



Brucella Epididymo-Orchitis: An Evaluation of Eight Cases

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Abstract

Aim: In this study, clinical properties and treatment outcomes of 8 patients with unilateral epididymo-orchitis are evaluated.

Material and Methods: A total of 8 cases were diagnosed with brucella induced epididymo-orchitis at the Urology and Infectious Diseases Clinics of Mus State Hospital within a period of 15 months. All related demographic data, clinical and laboratory findings, treatment progress and outcomes of these patients were evaluated, and the patients were followed for one year. The results obtained were statistically evaluated.

Results: The mean age of the patients was 46.12 years (ranging between 20 and 58 years). The infection involvement was in the left side in five patients and in the right in three patients. All patients had applied to practitioners with acutely developing scrotal edema and pain. Systemic fever was detected in 6 (%75) patients, and *Brucella spp.* developed in the blood cultures of two patients. Wright agglutination test was positive in all cases. The Doppler USG examination conducted displayed epididymal cyst in two patients and testicular abscess in one. All 8 patients received antimicrobial treatment of streptomycin 1g/day for 21 days, and tetracycline 2x100mg and rifampisin 600mg/day for 6 weeks. One of the patients developed relapse due to low adherence to the treatment.

Conclusion: In the endemic areas, brucella epididymo-orchitis must be considered in the possible diagnosis of the patients who apply with acutely developing scrotal pain and edema. Early diagnosis will prevent unwanted surgical interventions and complications such as infertility.

Key Words: Brucellosis; Epididymo-Orchitis; Urogenital Infections.

Brusella Epididimoorşiti: Sekiz Olgunun Değerlendirilmesi

Özet

Amaç: Bu çalışmada, bruselloza bağlı tek taraflı gelişen epididimoorşit olgularının klinik özellikleri ve tedavi sonuçlarının irdelenmesi amaçlanmıştır.

Gereç ve Yöntemler: Muş Devlet Hastanesi'nde 15 ay boyunca Üroloji ve Enfeksiyon Hastalıkları klinikleri tarafından tanı konulan 8 brusella epididimoorşit olgusu çalışmaya alındı. Hasta bilgileri, klinik ve laboratuvar verileri, tedavi protokolleri ve uygulanmış tedavi sonuçları incelendi. Hastalar bir yıl boyunca takip edildi. Elde edilen verilerin istatistiksel analizleri yapıldı.

Bulgular: Hastaların yaş ortalaması 46,12 (20-58) yıl idi. Beş hastada sol, üç hastada ise sağ testiste tutulum saptandı. Hastaların hepsi akut gelişen skrotal ödem ve ağrı şikayeti ile başvurmuştu. Altı (%75) hastada sistemik ateş bulgusu olup iki hastanın kan kültüründe *Brucella spp.* üremesi saptandı. Tüm hastalarda Wright aglütinasyon testi pozitif bulundu. Doppler USG incelemesinde iki hastada epididim kisti ve bir hastada da testiküler abse formasyonu saptandı. Hastalara 21 gün süreyle streptomisin 1gr/gün ve 6 hafta boyunca tetrasiklin 2x100mg ve rifampisin 600mg dozunda tedavi verildi. Bir olguda tedaviye uyum sorunundan dolayı relaps gelişti. Tüm hastalar verilen medikal tedavi başarılı oldu. Hiçbir hastada brusellaya bağlı komplikasyon gelişmedi ve cerrahi tedaviye gereksinim duyulmadı.

Sonuç: Brusellanın endemik olduğu bölgelerde akut gelişen skrotal ağrı ve şişlik ile başvuran hastalarda brusella epididimoorşiti ayırıcı tanıda düşünülmelidir. Doğru tanının erkenden konulması istenmeyen cerrahi girişimleri ve oluşabilecek infertilite gibi komplikasyonları önleyebilecektir.

Anahtar Kelimeler: Bruselloz; Epididimoorşit; Ürogenital İnfeksiyonlar.

INTRODUCTION

Though endemic in the Mediterranean basin brucellosis is a zoonosis that can be seen in almost all the world (1,2). Its seropositivity rate in the population has been reported to be 1.8% (3). In Turkey, it is more common in the Eastern Anatolia and Southeastern Anatolia regions (4). *Brucella spp.* is usually transmitted to humans through the consumption of contaminated animal products, their direct contact with skin or mucosa that is exposed to abrasion, ingestion, or inhalation. The bacteria enter the body, infect reticuloendothelial

system tissues, and cause clinical symptoms (4). Brucellosis is a systemic infection that can involve many organs. It most commonly effects the musculoskeletal system, however, the endocardium central nervous system involvement can also be observed. The second most common influence of the disease is on the genitourinary system (by 2-14%). In men, the disease usually exposes itself in the form of prostatitis, testicular abscess, seminal vasculitis, pyelonephritis, cystitis, and renal abscess; still the most widespread symptom in men is unilateral epididymo-orchitis (5, 6). If this type of involvement is not diagnosed early or if it is inadequately treated, it can give rise to serious complications such as

necrotizing orchitis and infertility in men; nevertheless brucellosis is major cause in acquired infertility. Therefore, brucellosis related epididymo-orchitis patients and their clinical characteristics should be determined adequately in order to plan the treatment and approaches (7-9).

