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Osteoarticular Involvements and Autoantibody Frequency in Patients With Brucellosis

Brusellozlu Hastalarda Osteoartiküler Tutulumlar ve Otoantikor Sıklığı

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Abstract

Introduction: Brucellosis is a chronic infectious disease with osteoarticular (OA) manifestations. It is difficult to distinguish between brucellosis and rheumatologic diseases in endemic areas. In this study, we aimed to report the clinical findings and autoantibody results of patients diagnosed with brucellosis in the rheumatology department.

Materials and Methods: In this study, 92 patients over the age of 18 with the diagnosis of "Brucellosis" were included. All patients' systemic and joint examinations were performed. In the presence of clinical signs, those with a detected value of ≥1:160 on the standard tube agglutination test were considered to be active brucellosis. Those with arthritis, arthralgia, tenosynovitis-bursitis, spondylitis/spondylodiscitis and sacroiliitis were detected on physical examination or magnetic resonance imaging, and those with low back or hip pain were recorded. Complete blood count, serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) and autoantibody; RF, anti-CCP, ANA and anti-DNA results were evaluated.

Results: The mean age of ninety-two patients (Female:54, 58.7%) was 39.3±13 years. In the OA findings respectively; arthralgia was detected with a ratio of 90.2%, arthritis with 33.7% (mono-oligoarthritis 77.4%), myalgia with 28.2%, sacroiliitis with 25% (78% active) and spondylodiscitis with 6.5%. CRP and ESR means were 19 mm/h with 2.1 mg\dL. RF was positive in 12 (13%), Anti-CCP in 5 (5.4%), ANA in 7 (7.6%) patients. There were no patients who were anti-DNA positive. The median treatment duration was 12 weeks.

Conclusion: The anti-CCP positivity rate was lower than in the literature, and the RF and ANA positivity were similar. Symmetrical involvement of small joints, higher CRP levels and high titer autoantibody positivity were at a higher risk of developing rheumatologic disease.

Keywords: Autoantibodies; brucellosis; findings; osteoarticular.

Özet

Amaç: Bruselloz, osteoartiküler (OA) bulguları olan kronik enfeksiyon hastalığıdır. Endemik bölgelerde bruselloz ve romatolojik hastalık ayrımı yapmak zordur. Bu çalışmada romatoloji bölümünde brusellla tanısı alan hastaların klinik bulgularını ve otoantikor sonuçlarını bildirmeyi amaçladık.

Gereç ve Yöntemler: Bu çalışmaya, "Bruselloz" tanılı 18 yaş üstü 92 hasta alındı. Tüm hastaların sistemik ve eklem muayeneleri yapıldı. Klinik bulgular varlığında, standart tüp aglütinasyon testi ≥1:160 saptananlar aktif bruselloz kabul edildi. Fizik muayenede veya manyetik rezonans görüntüleme ile artrit, atralji, tenosinovit-bursit, spondilit/spondilodiskit ve sakroiliit saptananlar ve bel veya kalça ağrısı olanlar kaydedildi. Tam kan sayımı, serum C-reaktif protein (CRP) ve Eritrosit sedimantasyon hızı (ESH) ve eş zamanlı yapılan otoantikor; RF, anti-CCP, ANA ve anti-DNA sonuçları değerlendirildi.

Bulgular: Doksan iki hastanın (Kadın:54, %58,7) yaş ortalaması 39,3±13 yıldı. OA bulgular; atralji %90,2, artrit %33,7 (mono-oligoartrit (%77,4), miyalji %28,2, sakroiliit %25 (%78 aktif) ve spondilodiskit %6,5 oranında saptandı. CRP ve ESH ortalamaları, 2,1 mg\dL (0-0,8) ile 19 mm/saat idi. Otoantikor profili; RF 12 (%13), Anti-CCP 5 (%5,4), ANA 7 (%7,6) hastada pozitif idi. Anti-DNA pozitif olan hasta yoktu. Ortanca tedavi süresi 12 hafta idi.

