

Brucellar Epididymo-Orchitis: A Retrospective Study

Brusella Epididimo-Orşiti: Retrospektif Çalışma

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Objectives: Epididymo-orchitis is a focal form of human brucellosis described in 2-20% of patients with brucellosis.

Patients and Methods: In this retrospective study, the records of 190 adult male patients (mean age 27.5 years; range 17 to 71 years) with brucellosis were evaluated. Ten of these cases presented with epididymo-orchitis. Among these cases, epididymitis or epididymo-orchitis were diagnosed on the basis of a typical history of gradual onset of scrotal pain and findings of enlarged tender testes and/or epididymis.

Results: The most common symptoms were fever, scrotal pain, and swelling (100%). There were different focal Brucellar involvements other than the epididymo-orchitis in eight patients (80%). All of the patients had unilateral epididymo-orchitis. A testicular abscess was detected in one patient. Combined antibiotic therapy was started and continued for 6-8 weeks. Orchiectomy was required for one patient (10%) and granulomatous orchitis was detected in the resected specimens. Relapse was not observed in any patient.

Conclusion: Brucellosis should be considered in the diagnosis of scrotal diseases in endemic areas. Clinical and serological data are sufficient for the diagnosis. Conservative management combined with antibiotic therapy is adequate for managing brucellar epididymo-orchitis.

Key words: Brucellosis epididymo-orchitis.

Amaç: Epididimo-orşit brusellozlu hastaların %2-20'sinde tanımlanan insan brusellozunun fokal bir formudur.

Hastalar ve Yöntemler: Bu çalışmada, brusellozlu 190 erişkin erkek hastanın (ort. yaş 27.5; dağılım 17-71) kayıtları retrospektif olarak incelendi. On hastada epididimo-orşit saptandı. Bu olgulara, yavaş yavaş ortaya çıkan skrotal ağrı öyküsü, testiste ve/veya epididimde hassasiyet ve büyüme gibi hastalığa ait tipik belirtilere dayanarak göre epididimit veya epididimo-orşit tanısı kondu.

Bulgular: En yaygın görülen semptomlar ateş, skrotal ağrı ve şişlik idi (%100). Sekiz hastada (%80) epididimo-orşitten başka farklı fokal hastalıklar da saptandı. Epididimo-orşit, hastaların hepsinde tek taraflı idi. Bir hastada testiküler abse saptandı. Kombine antibiyotik tedavisi başlandı ve 6-8 hafta süreyle kullanıldı. Hastaların birinde (%10) orşektomiye ihtiyaç duyuldu. Alınan örnekte granülomatöz orşit saptandı. Hiçbir hastada relaps gözlenmedi.

Sonuç: Bruselloz endemik olan bölgelerde görülen skrotal hastalıkların tanısında akılda bulundurulmalıdır. Tanıda klinik ve serolojik veriler yeterlidir. Antibiyotik tedavi ile birlikte yapılan konservatif tedavi brusella epididimo-orşitinin tedavisi için yeterlidir.

Anahtar sözcükler: Brusella epididimo-orşiti.

Brucellosis, which is also known as Mediterranean or Malta fever, is an endemic enzootic disease.^[1] In many parts of the world, including the Mediterranean countries and Middle East, Brucellosis constitutes a major health and economic problem.^[2,3] Recently, new brucellar infections in south and central Europe have been reported to be imported from the Mediterranean basin, and approximately 500,000 new cases of brucellosis are reported annually throughout the world, but it is estimated that only 4% of the cases are recognized.^[4]

Brucella spp. is transmitted through the gastrointestinal tract after consumption of contaminated meat or milk and its products, through direct contact with infected tissues, blood or lymph of infected or injured skin, through the respiratory system after inhalation in microbiological laboratories, and through the conjunctivae.^[5] The most frequent complications of Brucellosis are bone and joint lesions, hepatosplenomegaly, lymphadenopathy, endocarditis and meningoencephalitis. Overall, the complications of brucellosis are attributed to the involvement of many systems. In men, various genitourinary infections including epididymo-orchitis, prostatitis, testicular abscess and seminal vesiculitis have been attributed to brucellosis.^[6] The most frequent genitourinary complication of brucellosis is epididymo-orchitis.^[7,8] Brucellar epididymo-orchitis (BEO) is a focal complication of the human brucellosis and has been described in 2-20% of the patients with brucellosis.^[9]

In the present study, we retrospectively analyzed the epidemiologic, clinical and laboratory findings, treatment and outcome of epididymo-orchitis due to *Brucella melitensis* infection.

PATIENTS AND METHODS

This study was conducted retrospectively in the Gülhane Military Medical Academy, Department of Infectious Diseases and Clinical Microbiology between January 1997 and August 2008. The records were reviewed for all adult patients with brucellosis who presented with epididymitis or epididymo-orchitis.

