Neglected Case of Osteoarticular Brucella Infection of the Knee

Huseyin Yorgancigil, Guler Yayli¹, Orhan Oyar²

Departments of Orthopedics, ¹Clinical Microbiology and Infectious Diseases, and ²Radiology, Süleyman Demirel University School of Medicine, Isparta, Turkey

A 49-year-old farmer had a history of recurrent knee effusion for 20 years. He did not report undergoing any diagnostic or therapeutic procedures apart from repeated aspirations of the joint fluid. After the isolation of Brucella melitensis from the joint fluid, computed tomography-guided bone biopsy was performed and histopathologic examination of the biopsy sample confirmed the diagnosis of chronic Brucella osteomyelitis. Arthroscopic synovectomy combined with antimicrobial therapy with doxycyclin, rifampicin, and ciprofloxacin for six months resulted in clinical recovery. This case indicates that brucellosis should be suspected in patients with non-specific and chronic osteoarticular symptoms, especially in endemic regions.

Key words: arthritis, infectious; bone diseases, infectious; Brucella; Brucella melitensis; brucellosis; osteomyelitis

Brucellosis is primarily a disease of wild and domesticated animals (1). It is transmitted to humans through consumption of unpasteurized dairy products of infected animals, directly through contact with infected animals, or indirectly by environmental exposure (1). It is widespread in Turkey, as in many other Mediterranean and Middle Eastern countries. Brucellosis may commonly be misinterpreted because of its extremely variable clinical pictures and, in some chronic cases, microbiological and serological negativity (2). For this reason, suspicion of Brucella infection may sometimes be the key for correct diagnosis, especially in endemic regions.

We present a case of a patient with chronic brucellosis that manifested as an osteoarticular involvement of the knee joint and adjacent bones, without any diagnosis for 20 years.

Case Report

A 49-year-old male farmer presented with swelling and limited motion of the right knee. He reported that the symptoms had started before 20 years and that he had been treated only with the aspiration of fluid from the knee joint. He also reported that he had never undergone any biochemical or radiological examinations to clarify the cause of his condition. Joint fluid aspiration had been repeated several times due to recurrence of the symptoms before he came to our emergency department with a swollen knee but without any signs of acute inflammation. Laboratory tests revealed erythrocyte sedimentation rate of 24 mm/h, negative C-reactive protein, and white blood cell count of 5.7×10⁹/L. No microorganisms were isolated from blood cultures. All the other biochemical parameters were normal. Considering the prevalence of brucellosis in our region, we decided to search for Brucella in this particular patient having non-specific osteoarticular symptoms. Standardized Brucella tube agglutination test was performed on a serum sample (Pendik Veterinary Control and Research Institute, Istanbul, Turkey). To avoid post-zone phenomenon (3), the specimens were diluted up to 1:2,560 but yielded a negative result. Coombs test was also negative (Serologicals Ltd., Livingston, UK).

Macroscopic appearance of the joint fluid, which was slightly turbid and dark yellow, was consistent with chronic infectious arthritis. Fluid cell count was 3.0×10⁹/L, with differential count of 80% monocytes. No microorganisms were detected on Gram-stained smears. Biochemical analysis of the joint fluid revealed glucose concentration of 2.9 mmol/L, albumin concentration of 13.1 g/L, and globulin concentration of 15.0 g/L. The joint fluid was inoculated in blood agar and blood culture bottles, and Brucella melitensis was isolated from blood culture bottles on the sixth day.

X-ray of the right knee revealed lytic lesions in the proximal tibia and distal femur adjacent to the joint (Fig. 1A). These lesions were confirmed by magnetic resonance imaging, showing para-articular hyperintensities on T2-weighted sequence (Fig. 1B). Scintigraphy with technetium-99m methylene diposphonate revealed inflammatory hyperactivity in the
right distal femur and proximal tibia, and computed tomography-guided bone biopsy was performed. Together with osseous biopsy material from the proximal tibia and distal femur, some fluid similar to the joint fluid was obtained. No microorganisms were isolated after inoculation in blood agar, but *Brucella melitensis* was cultured after inoculation into blood culture bottles. Histopathological examination of the specimens revealed chronic nonspecific infection. Antimicrobial treatment was started with doxycycline 100 mg twice daily, rifampicin 300 mg twice daily, and ciprofloxacin 500 mg twice daily.