Sonuç: Anti-CCP pozitiflik oranı literatüre göre daha düşük, RF ve ANA pozitifliği ise benzerdi. Küçük eklemlerin simetrik tutulumu, daha yüksek CRP düzeyi ve yüksek titrede otoantikor pozitifliği varsa romatolojik hastalık gelişme riski yüksekti.

Anahtar Kelimeler: Bruselloz; osteoartiküler; bulgular; otoantikorlar.

Introduction

Brucellosis is a gram-negative bacterial infection with a zoonotic intracellular pathogen that is common all over the world (1). While brucellosis is still important endemically in various countries and regions around the World (Asia), many countries have brought the disease under control (2). Türkiye is one of the countries where brucellosis is endemic. Its annual incidence is per million people 262.2 in Turkey. It is still reported

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as endemic in Central Anatolia, Eastern and Southeastern Anatolia regions (3). It affects many tissues and organs, causing non-specific clinical symptoms such as high fever, night sweats, restlessness, loss of appetite, headache and muscle-joint pain, showing similarity to other infections and non-infectious diseases (4). Osteoarticular involvement is especially in the form of arthralgia-myalgia, peripheral arthritis, sacroiliitis and spondylodiscitis. Osteoarticular involvement is confused with rheumatologic diseases because they do not have specific clinics. An increase in autoimmunity occurs due to brucellosis infection. Brucellosis can cause immunologic reactions by affecting the reticuloendothelial system, producing Rheumatoid factor (RF), Anti-nuclear antibodies (ANA) and cyclic citrullinated peptide antibody (Anti-CCP) tests positive. RF low titer can be found in healthy people, and the positivity rate increases with age (2.5-17%) (5). RF is not specific to rheumatoid arthritis (RA) and it can be positive in connective tissue diseases (CTD), chronic infections, malignancies, sarcoidosis, and vasculitis (5,6). ANA may be low titer in healthy people and positive in dermatologic diseases, malignancies, infections and some medications. As its titration increases, the likelihood of autoimmune disease increases (≥1/160). However, in the European League Against Rheumatism (EULAR) / the American College of Rheumatology (ACR) 2019, ANA ≥1:80 was considered positive in the new classification criteria for SLE (7). Anti-CCP is a highly specific test for RA, with an incidence of about 1-3% in normal healthy people. However, in recent years, it has been reported that it may be positive in some infectious diseases such as pulmonary tuberculosis and FMF without joint involvement (8). Brucellosis is still an endemic disease in some parts of Turkey. It can manifest itself in a wide range of clinical signs and symptoms. The variety of clinical findings and the absence of specific findings often cause delays in the diagnosis of brucellosis. The disease becomes chronic, leading to severe damage and loss of function (9). The most common complication of brucellosis is Osteoarticular involvement and is reported in the range of 10-85% in various publications (10,11). Brucellosis can mimic rheumatologic diseases due to similarity in clinical findings, leading to misdiagnosis. Apart from its common OA involvements, brucellosis can rarely lead to a clinic similar to systemic vasculitis (12). Studies on the frequency of autoantibodies in brucellosis patients had different results. Herein, we aimed to report the follow-up data, clinical findings and autoantibody results of patients with brucellosis with Osteoarticular involvement diagnosed in the Rheumatology department around Lake Van, where brucellosis is endemic.

