Case Report

Exceptionally high titres in atypical presentation of occult epididymo-orchitis due to brucellosis

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A male patient of 32 years was referred for surgical drainage and orchidectomy of the right testis following a cycling injury. A Veneral Disease Research Laboratory (VDRL) test was requested by the surgery department to rule out secondary syphilis. Although serum samples gave a negative result in the VDRL test, qualitative screening was performed for Brucella antibodies, as per hospital policy, since brucellosis is endemic in this region. Following a positive reaction, a quantitative standard tube agglutination test was carried out yielding titres that were exceptionally high (STAT = 40,960 IU ml⁻¹; 2-ME = 1 : 5,120). This finding correlated with the patient's history which included a number of predisposing factors for contracting brucellosis including exposure to cattle, consumption of raw milk and assisting in the parturition of cattle. Consequently, surgery was postponed and treatment was changed from injections of ceftriaxone to the WHO regimen for the treatment of brucellosis: 1 g streptomycin once daily, administered intra-muscularly, plus 100 mg doxycycline twice daily, taken orally. Following 3 days of this treatment, the testicular swelling reduced considerably and orchidectomy was not required. Indeed, after a week, swelling was completely resolved and the patient was discharged. To our knowledge, this is the first case of such high titres in a patient as a result of epididymo-orchitis without the typical clinical presentation of fever and joint pain that is normally associated with brucellosis.

Case report

A 32-year-old male patient was admitted to the surgery department with a swelling of 5 cm in size in the right testis, which was acquired 7 days earlier due to blunt trauma to the previously normal testis, which occurred while cycling. The patient was afebrile and the swelling was associated with severe pain at the time of admission. The patient was a non-vegetarian, non-smoker and non-alcoholic with no elicitable history of mumps, sexually transmitted diseases, drug allergy or swelling of the testis prior to this incident. The patient was found to have no joint pain, organomegaly, deformities of limbs or rashes of the skin and there were no abnormal findings after examination of the respiratory, cardiovascular and central nervous systems.

Local examination revealed a swelling of 5 × 4 cm in size on the right side of the scrotum with pus discharging from an opening in the draining part of the swelling. Firm, tender and mobile lymph nodes were palpable in the right inguinal region. Differential diagnoses of haematoma, tuberculous orchitis, mumps orchitis and secondary syphilis were made. The haematological and blood biochemistry parameters were within normal ranges and ultrasonography of the testis demonstrated an enlarged right testis (5.0 × 4.0 × 4.0 cm), showing a heterogeneous echo texture with multiple hypoechogenic areas along with a collection of thick extratesticular fluid measuring 3.4 × 2.0 cm. The left testis was normal in size (3.9 × 2.3 × 1.8 cm) and showed a homogeneous echo-texture. A serum sample was sent to the serology section of the microbiology department for Veneral Disease Research Laboratory (VDRL) testing to rule out secondary syphilis. The patient was prescribed 1 g ceftriaxone, twice daily, via intravenous injection but as no favourable response was obtained, the patient was then referred for surgical drainage and orchidectomy.

Since brucellosis is endemic in this region, our department follows a policy to screen all the serum samples for Brucella by using a slide agglutination test using Rose Bengal Antigen, which is an 8 % suspension of pure killed cells of smooth Brucella abortus strain 99, which is phenolized, stained with Rose Bengal dye and buffered at pH 3.65 using lactic acid buffer. Therefore, despite being negative in VDRL tests and not showing any of the typical symptoms of brucellosis, the patient’s serum was subjected to slide agglutination test for Brucella antibodies where it elicited a strong positive reaction necessitating a subsequent standard tube agglutination test (STAT) to provide a quantitative...
estimation of the antibodies. The antigen used for the STAT was a suspension of pure culture of smooth *Brucella abortus* strain 99 in phenol saline, obtained from the Division of Biological Products, Indian Veterinary Research Institute (IVRI), which is the nodal agency and prepares antigens in accordance with the international reportage system as per the guidelines of the Veterinary Services Laboratories, Ames, Iowa, USA, and the FAO/WHO Collaborative Centre for Brucellosis, VLA Central Veterinary Laboratory, New Haw, Weybridge, Surrey, England. The slide agglutination test and STAT were performed according to the protocol provided by the IVRI. The end titres obtained in the STAT were 40 960 IU ml\(^{-1}\) and 1:5210 in 2-mercaptoethanol (2-ME), which was performed in parallel to the STAT to derive the IgG component of the total antibody titre obtained with phenol saline (2-ME dissolves the disulfide bonds between IgM molecules, thus agglutination observed in 2-ME tubes is due to IgG antibodies only). The presence of very high IgG titres along with significantly high IgM antibody titres (derived by difference of titres obtained in the STAT and the 2-ME test) suggested acute exacerbation of chronic brucellosis. These findings were immediately conveyed to the surgery department where blood and pus samples were collected from the scrotal wound (Fig. 1) and used to inoculate two sets of brain heart infusion biphasic medium collected from the scrotal wound (Fig. 1) and used to inoculate two sets of brain heart infusion biphasic medium.