In this study, our goal is to present clinical characteristics and treatment outcomes of 8 brucella spp. induced unilateral epididymo-orchitis cases in the light of literature.

MATERIALS AND METHODS

We have concentrated on 8 male patients who had been admitted to Mus State Hospital Urology Department in 2013. All 8 patients were hospitalised with a diagnosis of unilateral epididymo-orchitis due to brucella spp. We have recorded all the data about the patients, their clinical symptoms, physical examination findings, laboratory results, treatment protocols, and the results of treatment.

The diagnosis of epididymo-orchitis was done by getting patients' medical histories, from physical examination findings and laboratory tests, and applying radiological imaging methods (scrotal colour Doppler ultrasound). To ensure the epididymo-orchitis diagnosis, we applied tests like blood count, serum biochemistry, CRP, erythrocyte sedimentation rate, blood and urine cultures, and serum agglutination for brucellosis (Rose Bengal and Wright's agglutination). Those patients whose epididymo-orchitis could not be explained with other factors and who had Brucella spp. productivity in their blood cultures and significant positive values in their agglutination tests ($\geq 1/160$ titre in standard serum agglutination test for brucellosis) were defined as brucellosis-induced epididymo-orchitis cases.

After the diagnosis, we sent the patients to infectious diseases clinic and started a 6-week brucellosis-targeted treatment of streptomycin 1x1 g/day IM (for the first 21 days) with doxycycline PO (2x100 mg/day for 6 weeks) and rifampicin PO (1x 600 mg/day for 6 weeks). Acute symptoms remitted, the patients were discharged and

called to the outpatient clinic for monitoring every two weeks. Routine tests were repeated during the visits and all clinical symptoms were recorded. Having completed their six-weeks treatment, the patients were monitored on a monthly basis in the first three months and every three months in the next nine months, corresponding to an overall follow-up of one year.

RESULTS

Diagnosed with epididymo-orchitis, the 8 patients had a mean age of 46.12 years (20-58 years). 1 of the patients (12.5%) had had brucellosis prior to this with an insufficient (in terms of duration) and irregular treatment history. 2 of our patients (25%) were from the rural areas while 3 (37.5%) patients lived on stockbreeding. All 8 patients (100%) had consumed unpasteurised milk and dairy products. In addition, 1 of our patients (12.5%) had cystitis (dysuria, pollakiuria, etc.) while another (12.5%) underwent urological intervention (ESWL) in the last month; we could not determine any other factors in the remaining 6 patients (75%).

All of the patients visited a doctor with complaints of scrotal pain and swelling. Six patients (75%) showed signs of serious fever. Again, all patients had complaints like weakness, fatigue, and joint pain (back pain, hip pain, leg pain, etc.).

In all patients, the serum brucella Wright agglutination test was positive in favor of active infection. Their standard tube agglutination values were between 1/320 and 1/2560. Two of the patients (25%) had Brucella spp. productivity in their blood cultures. However, no bacteria was observed in their urine cultures.

All the patients showed unilateral involvement in Scrotal Doppler ultrasonography. 5 (62.5%) patients had involvement in the left testes and 3 (37.5%) had involvement in the right testes. Apart from the epididymo-orchitis findings, one of the patients (12.5%) had signs of a tumour or abscess formation, 3 (37.5%) patients had varicocele, 2 (25%) patients had hydrocele, and 2 (25%) patients had giant ependymal cyst symptoms.

Table 1. Scrotal Doppler ultrasound findings, microbiological data, and the details of the follow-up treatment.

| AGE | STA (titre) | Blood Culture | Doppler USG (side) | Accompanying findings (EO+)* | Treatment Duration | Treatment Complications | STA* (first month) | STA* (third month) |
|-----|-------------|---------------|--------------------|--|--------------------|----------------------------------|--------------------|--------------------|
| 37 | 1/640 | none | Left | none | 6 weeks | none | 1/40 | 1/40 |
| 58 | 1/1280 | Brusella spp | Left | Right hydrocele + suspected giant ependymal cyst | 6 weeks | Hearing loss | 1/20 | (-) |
| 20 | 1/1280 | none | Left | Abscess on the left, suspected tumour | 6 months | leucopenia | 1/320 | 1/640 |
| 58 | 1/1280 | Sterile | Right | Left varicocele | 6 weeks | nausea, vomiting, abdominal pain | 1/40 | 1/80 |
| 47 | 1/320 | CNS* | Right | Left varicocele | 6 weeks | none | 1/80 | 1/20 |
| 39 | 1/320 | none | Left | none | 6 weeks | none | 1/40 | (-) |
| 26 | 1/2560 | Brusella spp | Left | Giant ependymal cyst on the right | 8 weeks | none | 1/80 | 1/80 |
| 25 | 1/320 | Sterile | Right | Left varicocele | 6 weeks | none | (-) | (-) |

*EO: epididymo-orchitis, STA: Standard tube agglutination, CNS: Coagulase negative staphylococcus.

