

Brucella Prostatitis: A First Case Report Diagnosed in Korea

Seong Yeol Ryu · Hyun Ah Kim
Jiyoung Park¹ · Misun Choe¹
Kunyoung Kwon¹

Departments of Internal Medicine and
¹Pathology, Keimyung University School of
Medicine, Daegu, Korea

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Corresponding Author

Misun Choe, M.D.
Department of Pathology, Keimyung University
School of Medicine, 56 Dalseong-ro, Jung-gu,
Daegu 700-712, Korea
Tel: +82-53-580-3815
Fax: +82-53-580-3823
E-mail: msc@dsmc.or.kr

Brucellosis is a zoonosis caused by several species of *Brucella*. Brucellosis is usually an acute or sub-acute febrile illness that histologically develops granulomatous inflammation. *Brucella* prostatitis is a very rare complication and is usually accompanied by epididymo-orchitis. We now report a case of histologically proven granulomatous prostatitis due to *Brucella* without clinical evidence of epididymo-orchitis. A 61-year-old farmer presented with myalgia, low back pain, and fever. A needle biopsy of the prostate was performed due to symptoms of urinary frequency and high prostate specific antigen levels (17.3 ng/mL). Histologically, the prostate showed granulomatous inflammation without caseous necrosis. Polymerase chain reaction (PCR) studies of blood and prostatic tissue for *Brucella* were positive, while a PCR study for *Mycobacterium tuberculosis* was negative. The patient was treated with doxycycline and rifampin. A possibility of *Brucella* prostatitis should be considered in the differential diagnosis of granulomatous prostatitis or prostatitis of unknown origin associated with or without epididymo-orchitis.

Key Words: *Brucella*; Prostatitis; Granuloma

Globally, brucellosis is the commonest zoonotic disease with annual new occurrence of 500,000. It is an important cause of travel-associated morbidity.¹ It is prevalent in countries of the Mediterranean basin, the near east, central Asia, South America, and sub-Saharan Africa.¹ In Korea, brucellosis was classified as a type 3 notifiable disease in the Communicable Disease Prevention Act in 2000. The first documented case of human brucellosis in Korea was reported in 2002.² Since then, the incidence of human brucellosis has drastically increased with a peak in 2006 and has subsequently been decreasing.³ The outbreak of human brucellosis was concurrent with a drastic increase of bovine brucellosis in Korea.^{4,5}

Brucellosis usually presents with an acute or sub-acute febrile illness and histologically develops granulomatous inflammation.⁶ Many systems, including skeletal, genitourinary, gastrointestinal, cardiovascular, hematopoietic, nervous, pulmonary, and cutaneous systems, may be involved as a complication. In men, genitourinary localization is reported in 2-20% of cases.^{7,8} Unilateral epididymo-orchitis is the usual manifestation of genitourinary involvement and prostatitis is a very rare complication. To the best of our knowledge, no cases of prostatitis by *Brucella* have been reported in Korea. We now report a case of biopsy-proven granulomatous prostatitis by *Brucella* without evidence of epididymo-orchitis.

CASE REPORT

A previously healthy 61-year-old stockbreeder presented with myalgia, low back pain and fever for ten days. Two weeks previously, he had three *Brucella* infected-cattle killed. On physical examination, he had a 37.9°C fever and findings were otherwise unremarkable. No tenderness or swelling was observed in the scrotum. Laboratory findings including urinalysis were within normal ranges. Radiologic examination of the lumbar-spine under the impression of brucellosis spondylitis was unremarkable. After admission, he complained of aggravated urinary frequency and his serum prostate specific antigen (PSA) level was high (17.3 ng/mL). An ultrasonogram of the prostate revealed benign prostatic hyperplasia (32 g) and several hypochoic lesions. Needle biopsy of the prostate was performed under the impression of malignancy. On histologic examination, the prostatic tissue showed granulomatous prostatitis without caseous necrosis (Fig. 1). The granuloma was composed of epithelioid histiocytes and surrounding lymphocytes with scattered multinucleated giant cells (Fig. 2). Some granulomas were centered on the acini, obscuring the epithelia (Fig. 3). Special staining including periodic acid-Schiff, Gomori methenamine silver and Ziehl-Neelsen stain revealed no organisms. The standard tube agglutination tests for *Brucella* were negative (1:40 during acute phase

