompanied by osteomyelitis and abscess formation in the iliac muscle. Magnetic resonance imaging (MRI) has a high sensitivity in the diagnosis[13]. Figure 1 shows the MRI of a patient with sacroiliitis.

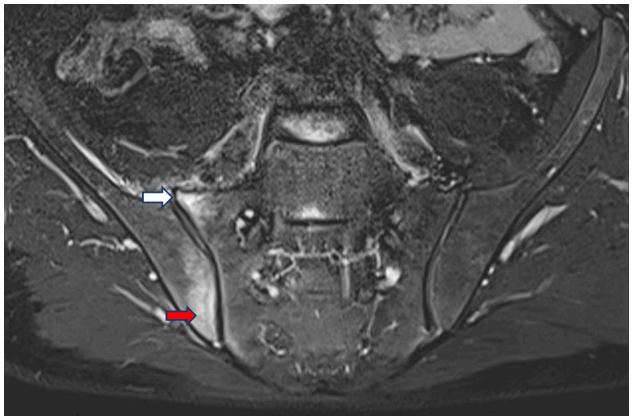

Figure 1. *Sacroiliac joint magnetic resonance image from a 38-year-old man with Brucellar sacroiliitis. Coronal T2-weighted fatsat image shows significant signal increase inferior to the iliac bone (red arrow) and superior to the sacral bone (white arrow) in the right sacroiliac joint.*

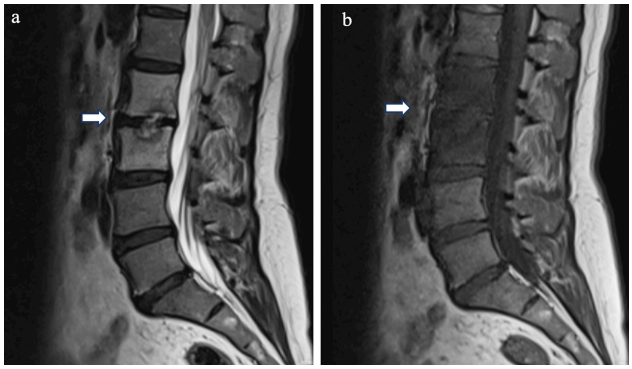

Figure 2. *Lumbar magnetic resonance images from a 47-year-old woman with Brucellar L2-L3 spondylodiscitis. T2-weighted sagittal image shows hyperintense signal intensities in L2-L3 vertebral bodies and the intervertebral disc (white arrow) (a). T1-weighted sagittal image shows homogeneous hypointensity in L2-L3 vertebral bodies and the intervertebral disc (white arrow) (b).*

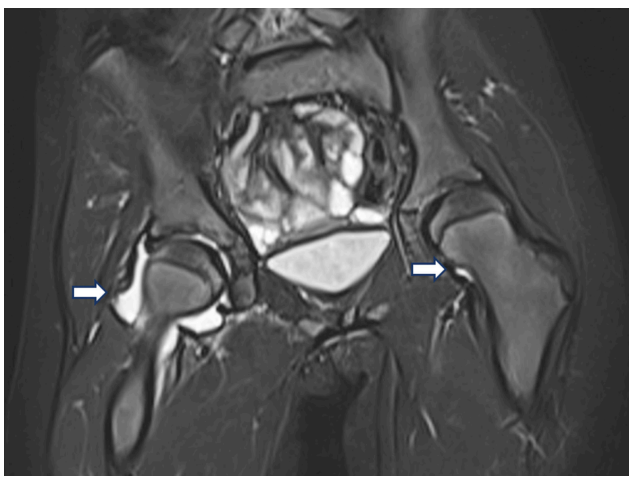

Figure 3. *Bilateral hip magnetic resonance image from a 10-year-old girl with prominent bilateral hip arthritis on the right. T2-weighted coronal image shows hyperintense areas that indicate joint effusion (white arrows).*

Spinal joints are frequently affected; the most common types of spinal involvement are spondylitis and spondylodiscitis. While patients generally complain of low back pain, radicular findings may also accompany them[8,14]. Brucella spondylodiscitis seen in our study was mostly involved in the lumbar region, followed by the thoracic region, while we did not have any cases showing cervical involvement. In the literature, similar to our data, the frequency of spondylodiscitis involvement was reported as lumbar, thoracic and cervical regions[11,15]. Although the L4-L5 segment is frequently affected, focal or multifocal involvement can be observed[7,16]. Paravertebral abscess and neurological complications may develop in cases of spondylodiscitis[17]. Due to the relatively low number of cases, we did not find any cases with paravertebral abscess, neurologic complications or involvement of the cervical region in our cases. Figure 2 shows MRI scans of a patient with spondylodiscitis.

Peripheral arthritis is a common osteoarticular involvement. The incidence of Brucella-induced arthritis ranges from 3% to 77% in various series. It may show monoarticular, oligoarticular or polyarticular distribution and may be in septic or reactive form. The peripheral joints most commonly affected by brucellosis include the knee, hip, and ankles. Shoulders, wrists, elbows, interphalangeal and sternoclavicular joints may be affected less frequently[16]. In our data, the knee joint was the most commonly affected joint, parallel to the literature. The most common type of osteoarticular involvement in children is monoarthritis. Hip and knee joints are frequently involved, and there may be accompanying osteomyelitis of the adjacent bone[13]. Among our cases, hip arthritis was present in only one pediatric patient. Difficulty in the diagnosis and treatment process can lead to serious complications such as femoral head dislocation and necrosis in hip arthritis[18]. It is important to remember it in the differential diagnosis, especially in endemic regions, to prevent possible complications and permanent disabilities. The MRI of the case in which hip arthritis was detected is shown in Figure 3.

Our data did not detect a significant correlation between laboratory parameters and the presence of arthritis, sacroiliitis, and spondylodiscitis. There were series in which acute phase reactants were found to be higher in patients with osteoarticular involvement than in those without osteoarticular involvement[11,19–21]. We found elevated CRP in 48.93% of our patients, elevated ESR in 27.65%, and anemia in 31.91%. Türkoğlu-Yilmaz et al.[22] found

elevated CRP in 91.5% and elevated ESR in 48.3% of Brucella cases. In the retrospective publications of Kiş et al.[23] CRP elevation was 39.6%; elevated ESR and anemia were detected in 32.4% and 37.8% of patients, respectively. In another study conducted in our city, CRP elevation was found in 83.3%, ESR elevation in 40%, and anemia in 51.6% of the patients[19]. These differences are due to the inclusion of only patients with osteoarticular findings in our study. It may be due to not knowing whether the patients are acute, subacute or chronic. While the analysis of osteoarticular findings in a region where Brucella infection is endemic is the strength of our study, the relatively low number of cases and the absence of a control group in the analysis of biochemical parameters are the weaknesses of our study. Another limitation is the lack of knowledge of Brucella species, which may impact clinical findings, prognosis, and treatment.

Conclusion

Physical medicine and rehabilitation outpatient clinics are typically the first point of contact for patients with musculoskeletal complaints. Brucellosis often affects the musculoskeletal system and can present with various findings. Brucella infection should be considered in the differential diagnosis to prevent potential complications through early diagnosis and treatment, especially in regions where brucellosis is endemic.

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