After the treatment, the clinical improvement that has been observed throughout was confirmed by the agglutination conducted in the follow-up tests for all the patients. The results of the scrotal Doppler ultrasound test, that had been performed for all patients during the admission control, were normal for all our patients, too. We did not observe abscess formation in any of the patients during or after the treatment; we did not feel the need for scrotal surgery, either. On the seventh day of the specific treatment (5th through 10th days), all the epididymo-orchitis findings were improved. We have presented the Scrotal Doppler ultrasound findings, the related microbiological data, and the details of the follow-up treatment in Table 1.

DISCUSSION

Brucellosis may involve many organs and systems. As an infectious disease with different clinical spectrum, osteoarticular involvement is quite common in brucellosis (1,2). Genitourinary system involvement occurs relatively rarely; epididymo-orchitis has been reported to occur with a frequency percentage of 2%-14% in males (6,7). After the testicular involvement of the bacteria, there develops granulomatous inflammation in the testis along with focal necrosis. Either the testes themselves or epididymis are infiltrated by lymphocytes and plasma cells in addition to a possible atrophy development in the seminiferous tubules. Brucellosis induced acute testicular involvement can be distinguished by tuberculosis, trauma, malignancy, and other infective, post-operative or idiopathic causes (8, 10).

The brucellosis related epididymo-orchitis usually comes up unilaterally with acute or chronic symptoms (2, 11, 12). The disease can be differentiated from other infectious reasons by a history of unpasteurised milk and dairy products consumption, long-lasting complaints, not responding to conventional treatments, presence of typical accompanying clinical symptoms such as high fever, fatigue, joint pain, the presence of minimal local inflammation, and, generally, the absence of lower urinary tract symptoms (13).

The most critical processes in patients with brucella epididymo-orchitis is the early final diagnosis of brucellosis. Otherwise, the risk of permanent complications due to infection increases (7). There are studies in the literature that report testicular abscess development followed by orchiectomy intervention in late diagnosis, incorrect and inappropriate treatment of brucellosis (14). Colmenero et al. state that permanent complications due to brucella are significantly higher in developing countries because doctors do not know brucellosis very well and delay the diagnosis and specific treatment of brucellosis. The most important of these complications is male infertility (15).

Clinical recognition of the patient's history and physical examination findings are very important in brucella epididymo-orchitis cases. Systemic brucellosis symptoms like undulant fever and arthralgia generally accompany

unilateral epididymo-orchitis involvement in physical examination. The urine analysis results are generally within the normal range and urine culture for general uropathogens is negative (2, 11, 12). Therefore urine culture may be insufficient in diagnosing genitourinary brucellosis. The reason why brucellosis may not be visible in urine culture is often due to poor microbiological techniques (7). The urine cultures in our study were all sterile. To find out about brucellosis induced testicular involvement, it is quite useful to use stained scrotal Doppler ultrasound and Brucella agglutination tests along with blood cultures (16, 18).

In this study, we have evaluated 8 cases that have been diagnosed with brucella epididymo-orchitis and have been treated in about 15 months. Analysing the medical history of our patients, it is remarkable to see that all the patients were mostly middle-aged people. All the presenting symptoms of our patients were acute symptoms (≤ 30 days) parallel to those in Khan et al. (8) and Akıncı et al.'s (19) data. We could not detect any seasonal variation between the patients' application times though complaint start times and the duration between the start of the complaints and clinic visits were similar with an average of five (3-7) days. One of the patients had previously been diagnosed with brucellosis though he had not been fully treated. In the period before the emergence of symptoms of the disease, all of our patients shared a history of milk and milk products (provided by the farms around the region) consumption. Again, as the physical examinations showed, all the patients had applied to the clinic due to scrotal pain and swelling. Six of these patients had presented with high fever. Because of the findings mentioned above in addition to the fact that the patients did not respond to nonspecific antibiotic treatment and that Muş is an endemic region as far as brucellosis is concerned, brucellosis epididymo-orchitis was the first option we evaluated in the differential diagnosis.