Blood samples were cultured by use of an automated culture system (Organon Tecnica BacT/Alert 460 bioMérieux, France) and incubated for 30 days. All isolates were identified as recommended by Hausler et al.^[10]

Standard tube agglutination testing, the Rose Bengal test, and the Coombs test for antibodies to *Brucella* species were performed according to standard methods.^[11] A positive blood culture or high agglutination titers of $1 \geq 160$ and positive clinical manifestations of brucellosis (e.g., orchitis and fever, sweating, arthralgia, hepatomegaly, splenomegaly, signs of focal disease) were accepted as the main criteria for diagnosing brucellosis.^[12,13]

Among these patients with brucellosis, the diagnosis of epididymitis or epididymo-orchitis was based on clinical symptoms (scrotal swelling, pain or tenderness) and by ultrasonographic examination.^[14]

RESULTS

During the 11-year period, 190 male patients (median age 26 years; range 17 to 71 years) with brucellosis were detected in our department. Ten of the cases had epididymo-orchitis (5.2%). The investigation of seasonal distribution revealed a predominance of patients to spring and summer.

Eight of 10 BEO patients were in the 21-30 years of age interval and the remaining two cases were over 30 years of age. The median age was 24. A total of five patients (50%) lived in rural areas; six (60%) had consumed unpasteurized dairy products, which is a risk factor for brucellosis, and four (40%) presented occupational exposure.

The onset of symptoms was acute (≤ 1 month) in four patients (60%) and subacute or chronic (≥ 4 months) in six patients (60%). The time from onset of symptoms to diagnosis of epididymo-orchitis was 7-240 days (median, 45 days). For two patients (20%), the diagnosis of brucellosis and orchitis were made almost simultaneously. One patient (10%) was diagnosed with brucellosis and two weeks later orchitis was obvious. Seven patients (70%) were diagnosed as orchitis

Table 1. Other concordant focal diseases in eight patients with BEO

Focal disease	n	%
Osteoarticular involvement	3	30
Sacroileitis	2	20
Peripheral arthritis	2	20
Hepatitis*	1	10

*Alanin aminotransferase ≥ 50 IU/L

1-12 months before the detection of brucellar infection. We found different focal brucellar involvements other than the epididymo-orchitis in eight patients (80%; Table 1). The symptoms reported at presentation are shown in Table 2. None of the patients was asymptomatic.

Scrotal pain and swelling, fever, sweating were the most common symptoms. In four patients (40%), the fever was continuous. Three patients (30%) presented with undulant fever. Laboratory findings in patients with BEO were shown in Table 3.

Cultures of blood specimens from five (50%) of 10 patients with epididymo-orchitis were positive for *Brucella* species. Blood cultures were positive for two patients whose standard tube agglutination tests were measured very high ($\geq 1:160$) titers. All of five patients with negative blood cultures had received antibiotic therapy previously. There was no record of anemia. All patients received combined antibiotic therapy, which is presented in Table 4. Duration of therapy varied according to clinical response

Table 3. Laboratory findings in patients with BEO

Laboratory data	n	%
CRP >5 mg/dl	10	100
Mean CRP, mg/dl	49	
ESR >20 mm/h	8	80
Mean ESR, mm/h	38	
ALT >40 IU/l	1	10
ALP >150 IU/l	2	20
WBC $>10.5 \times 10^9/l$	3	18
Platelets $<150 \times 10^9/l$	3	18
Positive Rose Bengal test	10	100
Positive Wright agglutination ($\geq 1:160$)	10	100
Positive Coombs Test	4	40

Table 2. Characteristics of patients with BEO

Findings	n	%
Scrotal pain and swelling	10	100
Fever (temperature, $\geq 38^\circ\text{C}$)	10	100
Sweating	8	80
Scrotal redness	5	50
Arthralgia	4	40
Hepatosplenomegaly	4	40
Weight loss	3	30
Dysuria	3	30
Anorexia	2	20
Abdominal pain	1	10
Vomiting	1	10

Note: Some patients had >1 signs and symptoms

and the presence of focal disease other than epididymo-orchitis.

Ultrasonography was performed in 10 patients. According to ultrasonographic examination, all of the patients had unilateral involvement of epididymis and testes. Bilateral involvement was not seen in any patient. Enlargement and hypoechoic echo texture were detected in the affected testes and epididymis. Orchiectomy was required in one patient. This patient had a testicular abscess and pathological examination revealed necrotizing granulomatous orchitis. Relapse did not occur in any patient. All patients improved with therapy; the fever subsided in 2-5 days and there was local regression of the scrotal enlargement and decreased tenderness. The median (range) duration of hospital stay was 7 (4-14) days. Only two patients (20%) had a hospital stay of longer than 10 days. The follow-up at 3-month intervals did not show any relapse in our patients.

DISCUSSION

Brucellosis remains an important clinical problem worldwide, and needs to be highlighted as a continuing cause of morbidity in southern Europe and in many developing countries. In parallel, epididymo-orchitis is a common clinical entity in medical practice, and inappropriate management may result in serious complications such as testicular abscess, atrophy and male infertility.^[15]

Table 4. Therapeutic protocols of the patients with BEO

Patients	DOXY 2X100 mg/day + RIF 1X600 mg/day (peroral six weeks)	DOXY 2X100 mg/day + STREPTO 1 gr/day (IM three weeks)
BEO (Orchiectomy) (n=1)	Once	Once
BEO + Sacroilitis (n=2)		
1st case	Twice	Once
2nd case	Twice	Once
BEO + Osteoarticular involvement (n=3)		
1st case	Twice	Once
2nd case	Twice	
3rd case	Twice	
Others patients (n=4)		Once

DOXY: Doxycycline; RIF: Rifampicin; STREPTO: Streptomycin; IM: Intramuscular.