Materials and Methods

In this retrospective study, 92 patients with Osteoarticular involvement and whose data were fully available were included from 232 patients over the age of 18 who were diagnosed with "Brucellosis" in the Rheumatology Department between February 2014 and June 2018. Previous cases of brucellosis or chronic brucellosis are followed up with the diagnosis of rheumatologic disease, while those diagnosed with brucellosis, additional comorbid conditions, those with active/chronic infections, chronic liver disease, chronic renal failure, and malignancies were excluded from the study. Rose Bengal test was performed on all patients. Patients were diagnosed with active brucellosis in the presence of clinical signs such as fever, joint pain, joint swelling or inflammatory low back pain (LBP) with a titer of ≥1:160 by the standard tube agglutination test (STA). *Brucella* STA tests are routinely ordered for the etiology of sacroiliitis. Histories of all patients were taken; system queries and muscle-joint examinations were performed. Demographic characteristics were recorded from the hospital data system. Through physical examination or magnetic resonance imaging (MRI), patients with Osteoarticular involvement such as arthritis, arthralgia, tenosynovitis-bursitis, spondylitis/spondylodiscitis and sacroiliitis, LBP or hip pain were recorded. Complete blood count, serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) and concomitant autoantibody; RF, anti-CCP, ANA, anti-DNA results were evaluated. After completion of brucellosis treatments, seven patients were diagnosed with rheumatologic diseases according to ACR/EULAR classification criterias 5 (5.43%) RA and 2 (2.17%) primary Sjögren's syndrome (pSjS). Patients were divided into 2 groups, the first group included those with OA brucellosis who were diagnosed with arthritis-bursitis tenosynovitis-spondylitis or sacroiliitis by physical examination or imaging methods, and those who were diagnosed with rheumatologic disease in the follow-up of brucella treatment were included in the second group. These two groups were compared in terms of demographic and clinical characteristics, CRP, ESR, leukocyte, lymphocyte count, STA and autoantibody titers.

Ethical approval: In our study, written consent was obtained from all cases in accordance with the

Declaration of Helsinki. This study was approved by the Ethics Committee of Van Training and Research Hospital (Date: 05.07.2018-Decision no: 2018/11).

Table 1: Demographic characteristics of patients with brucellosis

Demographic characteristics, n:92	Result
Female, n (%)	54 (58.7)
Male	38 (41.3)
Age (year), Mean±SD	39.3±13
RF positivity (>25 IU\mL), n (%)	12 (13)
Anti-CCP positivity (>17 U/ml), n (%)	5 (5,4)
ANA positivity (≥1:100, IFA), n (%)	7 (7.6)
Anti-DNA positivity, n (%)	0 (0)
Rose Bengal test positivity, n (%)	92 (100)
Brucella STA positivity, n (%)	92 (100)
Titer, median (Min-Max)	640 (160-5120)
Leukocyte Count, (10^9/L)	
Mean±SD (Min-Max)	7037±1969 (1170-12810)
Lymphocyte Count, (10^9/L)	
Mean±SD (Min-Max)	2456±642 (1310-4540)
CRP mg\dL, (0-0.8)	
Mean (Min-Max)	2.1 (0.1-15)
ESR, mm/hour (0-25)	
Mean (Min-Max)	19.4 (1-80)

Mean± SD: Mean± Standard Deviation, **STA:** standard tube agglutination test, **RF:** Rheumatoid factor, **ANA:** Anti-Nuclear Antibodies, **CRP:** C-reactive protein, **ESR:** Erythrocyte Sedimentation Rate, **Min-Max:** Minimum-maximum,

Statistical analysis: Statistical evaluation was performed with SPSS 20.0 package program. Mean, median, standard deviation, minimum and maximum values were calculated for numerical variables and percentage ratio was given for categorical variables. Student's t-test was used for mean values between groups and chi-square test was used for categorical data. The $p<0.05$ was accepted as statistically significant in the obtained data.

Results

The mean age of 92 patients (Female: 54, 58.7%) was 39.3±13 years. All patients had positive Rose Bengal tests and STA test ≥1/160. The median serum antibody titrations of STA were 640 (160-5120). Leukocyte and lymphocyte count averages were in the normal range of 7037±1969 and 2456±642 µL. Three patients had leukopenia, 5 (5.43%) had leukocytosis, 5 (5.43%) had anemia, and 4 (4.34%) had lymphopenia. There were no patients with thrombocytopenia. The mean of CRP and ESR were 19 mm/h with 2.1 mg\dL, respectively. When the autoantibody profile is examined; RF was positive in 12 (13%), anti-CCP in 5 (5.4%), and ANA in 7 (7.6%) patients. There were no patients who were anti-DNA positive. Demographic characteristics and laboratory parameters are given in Table 1.