The patient was interviewed regarding his lifestyle in the context of potential exposure to risk factors for brucellosis. The patient was found to be a farmer residing in an area that is endemic for brucellosis and provided a very significant history of exposure to cattle, consumption of unboiled milk and assisting in parturitions of cattle, all of which are strong risk factors for contracting brucellosis. Following the serology reports, the surgery was deferred, ceftriaxone injections were desisted and the patient was administered injections of 1 g streptomycin once daily, administered intramuscularly, and 100 mg doxycycline tablets twice daily, taken orally, for 6 weeks as per the WHO recommended regimen for the treatment of brucellosis. The patient responded favourably to this drug regimen and within 3 days the swelling reduced considerably with complete resolution of pus, leading to closure and healing of the pus-discharging opening within a week. Surgical intervention and orchidectomy were not needed.

Blood cultures remained sterile, even after 6 weeks of incubation, but growth was observed on the fourteenth day of incubation from cultures of the pus sample taken from the scrotal wound inoculated in biphasic medium. The culture was identified as *Brucella melitensis* by Gram staining and standard biochemical reactions. The evidence, including growth of *Brucella* from pus samples, positive serology and excellent response to *Brucella*-specific therapy, established that the aetiological agent of this case of epididymo-orchitis was *Brucella*.

**Discussion**

Human brucellosis is a zoonotic disease endemic in South-East Asia, Mediterranean countries, the Arabian Gulf, Latin America, Asia, parts of Mexico, the Indian sub-continent and other developing countries. According to the WHO fact sheet, half a million new cases of brucellosis are reported every year worldwide (WHO, 1997), and it is estimated that for every case of human brucellosis that is diagnosed, four cases are missed (Radolf, 1994). Together, these figures suggest the disease is a significant problem and its prevalence may be linked to cases of human brucellosis where exacerbation of acute illness is followed by long symptom-free remission periods. Testicular lesions due to *Brucella* can be seen in 2–21 % of male patients (Patil et al., 1986; Forbes et al., 1954). However occult epididymo-orchitis with antibody titres of 40 960 IU ml\(^{-1}\) in an apparently healthy person with an absence of fever and joint pain or any other symptoms that are typical of brucellosis, has, to our knowledge, never been reported in scientific literature.

The patient was in the remission phase of brucellosis which is evident from presence of significantly high IgG titres in the absence of any typical symptoms. *Brucella* infection has been known to involve the testis (Colmenero et al., 1996) and because the scrotal injury in this patient was not an open wound to begin with, the source of the *Brucella* in the pus had to be endogenous. In our opinion, the focal presentation of the disease, in form of testicular abscess in this patient, was probably precipitated by the blunt trauma to the scrotum, due to the forceful impact of a central steel bar of a bicycle, resulting in a breach of the anatomical layers of testis and subsequent collection of thick extratesticular fluid in the right testis, from which *Brucella melitensis* was isolated in the culture.

Serological diagnostic methods are the mainstay of diagnosis of brucellosis, especially in culture-negative cases, but

**Fig. 1.** Photograph showing the pus-discharging opening on the scrotum of the patient.

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*IVRI*: Indian Veterinary Research Institute

*WHO*: World Health Organization

*STAT*: Slide agglutination test

*2-ME*: 2-mercaptoethanol

*IVRI*: Indian Veterinary Research Institute
one-time estimation of titres (especially if they are <160 IU ml<sup>-1</sup>) are not considered definitive, especially in areas endemic for brucellosis. Molecular techniques, if available, play an important role in providing the confirmatory evidence (Morata et al., 2001; Romero et al., 1995) but in cases where these methods are unavailable, primary isolation of <i>Brucella</i> in culture is still the conventional gold standard. In the present case, we attempted culture from both blood and pus samples, of which only the pus sample yielded growth of <i>Brucella</i>. Blood culture was negative in this case, which may be because of intermittent bacteraemia and variable culture yields, ranging from 15 to 60%, that are known to occur in brucellosis testing (Yagupsky, 1999); blood cultures can also be negative in localized infections such as the presence of localized lesions only, which was the case in this patient.

<i>Brucella</i> has been isolated from sperm (Vandercam et al., 1990) and banked spermatozoa samples (Corbel, 2006) and there are few reports of probable transmission of <i>Brucella</i> via a sexual route (Goossens et al., 1983; Stantic-Pavlinic et al., 1983; Ruben et al., 1991; Lindberg & Larsson, 1991), but this is yet to be proved conclusively. The patient in this case report had been married for 5 years and there was no conception during the last 3 years despite regular sexual activity with his wife and the couple was not using any contraceptive measures. We wanted to explore the possibility of <i>Brucella</i> being a cause of secondary infertility in this case but the patient refused to provide his sperm sample for analysis and also declined the examination of his wife despite our persuasions and assurance of complete confidentiality.

**Conclusion**

We would have missed this very unusual presentation of epididymo-orchitis caused by <i>Brucella</i> infection if the department did not have a policy to screen for this endemic bacterium. The existence of the easy-to-perform, rapid, sensitive and economical slide agglutination test has enabled our department to adopt this policy, and as shown here, has been invaluable given the diverse presentations of <i>Brucella</i> infection.

**References**


