CORRESPONDENCE

Brucella epididymo-orchitis relapsing three times despite treatment

Brucellosis is a chronic multi-systemic epizoonotic infection that may involve a variety of tissues and organs. Genitourinary complications are not infrequent (2–10% of patients with brucellosis may be affected) and include epididymo-orchitis, pyelonephritis, glomerulonephritis, interstitial nephritis, oophoritis, and abortion. The incidence of epididymo-orchitis in brucellosis ranges from 1.6% to 12.7% according to the recent medical literature.\textsuperscript{1–4} Brucella epididymo-orchitis generally occurs in the subacute phase of the infection and usually requires prolonged therapy lasting for at least six weeks.\textsuperscript{1,2,4} Despite the tendency of Brucella species to cause illness with frequent relapses, more than two episodes of relapse is rare. We report herein the triple relapse of epididymo-orchitis in the same testis in a sexually active young man, despite favorable treatment.

A 33-year-old man was admitted to the hospital with a four-week history of high fever, chills, and profuse night sweats. His history was otherwise unremarkable and physical examination showed a fever of 37.5°C and pulse rate of 80/min; he appeared sick and in pain. Initial blood tests showed a white blood cell count (WBC) of 3.9 \times 10^9/l with a differential of 49% lymphocytes, 43% neutrophils, and 8% monocytes. The erythrocyte sedimentation rate (ESR) was 24 mm/h, CRP 42 mg/l (normal: <5 mg/l), AST 58 U/l (within the normal range), and ALT 74 U/l (levels twice the normal). The standard Brucella tube agglutination test (STA) was positive at a titer of 1:640. Specific antibiotic therapy for brucellosis was started with rifampin (600 mg/day) plus doxycycline (200 mg/day), for six weeks. Brucella spp was also recovered from his blood cultures; the antibiotic susceptibility test was not performed.

Within one week of treatment, enlargement and tenderness had developed on the left scrotum. Ultrasonography of the scrotum revealed unilateral left epididymo-orchitis and a moderate hypoechoic area was detected. This was considered as focal orchitis. Testicular elevation was applied according to the urological recommendation. At the end of antimicrobial therapy, his fever and scrotal swelling resolved and STA decreased to 1:160. One month later he was readmitted to the hospital with fever and left testis tenderness. STA was positive at a titer of 1:320 and left epididymo-orchitis was again detected in the scrotal ultrasonography. Considering this a relapse of brucellosis, we started him on a further six-week treatment with rifampin plus doxycycline. At the end of the treatment the Brucella STA had decreased to 1:160, and ESR and CRP had returned to normal levels. Unfortunately, one month later the patient was readmitted to our hospital with the same complaints as before (high fever, left scrotal pain and tenderness). Scrotal ultrasonography revealed the same findings and the Brucella STA had increased to a titer of 1:640. Repeated blood cultures were negative. A search for focal involvement was started for any abscess formation in other parts of the body, and magnetic resonance imaging (MRI) showed thoracic spondylitis in the T10–11 space. We added trimethoprim–sulfamethoxazole to doxycycline plus ciprofloxacin for Brucella spondylitis and epididymo-orchitis, and the duration of therapy was extended to three months. As a result of the treatment, the Brucella STA returned to 1:80 after two months and to 1:40 at the end of the fourth month, and the patient’s signs and symptoms were all resolved. On the final follow-up visit after six months he was all well.

Epididymo-orchitis is the most common and abrupt genitourinary complication of brucellosis. In reported cases, the relapse rates of epididymo-orchitis in areas where the disease is endemic show regional differences. For instance, while Akinci et al.\textsuperscript{4} and Memish and Venkatesh\textsuperscript{1} reported a very low relapse rate from Central Anatolia, Turkey, Navarro-Martinez et al.\textsuperscript{5} reported a significantly high rate (25%) from Spain. In these serial reports, the exact duration of treatment and effective combinations of antimicrobials were not clearly stated.

In this case, the patient who had received rifampin plus doxycycline treatment previously at two different times was admitted for a third time with recurrence of the same side epididymo-orchitis due to brucellosis. We did not think this a compliance problem (though it is possible), because his adherence to treatment was good at the hospital, and after discharge the records on his drug card supported compliance. Although there are some studies showing a high relapse rate with this combination and failure of treatment of genitourinary brucellosis, in other studies no significant differences were found between different treatment combinations.\textsuperscript{6–8} As clearly seen in our patient (Figure 1), the CRP levels surging up and down and serological fluctuations are indicative of the relapses.
The failure of cure of epididymo-orchitis with doxycycline plus rifampin combination was interesting. The triple relapse in our case may indicate that this combination is not an adequate choice for therapy when this tissue is involved or that there may be a resistance to one or both of the drugs. On the other hand, a period of six weeks may not be sufficient for treatment. For similar patients referred to our institution, it is essential to obtain an adequate level of combined antibiotics in the testicular tissue to resolve the inflammation rapidly and save the organ from necrotizing orchitis that usually requires orchiectomy. In conclusion, multiple relapses in patients with Brucella epididymo-orchitis should suggest other organ involvement such as osteoarticular tissue sources or associated brucellar bacteremia or necrotizing orchitis; such phenomena must carefully be considered.

Conflict of interest: No conflict of interest to declare.

References


**Cervical cancer vaccine in Pakistan: let’s start thinking**

Khan et al. have very meticulously demonstrated an almost synonymous seropositivity of human papilloma virus 16 (HPV16) among cervical cancer patients in Pakistan.¹ The results call for immediate measures to be taken by the health authorities in the country, and the suggested connotation regarding a regular HPV screening of Pakistani women is verily justified. However, I believe that the implications of this finding should not be limited to a regular general population HPV screening only.

Cervical cancer remains one of the most common malignancies among women around the globe and is the second leading cause of cancer-related death among women.² Strong religious and cultural constraints have so far prevented a cervical cancer epidemic in Pakistan, with the incidence in the female population much lower than breast and ovarian cancers.³,⁴ However, with the loosening of cultural boundaries, this may not hold true in a couple of decades time. Lately, it has been suggested that HPV may have a causal association with anal, vulvar, and oropharyngeal cancers as well.⁵

Khan and co-workers’ elucidated finding that HPV serotype 16 is responsible for almost all cases of cervical cancer in Pakistan, implies a lot more than just general population HPV screening. Two commercial vaccines that cover HPV16 manufactured by Merck and GlaxoSmithKline have undergone successful advanced clinical trials in the USA.²,⁶ Moreover, it has been shown that vaccination against certain viral proteins of HPV16 induces an anti-viral response that neutralizes across all known strains of HPV.⁷ Owing to the success of the vaccines, the American Cancer Society now recommends a routine HPV vaccination for females aged 11–12 years.⁸ An overwhelming seropositivity of HPV16 among cervical cancer patients in Pakistan indicates that preventing the infection of HPV16 by applying the vaccination strategy could substantially reduce the incidence of the malignancy in this country.

It is true that the cost–utility of the suggested wide-population HPV vaccination is yet to be gauged. It does, however, stand out as a strategy that health authorities in Pakistan and other developing countries should seriously consider in the near future, if not now.

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**References**


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