Osteoarticular manifestations: 83 (90.2%) patients had joint pain, 26 (28.2%) had myalgia, and 31 (33.7%) had arthritis. Distribution of arthritis: mono-oligoarthritis (1-4) and polyarthritis (≥5 joints) were divided into two groups. There were twenty-four (77.4%) patients with mono-oligoarthritis and 7 (22.6%) with polyarthritis. The most common sites of involvement were ankle 16 (17.3%), knee joint 13 (14.1%) (Table-2). When the distribution was examined, unilateral involvement of the peripheral large joints of the lower extremity was higher. There were 6 (6.5%) patients with bursitis-tendinitis. There were 37 patients (40.2%) with LBP and 10 (10.8%) patients with mechanical low back pain (MBP). LDH was detected in 17 (18.5%) patients who underwent lumbo-sacral MRI. Sacroiliac MRI was performed in 38 (41.3%) patients to show acute/active sacroiliitis, of which 18 (78.2%) were active and 5 (21.8%) were chronic, and 23 patients had sacroiliitis findings. Spondylodiscitis was detected in 6 (6.5%) patients. The most common site was L4-5 vertebrae (50%) (Table-2). Of the ninety-two patients, 66 (71.7%) had used rifampicin+doxycycline. The median duration of treatment was 12 (6-36) weeks.

Table 2: Osteoarticular findings of brucellosis

Osteoarticular findings	n (%)
Atralgia	83 (90.2)
Myalgia	26 (28.2)
Arthritis	31 (33.7)
Mono-oligoarthritis	24 (77.4)
Polyarthritis	7 (22.6)
Joint involvement locations	
Fingers	7 (7.6)
Wrist	8 (8.6)
Elbow	2 (2.1)
Shoulder	2 (2.1)
Hip	3 (3.26)
Knee	13 (14.1)
Ankle	16 (17.3)
Toe	2 (2.1)
Bursitis-Tendinitis	6 (6.5)
Spondylitis/Spondylodiscitis	6 (6.5)
Involvement locations	
L4-5	3 (50)
L3-4-5	1 (16.6)
L5-S1	2 (33.3)
Inflammatory low back pain	37 (40.2)
Mechanical low back pain	10 (10.8)
AP Pelvis X-ray	59 (64.1)
Sacroiliac MRI	38 (41.3)
Sacroiliitis (MRI)	23 (25)
Active sacroiliitis	18 (78.2)
Chronic sacroiliitis	5 (21.8)
LS-MRG	
Presence of lumbar disc herniation	17 (18.5)

LS-MRI: lumbosacral magnetic resonance imaging

Follow-up data: There were 7 patients who developed rheumatologic disease while being followed up with brucellosis. Five patients met the ACR 2010 classification criteria for RA. Two patients met the ACR/EULAR 2016 pSjS classification criteria. When these patients were examined: the first patient was a 51-year-old male with symmetrical polyarthritis of the hand joints, anti-CCP antibody level specific for RA positive at a high titer of 300 (0-17 U/ml), RF level positive at 100 (0-25 IU\mL) and ANA positive at 1/100 dilution. The second RA patient, a 42-year-old woman, had symmetrical wrist polyarthritis, was anti-CCP 49, RF negative and ANA 1/80 dilution positive. The third RA patient, a 48-year-old woman, was negative for RF and ANA, while anti-CCP was reported as suspected in low (11 U/ml) titer. She had small joints of the hand and prolonged polyarthritis and acute phase elevation. The fourth RA patient, a 42-year-old woman, was positive for high titer anti-CCP (238 U/ml) and ANA 1/1000 dilution, while RF was negative. The fifth RA patient, a 61-year-old male, had polyarthritis in the small joints of the hand and was RF negative while anti-CCP (500 U/ml) was positive at high titer and ANA 1/100 dilution. The first pSjS patient, a 27-year-old woman, was diagnosed as anti-CCP negative in the presence of polyarthritis, was strongly positive at ANA 1/1000 dilution and RF (100 IU/mL) positive, as well as having symptoms of dry mouth and eye and pSjS based on minor salivary gland biopsy. The second pSjS patient, a 38-year-old woman with polyarthritis, was anti-CCP negative, ANA 1/320 dilution positive and RF (84 IU/mL) positive. Common characteristics of the seven cases are; symmetrical retention of the small joints of the hand and the absence of sacroiliitis or spondylodiscitis. When we compared the two groups, there was no significant difference between age and sex, ESR, leukocyte and lymphocyte ($p>0.05$). The median STA antibody