Studies suggest that leukocytosis at the time of the first application to hospitals cannot be a decisive laboratory finding indicating brucellosis (20). Similarly, because leukocytosis is detected in only 10% of patients with brucellosis epididymo-orchitis, this finding can help practitioners in distinguishing the disease from other infective causes (21). Having observed leukocytosis in only two of our eight patients (25%), we think that the assumption is a suggestive idea. Moderate anemia and leukopenia that often accompany brucellosis are among other hematologic findings for the disease. Pancytopenia and thrombocytopenia, on the other hand, are rarely observed (22). Three of the patients presented in our study (37.5%) had anemia and these cases were evaluated in favor of chronic disease anaemia. One of our patients (12.5%) developed leukopenia in the second week of the treatment, but this situation was resolved spontaneously in the following weeks. However, no thrombocytopenia was observed in our patients; serum biochemical parameters were within normal limits, too.

The sensitivity of blood culture is approximately 50% and it come to an end in approximately 1-3 weeks. Studies report that the dominant factor in blood cultures in about half of brucellosis epididymo-orchitis patients is isolated (15). *Brucella* spp. productivity was positive in the blood cultures of two patients (25%) in our study (Table 1). It is also reported that microorganisms can be isolated in the material collected through epididymal aspiration, which is an additional test to blood cultures (7). We did not perform epididymal aspiration in our study even though we studied the urine cultures, which were all negative.

The most helpful method for an accurate diagnosis of brucellosis is serum brucellosis agglutination tests (1-3). Throughout our study, all eight brucellosis epididymo-orchitis cases showed positive results in standard agglutination tests; the reaction to the Wright agglutination test was also in high titer (Table 1). Doppler ultrasound is useful in the diagnosis but its actual use is to support clinical diagnosis and help differentiate abscesses, torsion, and tumours (23).

A combined antibiotics treatment for at least 6-8 weeks is generally sufficient in treating brucellosis epididymo-orchitis. Rifampicin or doxycycline and streptomycin combinations are commonly used (7, 21). Almost all the studies on the treatment protocols for brucellosis epididymo-orchitis are limited series with a small number of cases. Therefore, the present treatment plans for these patients have not been fully standardised. The general opinion that offers the traditional brucellosis therapy for these patients is usually regarded to be appropriate (6, 7). However, in spite of adequate and appropriate treatment for brucellosis epididymo-orchitis, the relapse rate is about 10% (24). In their brucellosis epididymo-orchitis series of 13 cases, Afsar et al. (25) have administered orchiectomy for two of their patients having seen that the patients have not responded to doxycycline and rifampin therapy. Kadıköy et al. (26) have cured 16 cases of brucellosis epididymo-orchitis with the same combination and have detected relapse in only 2 patients. In a series of 59 patients, Navarro and Martinez (7) have tried different treatment modalities such as doxycycline and an aminoglycoside (in 39 patients), doxycycline combined with high-dose rifampicin (1x900 mg/day) (in 10 patients), tmp/SMX and rifampicin (in 7 patients), and mp/SMX and high-dose rifampicin (1x900 mg/day) (in 3 patients). However they were unable to get clinical response in five patients and they had to apply abscess drainage (for 2 patients) or orchiectomy (for 3 patients). Skalsky et al. (27) claim that a triple combination of aminoglycosides, doxycycline, and rifampicin therapy may be more effective in patients with brucellosis epididymo-orchitis.

In our study, we also administered a triple combination therapy of streptomycin 1g/day IM for the first 21 days followed by doxycycline (200 mg/day) and rifampicin (600 mg/day) for 6 weeks. One of our patients (12.5%) developed severe nausea, vomiting and abdominal pain due to the doxycycline therapy in the first week of treatment but the symptoms disappeared after the

symptomatic treatment we started without interrupting the medication. One of the patients (12.5%) stated that he had hearing loss on the 19th day of the streptomycin 1g/day IM therapy and was given a hearing test. Presuming that the drug use was the cause, the streptomycin treatment was cut and the current treatment continued with the other two drugs. Another patient (12.5%) developed leukopenia during the follow-up treatment, but he recovered spontaneously without any interruption of the drug treatment; the patient returned to normal after the fifth week. The combined therapy we conducted gave complete clinical response in six patients. In one of the patients we observed weakness, fatigue and joint pain after the six-week treatment. For this patient we extended the treatment and discontinued the drugs at the end of the eight week due to signs of clinical recovery. We think that in only one of the patients the disease relapsed because at the end of six-month treatment, he still had ongoing fatigue and joint pain. The Wright test and serum tube agglutination titre was 1/640 in this particular patient.

Brucellosis is still an endemic disease in certain geographic areas including Turkey. In these areas, brucellosis epididymo-orchitis should be taken into consideration in patients with an acute onset of scrotal pain, swelling, and tenderness. This will save time in commencing the appropriate treatment. Late or incorrect diagnosis and treatment may results in testicular abscess, atrophy, or infertility. For that reason the genitourinary system examination of each patient must be carried out with care.

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