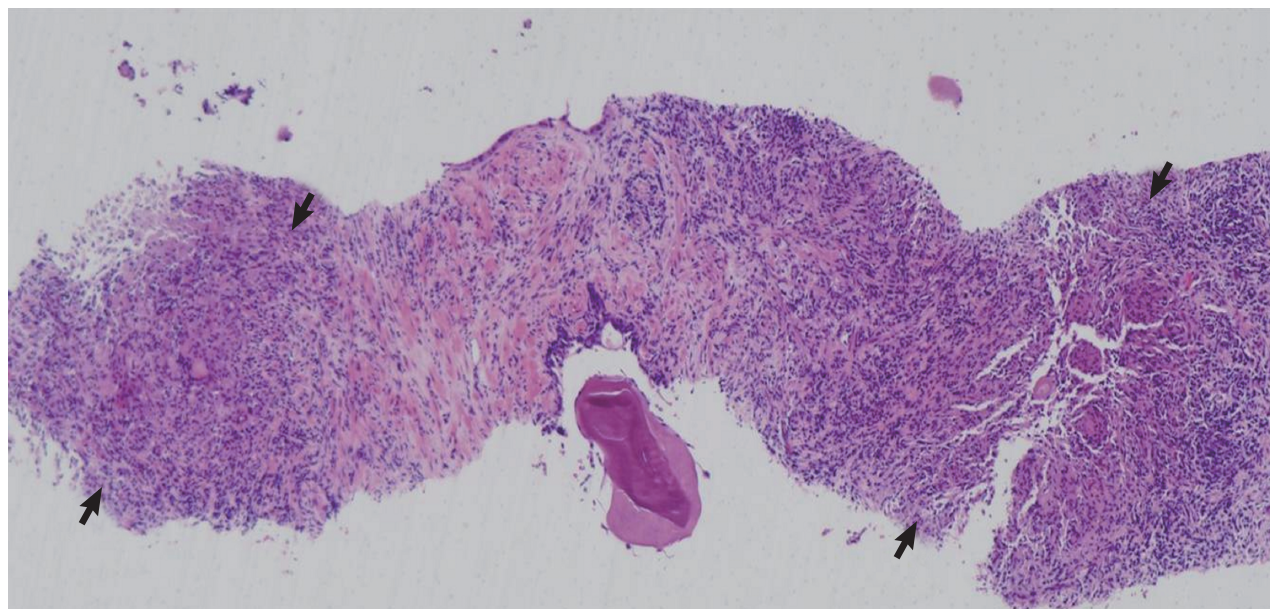


Fig. 1. Histologically, the prostate shows granulomatous prostatitis without caseous necrosis (arrows). Neoplastic lesions are not associated. No organisms are found on Gomori methenamine silver, Ziehl-Neelsen and Gram stains.

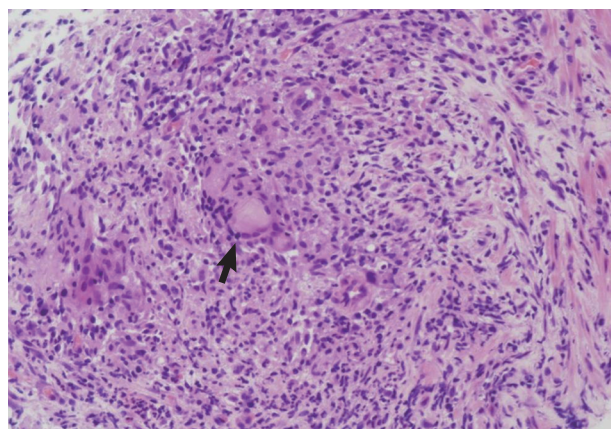


Fig. 2. The granulomatous lesion is composed of epithelioid histiocytes with multinucleated giant cells (arrow) surrounded by lymphocytes.

to 1:80 during recovery phase) and blood cultures were also negative. However, polymerase chain reaction (PCR) studies of blood and prostatic tissue for *Brucella* were positive. The target genes of primers used for the PCR study were a gene encoding a 31-kDa *Brucella abortus* antigen (BCSP31) and a gene encoding an outer membrane protein (omp-2). AMOS-PCR failed to differentiate among *Brucella* species. A PCR study for *Mycobacterium tuberculosis* was negative. Repeated physical examinations of the scrotum after the diagnosis of *Brucella* prostatitis were unremarkable. The patient was treated with doxycycline and ri-

fampin. One week after initiation of treatment, the symptoms were reduced and after three months, the level of serum PSA was normalized to 1.7 ng/mL.

DISCUSSION

Brucella is an intracellular gram negative coccobacillus.⁴ Traditionally, classification of *Brucella* species is based on its main hosts and there are 8 known species. Among them, *B. melitensis*, *B. abortus*, *B. suis*, and *B. canis* are known to cause human brucellosis.⁶ In Korea, both human brucellosis and bovine brucellosis are caused by *B. abortus*.^{4,5} It is transmitted mainly from animals to humans through direct contact, contaminated animal products (mainly unpasteurized milk products) and by inhalation of aerosolized infectious particles.⁹ Brucellosis is a kind of occupational disease, usually occurring in livestock workers, veterinarians, and personnel in microbiologic laboratories.⁶ Person to person transmission is extremely rare. After invasion into a host, *Brucella* is engulfed by phagocytes, where a minority of them survives and multiplies.⁶ Preferentially, they spread into the reticuloendothelial system, thus producing lymphadenopathy or hepatosplenomegaly. There was no demonstrable lymphadenopathy or hepatosplenomegaly in the present case.

The clinical manifestations of brucellosis cover a wide-spectrum and are non-specific. The most consistent feature is fever.