Table 3: Comparison of OA brucellosis and rheumatologic disease group

Demographic characteristics and laboratory parameters	OA Brucellosis Group (n=85)	Group with rheumatic disease (n=7)	p
Gender			
Female, n (%)	49 (57.6)	5 (71.4)	0.695
Male, n (%)	36 (42.4)	2 (28.6)	
Age, year (Mean ± SD)*	38.9±13.2	44.1±10.6	0.310
CRP mg/dl (Mean ± SE)**	1.84±0.3	5.25±1.95	**0.005**
ESR mm/hour (Mean ± SE)	19.05±1.71	23.71±6.13	0.601
Leukocyte count, (10^9/L) (Mean ±SD)	7040±1977	7000±2014	0.757
Lymphocyte count (10^9/L) (Mean±SD)	2502±634	1900±495	0.59
Brucella STA titer, Median	1280	640	0.196
RF positivity, n (%)	9 (10.5)	3 (42.8)	**<0.05**
Anti-CCP positivity, n (%)	1(1.2)	4 (57.1)	**0.005**
ANA positivity, n (%)	2 (2.4)	5 (7.4)	**<0.001**
Arthritist, n (%)	24 (28.2)	7 (100)	**<0.001**
Polyarthritis, n (%)	2 (2.4)	5(71.4)	**<0.001**
Active sacroiliitis, n (%)	18 (21.2)	0 (0)	
Spondylodiscitis, n (%)	6 (7.1)	0 (0)	

Mean ± SD:** Mean± Standard Deviation,* Mean ± SE:** Mean± Standard Error, **CRP:** C-Reactive protein, **ESR:** Erythrocyte sedimentation rate, STA: Standard tube agglutination, **RF:** Rheumatoid Factor, anti-**CCP:** Anti-cyclic citrullinated peptide, **ANA:** Antinuclear antibodies, p: **P value:** Statistically significant values are shown in bold.

titer was 1280 in the OA brucellosis group, while the median STA antibody titer (640) in the rheumatologic disease group was lower (p=0.196). The mean CRP in the brucellosis group (1.84 mg/dl) was lower than the mean in the rheumatologic disease group (5.25 mg/dl), and the difference was statistically significant (p=0.005). In the group that developed rheumatologic disease, arthritis with high titer RF, ANA, anti-CCP positivity was more common, while there were no patients with active sacroiliitis and spondylodiscitis. Table 3 shows a comparison of both groups.