Villous synovial hypertrophy was observed at arthroscopy, and a multi-portal arthroscopic synovectomy was performed. Chronic nonspecific synovitis was confirmed histopathologically. There was no microbiological growth in synovectomy specimens. The case was diagnosed as a rare form of brucellosis with osteoarticular involvement and osteomyelitic lesions of the distal femur and proximal tibia secondary to chronic infectious arthritis of the knee caused by *Brucella melitensis*.

The medical treatment continued for six months, including anti-inflammatory agents and physiotherapy. There were no symptoms, such as swelling or pain, to implicate recurrence of the infection throughout the follow-up period. The patient made a complete clinical recovery at the latest control examination at 24 months.

**Discussion**

Osteoarticular involvement in brucellosis most commonly affects the vertebral column, sacroiliac, and peripheral joints. Although the leading manifestation is bone and joint inflammation, there are rare reports of osteomyelitis (4-8). However, metaphyseal location of osteomyelitis is undemanding because of the histological nature of that part of the bone. The question in this case may be whether the initial infection was in the joint or in adjacent metaphyses.

Although *Brucella melitensis* was initially isolated from the joint fluid in our patient, no microorganisms were found in the later arthroscopic synovectomy specimens. This may be due to antimicrobial therapy that was started immediately after the first isolation. There was also no joint destruction, as reported elsewhere (5). It may be speculated that metaphyseal bone involvement and subsequent erosion was the result of a local dissemination of untreated *Brucella* arthritis for about 20 years.

Zwass and Feldman (7) reported a case of chronic multifocal osteomyelitis in a patient with an established diagnosis of chronic brucellosis that lasted for 14 years. However, the diagnosis in our patient was reached on the basis of inoculation of the joint fluid in blood culture bottles to isolate the microorganism. Further factors raising suspicion of brucellosis were the fact that the patient lived in an endemic region and that he could be environmentally exposed to *Brucella* due to his occupation. Clinical or laboratory findings did not suggest a *Brucella* infection in our patient; serological tests and blood cultures were negative. On the other hand, other authors mostly reported positive agglutination titers in cases of *Brucella* osteomyelitis (4-8). However, the diagnosis of brucellosis cannot be excluded even if the serum agglutination tests are negative (2).

Although brucellosis in humans often has to be diagnosed without the isolation of a casual organism, laboratory investigation of aspiration fluid and tissue specimens obtained at biopsy aided in identification of the disease in our patient. *Brucella melitensis* was cultured from both joint fluid and bone biopsy specimens. The important fact is that the growth of the microorganism was possible only after inoculation of these specimens into blood culture bottles. This can be expected, as *Brucella spp* are known to be delicate bacteria (2). We usually obtain higher rates of isolation of microorganisms from joint and other body fluids when using blood culture bottles, than incubation in standard plates. Considering the characteristics of our region, we routinely inoculate these specimens into blood culture bottles in our institution.

In our patient, the insidious course of the disease and negligence in previous medical handling caused a 20-year delay in diagnosis of the disease. If possible, enzyme linked immunosorbent assay (ELISA) can be used in detection of antibody when conventional serological tests are negative (9). We did not have to confirm serological diagnosis with ELISA in our patient, because culture results were positive for both synovial fluid and bone biopsy specimens.

One should bear in mind that osteomyelitis and infectious arthritis due to *Brucella* may present as a low-grade infection. In spite of its rarity, brucellosis should be considered in differential diagnosis of patients with recurrent knee joint effusion, even when they have no systemic symptoms or laboratory evidence, especially in areas where the disease is endemic and in patients with epidemiological risk factors for the infection.

**References**


Received: January 9, 2003
Accepted: June 20, 2003

Correspondence to:
Huseyin Yorgancigil
Post Office Box (PK): 90
32000 Isparta, Turkey
huseyin@med.sdu.edu.tr