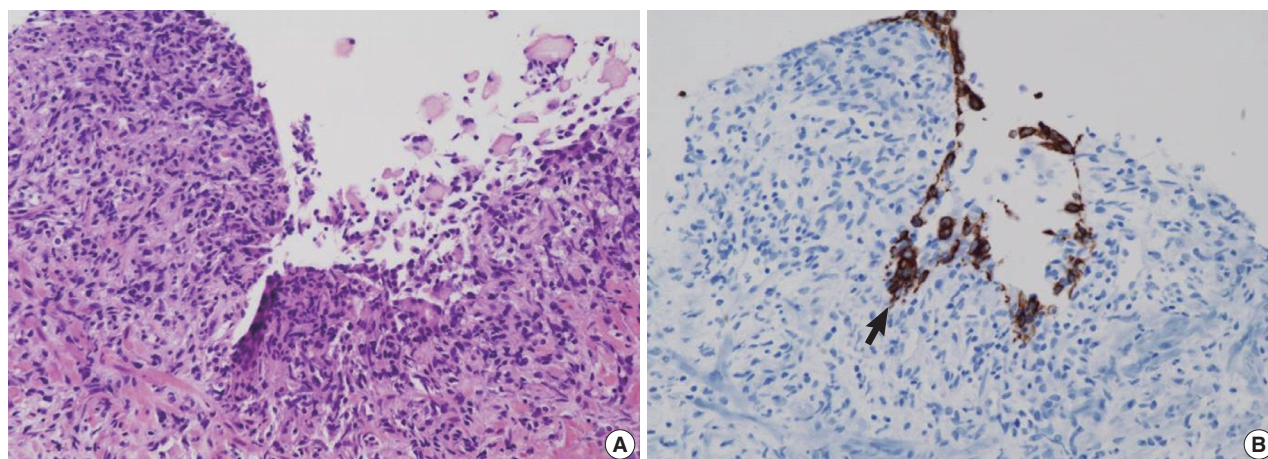


Fig. 3. (A) Some granulomatous inflammation is centered on prostatic acini, obscuring epithelium of acini. (B) Immunohistochemical staining (IHC) for cytokeratin highlights the epithelia (arrow) of residual prostatic acinus structures (IHC).

Fatigue, malaise, chill, sweating, and arthralgia are generally associated.^{5,6} The most common complication is osteoarticular disease. Chief complaints in the present case were fever, myalgia, and low back pain. The reproductive system is the second most common site of complications. In man, it usually presents as epididymo-orchitis with an incidence of 2-20% of patients.^{5,7} The *Brucella* epididymo-orchitis patient usually presents with scrotal pain and swelling. In Korea, several cases of *Brucella* epididymo-orchitis but no *Brucella* prostatitis have been reported.^{5,10,11} *Brucella* prostatitis is very rare and the incidence is not clearly defined. It is usually accompanied by epididymo-orchitis. Navarro-Martínez *et al.*⁷ reported that prostatitis accompanied 5% of *Brucella* epididymo-orchitis patients. *Brucella* prostatitis may present with lower urinary tract symptoms like dysuria, urinary frequency, or weak stream.¹² The present case presented with an aggravated lower urinary tract symptoms and high PSA levels without clinical evidence of epididymo-orchitis. The histologic examination of a prostatic needle biopsy specimen revealed granulomatous prostatitis. The histologic differential diagnoses of granulomatous prostatitis include infectious diseases such as tuberculosis, iatrogenic causes like BCG-instillation, systemic granulomatous disease such as sarcoidosis, and idiopathic prostatitis. *Brucella* prostatitis may be easily mistaken for tuberculosis in that tuberculosis is a leading cause of granulomatous inflammation in Korea, or for idiopathic prostatitis. For differential diagnoses, a previous history, ancillary tests including special stains and molecular tests for microorganisms, and thorough histologic evaluations are mandatory. The confirmation of brucellosis is made in a clinically compatible case that is laboratory confirmed. Laboratory criteria for diagnosis require

isolation of *Brucella* sp. from a clinical specimen, or fourfold or greater rise in *Brucella* agglutination titer between acute- and convalescent-phase serum specimens or a titer above 1:160.^{6,13} The sensitivity of culture is relatively low, ranging from 15 to 70%⁶ and the culture study should be performed for at least four weeks.⁶ There are two broad categories of serologic methods for detection of brucellosis: serum agglutination tests and indirect enzyme-linked immunosorbent assays. Serologic methods have several shortcomings such as cross-reactions or a lack of seroconversion as in the present case.⁶ Recently PCR with primers for the 16S rRNA gene, *BCSP31*, and *omp-2* have been widely accepted for detection of genus *Brucella* DNA.^{10,14} For differentiation among *Brucella* species, multiplex PCR, especially AMOS-PCR, is used.¹⁵ Both serologic tests and culture studies of the present case were negative, but PCR studies of blood and prostatic tissue for *Brucella* were positive. In addition, histologic examination showed granulomatous prostatitis, which was consistent with *Brucella* prostatitis.

The present case was unusual in that it presented without epididymo-orchitis. A possibility of *Brucella* prostatitis should be considered in the differential diagnosis of granulomatous prostatitis or prostatitis of unknown origin associated with or without epididymo-orchitis.

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