Brucellosis is an endemic disease in Turkey. The seropositivity rate in the healthy population in all geographical regions of Turkey is between 2-6%.^[16] Incidences of human brucellosis in some Mediterranean countries such as Greece and Spain where the true incidence for BEO is meant to be 12% and 2-20% respectively are high.^[9,17] In a study from Saudi Arabia, the incidence was noted as 1.6%.^[7] Presentation of the brucellosis as BEO is not a common finding. In the present study, BEO occurred in 5.2% of male patients with brucellosis. In the literature, the incidence of BEO in Turkey was noted between 2-12.7%.^[18-20] The demographic as well as clinical characteristics of the patients in this study were similar to those of groups of patients with BEO described elsewhere,^[21-24] and most patients in this cohort had risk factors for brucellosis.

In this study, the age of the BEO patients was relatively young (median age 24). In other studies, patients with BEO were also found to be young.^[6,7,9,22,25] This study suggests that the development of BEO in systemic brucellosis is more frequently seen in younger patients.

In one study, it was suggested that the onset of brucellar epididymo-orchitis was mostly insidious.^[21] In some other reports, patients with epididymo-orchitis generally had acute onset, although that was the case only in four of our patients.^[9,26] However, an acute, subacute and chronic classification seems to be uninformed

time periods and they may overlap according to our data.

CRP levels were also significantly higher in these patients. This is probably associated with the acute onset of the disease. Abnormal blood test results are usually mild and nonspecific. No severe blood leukocytosis was present. The hemoglobin level may be lower as a result of prolonged infection, and a moderately elevated ESR is found in most cases. Liver function tests disclose a mild to moderate increase in the hepatic transaminase serum levels.^[27] The abnormalities in liver function tests may be caused by the liver involvement.^[25] The disturbances in liver function tests were found only in one case in our study.

Urinary tract symptoms were present in 30% of the patients in our cases. Similarly, urinary tract symptoms were reported at a lower rate in other studies.^[7,22] In all of these studies, urine analysis and urine cultures were normal in most of the patients, which was also the case in our study.

All patients had unilateral involvement and all of them had epididymo-orchitis. These results were compatible with the literature.^[7,21,22] Ultrasonography plays an important role in the diagnosis, assessment, and management of patients with BEO. Granulomatous lesions of the testis result from a group of illnesses that are clinically and pathologically similar. Because

granulomatous inflammation can be associated with focal necrosis, clinical and ultrasonographic findings resemble those seen in testicular tumors. In patients with focal hypoechoic lesions in the testis seen on ultrasonography, orchiectomy is usually performed.^[28,29] Orchiectomy was required in one patient. This patient had a testicular abscess and was unresponsive to the therapy. Pathological examination revealed necrotizing granulomatous orchitis. In the literature, orchiectomy is usually reserved for cases unresponsive to antibiotics, or with a suspicion of testicular abscess or tumor.^[22,25,30] Radical orchiectomy is not recommended on the basis of sonographic findings alone, but in patients with focal hypoechoic testicular lesions that are suspected of being neoplasm.^[30] An unnecessary orchiectomy could be prevented as a consequence.

We found different focal involvement other than the epididymo-orchitis in eight patients (80%). The most common symptoms were scrotal pain and swelling. Fever was detected in more than half of the patients. These symptoms were reported as the most frequent symptoms of BEO in the literature.^[7,21,22]

Human brucellosis continues to pose a therapeutic problem because of the intracellular localization of the *Brucella* within the host's reticulo-endothelial cells, a site relatively inaccessible to antibiotics. Inappropriate choice, dosage and length of antimicrobial therapy, failure of patients to take prescribed drugs and, very rarely, antibiotic-resistant *Brucella* strains are associated with unpredictable relapses after treatment.^[31] Hence, the institution of a proper combination of antibiotics for longer periods is warranted to improve the outcome and prevent relapses. In the present study, use of combined therapy resulted in a steady improvement, subsiding of fever in 2-5 days, and regression of scrotal enlargement and tenderness. In the present study, none of patient relapsed during the follow-up. In other studies, rifampicin plus doxycycline or doxycycline plus streptomycin combinations were usually preferred for the treatment of BEO and the treatment continued for at least six weeks.^[6,7,21,22] In most of these studies, cases of relapse or failure

with antibiotic therapy were low and most of the patients improved.

In conclusion, brucellosis is still a public health problem in countries where the infection is endemic. Brucellar epididymo-orchitis should be a consideration in the differential diagnosis of patients presenting with signs and symptoms of this entity in endemic areas of brucellosis. A conservative approach with administration of combined antibiotic therapy is usually adequate for managing BEO. The eradication of brucellosis in animals is the key to human prevention. An organized national brucellosis control program to eradicate the disease has long been in use in Turkey.

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