Journal of Microbiology, Immunology and Infection (2016) xx, 1–6

Available online at www.sciencedirect.com
ScienceDirect
journal homepage: www.e-jmii.com

ORIGINAL ARTICLE

Testicular infection in brucellosis: Report of 34 cases

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Received 20 August 2015; received in revised form 9 November 2015; accepted 1 February 2016
Available online ■ ■ ■

KEYWORDS
brucellosis;
epididymitis;
orchitis;
relapse;
treatment

Abstract *Background/Purpose:* To present clinical and laboratory features, treatment options, and outcome in patients with brucellar testicular infection and to compare them with analogous in brucellar patients without testicular involvement.
Methods: Thirty four brucellar patients with testicular infection treated in two general hospitals in the Republic of Macedonia, during the period 1998–2009, were retrospectively analyzed. Their clinical and laboratory characteristics were compared with analogous in 364 male brucellar patients without testicular infection, who were treated at the same hospitals during the same time period.
Results: Brucellar testicular infection was evident in 34 (8.5%) out of 398 male patients with brucellosis. The median age of the patients was 46.5 years. In all patients testicular involvement was presented as an acute form with a median duration of 5 days (range, 2–14 days) prior to diagnosis. Twenty-three of the patients had at least one other simultaneous focal infection. After starting with the treatment testicular infection lasted a median 10 days, range 7–21 days. Brucellar patients with testicular infection when compared with other brucellar patients more frequently manifested fever (97% vs. 61%), concomitant spondylitis (32% vs. 16%), and urinary system involvement (12% vs. 2%). Also, the relapse rate in patients with testicular involvement was significantly higher (24% vs. 9%).
Conclusion: In endemic regions brucellosis should be taken into consideration in any patient with testicular infection. Brucellar testicular involvement is usually characterized with a severe acute clinical presentation and a high percentage of relapses which entails the need of timely recognition and proper treatment duration of at least 60 days.

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http://dx.doi.org/10.1016/j.jmii.2016.02.004

Please cite this article in press as: Bosilkovski M, et al., Testicular infection in brucellosis: Report of 34 cases, Journal of Microbiology, Immunology and Infection (2016), http://dx.doi.org/10.1016/j.jmii.2016.02.004

Introduction

Human brucellosis is a zoonosis that is characterized by a wide clinical heterogeneity affecting different systems of the human body. Genitourinary involvement is among the commonest focal manifestations of human brucellosis,[1–4] presented as epididymo-orchitis, prostatitis, cystitis, interstitial nephritis, pyelonephritis, immunoglobulin A nephropathy, exudative glomerulonephritis, and renal and testicular abscess.[5,6] Brucellar epididymo-orchitis (BEO), by far the commonest genitourinary manifestation, was described for the first time by Hardy in 1928[7] and Wainwright in 1929.[8] This focal manifestation is a result of urine *Brucella* removal or as a blood-borne septic metastasis.[9–11] Clinical presentation of BEO is most frequently acute,[6,11–14] rarely subacute[10,15,16] or chronic.[6,15] BEO may cause complications like necrotizing orchitis,[5,17,18] testicular abscess,[11,15,19] infarction,[17,20] atrophy,[21] and suppurative necrosis.[17,20] Also, cases with aspermia and infertility have been described.[11,14,15]

Characteristics and prognosis of BEO have been described in many studies and communications, but comprising a small number of patients.[13,22–24] This clinical entity is also rarely presented in studies related to the Balkan Peninsula,[10,11] a region where brucellosis is considered to be an endemic disease. In this retrospective study we attempted to present the main demographic, clinical, and laboratory features, therapeutical experiences and outcome in patients with brucellar testicular infection in the Republic of Macedonia as an endemic region and to compare them with analogous in brucellar patients without testicular involvement.

Methods

The medical records and follow-up protocols of 34 brucellar patients with testicular infection treated at the Departments for Infectious Diseases in Veles and Bitola, Republic of Macedonia, during the period 1998–2009, were retrospectively analyzed. Their clinical and laboratory features were compared with analogous in 364 male brucellar patients, 18 years or older, without testicular infection that were treated at the same hospitals during the same period. The study was approved by the Ethics Committee of the Medical Faculty in Skopje, Republic of Macedonia.

The diagnosis of brucellosis was based on clinical findings compatible with brucellosis, supported by detection of specific antibodies at significant titers and/or demonstration of at least a fourfold rise in antibody titer in serum samples obtained 3–4 weeks apart. Antibody titers were determined by the standard tube agglutination, Brucella Coombs, and/or Brucellacapt assays as previously described.[25,26]

All of the patients underwent standard diagnostic protocol including detailed history, physical examination, and laboratory analysis—erythrocyte sedimentation rate, C-reactive protein, hemoglobin, white blood cells, lymphocytes, platelets, urine analysis, alanine aminotransferase, and serological tests for brucellosis. Patients were treated with various antimicrobial combinations that contained two or three of the following antimicrobials: oral doxycycline 100–200 mg/d; oral rifampin, 900 mg/d; oral trimethoprim/sulfamethoxazole (co-trimoxazole) 960 mg twice daily; and intramuscular gentamicin, 5 mg/kg/d. Gentamicin was administered 7–14 days, and the other drugs were given 45 days or longer if spondylitis, brucellosis of the central nervous system or therapeutic failure was evident. After finishing the treatment all patients were followed-up clinically and serologically every other month during the first 3 months, and every 3–4 months afterwards.

The investigated patients were divided into two groups: with ($n = 34$) and without ($n = 364$) testicular infection. The comparisons were performed in terms of the demographic and epidemiological data, clinical manifestations, laboratory characteristics, and outcome. Orchitis and epididymitis were diagnosed by the presence of acute scrotal pain, swelling and tender scrotal, and/or epididymal enlargement which were associated with the first episode of the actual disease and could not be attributed to other causes. Duration of testicular infection was defined as the number of days that elapsed from the start of treatment until the disappearance of all inflammatory signs. Relapse was accepted as the reappearance of symptoms and signs after the antibrucellar treatment was completed and therapeutical failure as persistence of symptoms and signs of the disease for more than 45 days of antibiotic therapy initiation.

The Chi-square test or Fisher's exact test (when Chi-square could not be applied) were used for comparison of qualitative variables between the groups. For quantitative variables Mann–Whitney *U* test was performed. A *p*-value of < 0.05 was considered significant.

Results

Among 398 male patients with brucellosis that were treated during the analyzed period at the Departments for Infectious Diseases in Veles and Bitola, 34 (8.5%) had testicular involvement. Besides orchitis and/or epididymitis, 23 of the patients had other coexisting focal forms of brucellosis: 13 peripheral arthritis; 11 spondylitis; three sacroiliitis; three radiculitis; three cystitis; two respiratory; two gastrointestinal; and one each of bursitis, tendinitis, and pyelonephritis (some of the patients had more than 1 simultaneous focal form). Out of the patients with brucellar testicular infection 21 manifested orchitis, 12 epididymo-orchitis, and one patient had epididymitis. Their distribution is presented in Table 1.

Testicular infection was the only manifestation of the disease in four patients, and in 30 other patients besides testicular, other symptoms and signs attributable to brucellosis e.g., fever, sweating, arthralgia, headache, loss of appetite, backache, malaise, hepatomegaly, splenomegaly, and osteoarticular involvement were also present. In three patients testicular manifestations appeared parallel with the general signs and symptoms; in one patient they were preceding them, whereas in the remaining 26 patients testicular infection appeared after initiation of brucellosis. In all cases the clinical presentation was acute and the brucellar etiology of testicular symptoms and signs

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