Discussion

In this study, we presented the data of brucellosis cases with OA involvement and their autoantibody results. Joint findings of brucellosis patients were evaluated. In particular, sustained arthritis, active sacroiliitis, and spondylitis cases were followed up by the rheumatology department. Out of 92 patients, 7 of them was diagnosed as inflammatory rheumatologic disease. According to population studies reported from different geographical regions, there are differences in the types and frequency of rheumatic symptoms and in the sites of skeletal involvement. Various factors, such as age, disease duration and types of brucellosis, can cause different symptoms of brucellosis (4,5,9). Buzgan et al. reported clinical signs and complications of 1028 adult cases of brucellosis. According to the study, the most common symptom was arthralgia (73.7%). Osteoarticular findings were detected in 25% of cases. LBP (21.2%), peripheral arthritis (14.3%), sacroiliitis (6.2%) and spondylitis (3.1%), while RF positivity 3.1% were reported in the results (11). In this study, the mean age 33.7 ±16.34 years and women's weight were similar to our study, while RF positivity and Osteoarticular findings were less. In a study by Heidari et al.,51 brucellosis patients were included and their rheumatologic symptoms were examined. Rheumatologic symptoms were observed in 94% of the patients, and the most common musculoskeletal findings (72.5%), sacroiliitis (31%), LBP (25.5%), especially peripheral arthritis (25%) and spondylitis (8%) in the form of mono-oligoarthritis involvement of the large joints of the lower extremities were detected (13). The rates of peripheral arthritis (33.7-25%), sacroiliitis (41.3-31%) and spondylitis (7.8-6.6%) in our study were similar to those in this study with similar mean gender and age. In the cohort study by Cüzdan et al., OA findings of 534 brucella patients with antibody titer of ≥1/160, a median age of 47 years and among which 207 (38.8%) were female, were reported as polyarthralgia 324 (60.7%), myalgia 172 (32.2%), LBP 69 (12.9%), peripheral arthritis 46 (8.6%), bursitis 19 (3.6%), spondylitis 41

Table 4: Autoantibody studies in patients with brucellosis

Series, years and n	RF, %	Anti-CCP, %	ANA, %	Anti-DNA, %
Kısacık, 2013 (113)	8.8	11.5	NA*	NA
Gökhan, 2013 (62)	12.9	**20.9**	**12.9**	NA
Ahmadinejad, 2016 (49)	**30.6**	16.3	8.2	**2**
Cüzdan, 2023 (514)**	8.8	11.7	15	NA
This study, (92)	13	5.4	7.6	0

*** NA**: data not available, ******Patients with Brucella STA titer ≥ 160. **n:** number of patients,
Highest values are given in bold.

(7.7%), and sacroiliitis 13 (2.4%). Peripheral arthritis was mostly seen in the mono-articular (87.0%) and knee joint (59.3%). Spondylodiscitis (6.0%) and L4-5 (26.8%) of the vertebrae have been reported to be most commonly involved (14). The mean age of our series was lower (39.3 years) and the female gender (58.7%) was higher. Among our cases, 83 (90.2%) had arthralgia, 26 (28.2%) had myalgia, and 31 (33.7%) had arthritis. The majority of arthritis was asymmetrical mono-oligoarthritis (77.4%), most commonly involving the ankle (17.3%) and then the knee joint (14.1%). Sacroiliitis was present in 23 (25%) patients and the majority of them were active sacroiliitis (78.2%). There were 6 (6.5%) patients with spondylodiscitis and the most common was L4-5 (50%) spinal involvement. Thirty-seven (40.2%) patients had LBP. In this study, the frequency of arthritis and sacroiliitis was low. In our series, one in 3 patients had arthritis. This situation can be explained by the fact that the admission to the rheumatology department. Akkoç et al. evaluated 185 pediatric brucellosis patients and reported Osteoarticular findings in 94 (50.8%) patients. The most common osteoarticular finding is; Peripheral arthritis was reported as sacroiliitis in 62 (78.8%) and 31 (33%) patients. Most commonly peripheral arthritis; hip joint 46 (63.9%) and knee joint 22 (30.6%) were involved. Spinal brucellosis was reported in seven (7.4%) patients (15). Joint involvements, contrary to our series and literature, may be mostly due to MRI of the hip joint and bilateral involvement. The hip joint is difficult to detect with a physical examination or USG. However, the cases of sacroiliitis and spinal brucella were similar to our series. The autoantibody was not given in this study. Brucellosis is known to trigger immunological reactions, producing autoantibodies. RF positivity in patients with brucellosis depends on the production of different antibodies and their cross-reactions with RF (5,14). Therefore, treatment of patients with subacute OA brucella with only antibody positivity and misdiagnosis of rheumatologic disease may worsen clinical symptoms and prognosis (5). So far, the most data have been related to RF and ANA, while in the last 10 years, anti-CCP has been added to these antibodies. Anti-DNA has been less studied. In our study, four antibodies were evaluated simultaneously. In a study by Ahmadinejad et al.; 49 brucellosis patients were included and positive values were detected for RF 15 (30.6%), ANA 4 (8.2%), anti-DNA 1 (2%), and anti-CCP 8 (16.3%) in the patients (5). Only RF was found to be significantly different from the control group. Patients with antibody positivity did not meet the rheumatologic diseases classification criteria. In our series, although there were more brucellosis patients, the frequency of RF and anti-CCP was lower and the ANA positivity was similar. We did not detect any anti-DNA positive patients. In this study, 76% of localized brucellosis cases had musculoskeletal involvement. Although OA brucellosis treatments take an average of 6-12 weeks, this period is longer in spinal brucellosis cases (10). Since the musculoskeletal findings were pronounced, the median duration of treatment (12 weeks) was high. In our patients with spondylodiscitis, this period was 29 weeks (24-36) on average. In his study, Kısacık et al. recruited 113 brucellosis patients and compared RF and anti-CCP, RA and healthy controls. Although positive in RF 10 (8.8%) and anti-CCP 13 (11.5%) patients, they were not different from the healthy control group (16). When the musculoskeletal involvements of brucellosis were examined, arthralgia was detected in 20 (17.6%) patients, while on the contrary, arthritis was reported in 74 (65.4%) patients. While mono-oligoarthritis was predominant in the distribution of arthritis, polyarthritis was present in 7 cases. The most commonly involved joints are; lower limbs and unilateral knee, ankle and hip joints. These data are similar to our series. In a study by Gökhan et al.; In 62 brucella cases with peripheral arthritis, anti-CCP was positive in 20.9%, RF and ANA were positive in 12.9%, and all anti-CCP positivity was negative after 12 weeks of treatment (17). In the results of the study by Cüzdan et al., RF 24

(8.8%), anti-CCP 14 (11.7%) and ANA 9 (15%) were detected as positive (14). While RF and anti-CCP were higher than the control group, there was no difference in ANA results. Of our 92 cases, 12 (13%) were positive for RF, 5 (5.4%) for anti-CCP and 7 (7.6%) for ANA. While the RF ratio was high, the anti-CCP and ANA ratio was found to be lower. The summary of the studies reporting autoantibody outcomes in brucellosis patients is given in Table-4. Autoantibody positivity is reported at different rates in patients with brucellosis. These rates vary according to years and regions, disease stages and age group, or only the characteristics of the selected group. While the presence of follow-up data in our study, the diagnosis of rheumatologic diseases in the follow-up of some brucellosis patients with OA involvement are positive aspects of our study. However, are the two diseases a coexistence or the development of rheumatologic diseases triggered by brucellosis? Large-scale prospective studies are needed to answer these questions.

Study limitations: The fact that the number of patients was relatively low, and the absence of antibody results in brucellosis patients and healthy individuals without joint findings were the limitations of our study.

Conclusion

According to our study, brucellosis patients with OA findings had a higher risk of developing rheumatologic disease if they had symmetrical small joint involvement, higher CRP level and high titer autoantibody positivity. Brucellosis can mimic rheumatologic diseases. High titer anti-CCP positivity can be used for discrimination. In the differential diagnosis of rheumatologic diseases, brucellosis should be considered in endemic regions.

Ethical approval: This study was approved by the Ethics Committee of Van Training and Research Hospital (Date: 05.07.2018-Decision no: 2018/11).

Conflict of interest: There is no conflict of interest.

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Author contributions: Concept (FY), Design (FY), Data Collection and/or Processing (FY), Analysis and/or Interpretation (FY).

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