Acute Brucellosis as a Cause of Infective Colitis

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ABSTRACT Gastroenterological manifestations of human brucellosis are relatively uncommon. A case of Brucella melitensis infection in a 39-year-old man accompanied by lesions of the colon, observed by colonoscopic and histopathologic examinations, and a brief review of the relevant literature are reported.

INTRODUCTION Brucellosis, a worldwide zoonotic disease, is a systemic infection caused by facultative intracellular bacteria of the genus Brucella that can involve many organs and tissues. Humans become infected by ingestion of animal food products, direct contact with infected animals, or inhalation of infectious aerosols. Brucellosis in humans has a strong association with military medicine, since it has a long history as an endemic threat on the battlefield. Moreover, the ease of transmission by aerosol suggests that Brucella organisms might be a candidate for use as a biological warfare agent. Undifferentiated febrile illness and arthritis-dominant syndrome with hepatosplenomegaly and lymphadenopathy are the usual modes of presentation. The gastroenterological manifestations of human brucellosis are relatively uncommon, ranging from the nonspecific, such as diarrhea and abdominal pain, to the pathologically distinct hepatic lesions, and to the rare colonic, pancreatic, and peritoneal involvement. We report a case of acute human brucellosis accompanied by colitis with a brief review of the relevant literature.

CASE REPORT A 39-year-old male officer was admitted to hospital because of a 2-week period of intermittent high-grade fever up to 38.5°C associated with chills, fatigue, malodorous night sweats, and mucosanguineous diarrheas up to five times a day, in addition to low back pain which had appeared 5 days previous to admission. His medical history included nephrolithiasis and appendectomy. A record of the consumption of unpasteurized dairy products during the previous months was also reported. There was no history of recent foreign travel, use of drugs, tuberculosis, or any type of infection during the preceding months. On physical examination the patient appeared ill. The head, neck, heart, and lungs were normal. The bowel sounds were normal, and no organs, mass, or tenderness was felt. The extremities were normal. A stool specimen was positive for occult blood. Laboratory tests showed the following values: hematocrit, 32.7%; hemoglobin, 10.3 g/dL; white blood cell count, 5,000 cells/mm³ (neutrophils 62%, lymphocytes 34%, monocytes 3%); platelet count, 375,000/mm³; erythrocyte sedimentation rate (ESR), 78 mm/h; C-reactive protein (CRP), 99 mg/L (normal: 0–8 mg/L); normal biochemical parameters; and urinalysis. Microscopic examination of three stool specimens revealed no ova or parasites. An electrocardiogram, a chest X-ray, and an abdominal ultrasound scan were within normal limits. Tests for the following were all negative: a tuberculin skin test (purified protein derivative), rheumatoid factor, anti-neutrophil cytoplasmic and anti-Saccharomyces cerevisiae antibodies, serological tests for salmonellosis, syphilis, leptospirosis, Lyme disease, gonorrhea, chlamydial infections, and infections by Rickettsia rickettsii, cytomegalovirus, herpes simplex virus, human immunodeficiency virus, hepatitis A virus, hepatitis B virus, and hepatitis C virus. Brucella agglutinin titer was positive at 1:640, and the blood culture using the BACTEC 9240 automated blood culture system (BD Biosciences, Franklin Lakes, New Jersey) had grown Brucella melitensis by the sixth day. Stool cultures were negative for Salmonella, Shigella, Campylobacter, Yersinia enterocolitica, Entamoeba histolytica, and other pathogenic microorganisms.

A colonoscopy performed on the third day of hospitalization showed areas in the colon with edematous mucosa, multiple petechiae, and exulcerations, suggestive of colitis (Fig. 1). The terminal ileum, ileocecal valve, cecum, ascending colon, and rectum appeared normal; the appendiceal orifice was identified. Microscopic examinations of biopsy samples taken from the mucosa of the above areas showed edema and hyperemia, aggregates of lymphocytes and plasma cells, such as numerous granulocytes that infiltrated the epithelium forming hidden mini-abscesses. After a putative diagnosis of acute brucellosis, the patient was administered...
doxycycline, 100 mg by mouth, twice daily for 6 weeks plus streptomycin, 1 g intramuscularly, for the first 21 days beginning on the fourth day of hospitalization, while awaiting the serological and cultural confirmation. Due to persistent low back pain and persistently elevated ESR and CRP, a bone scan with technetium-99m-methylene diphosphonate was obtained that revealed possible bilateral sacroiliitis. The patient refused the performance of magnetic resonance imaging scan. Because of a possible osteoarticular location of brucellosis, the patient was administered additionally rifampicine, 900 mg by mouth, daily for 6 weeks. Three days after the initiation of treatment, the patient ceased to suffer from diarrhea. Four weeks after the end of the treatment, a newly performed colonoscopy revealed disappearance of the previously described lesions. Six weeks after the admission, the low back pain disappeared and the ESR and CRP normalized.

DISCUSSION

Although human brucellosis has among its protean clinical manifestations a spectrum of gastrointestinal expressions, reports of documented specific gastrointestinal lesions caused by Brucella spp. are sparse. In a study among 25 Kuwaiti patients with brucellosis and gastrointestinal symptoms, upper gastrointestinal endoscopy revealed erosive gastritis only in 6 patents (24%). Diarrhea has been reported as prominent gastrointestinal symptom in 6 to 16% among 757 patients with brucellosis, but only two well-documented cases of B. melitensis colitis, to the best of our knowledge, have been described. The first case concerns a 16-year-old patient with osteomyelitis and simultaneous rectal bleeding from a friable colonic mucosa with multiple pseudopolyps; histology revealed acute and chronic inflammation and distortion of mucosal architecture with goblet cell depletion. The second case concerns a 22-year-old woman with fever, anemia, and disturbed liver function tests, without gastrointestinal symptoms. The colonoscopy revealed a reddened edematous ileocecal valve with multiple erosions and a descending colon with multiple erythematous patches; microscopic examination of biopsies from the ileocecal valve revealed acute and chronic inflammation beneath the surface epithelium and lamina propria. Some cases of brucellosis associated with clinical findings of colitis, without endoscopic or histopathologic confirmation, have also been reported. Ho et al. reported a 19-year-old woman with culture-proven B. melitensis infection, initially experiencing fever, abdominal pain (left lower quadrant), nausea, malaise, myalgias, and, later, loose bloody stools, suggestive of acute colitis. However, no colonoscopy or contrast roentgenogram were performed. Petrella and Young reported a case of an 11-year-old female with fever, arthritis, anemia, increased ESR, and a radiographically documented ileitis suggestive of Crohn’s disease. The true diag-

FIGURE 1. Colonoscopy performed on the third day of hospitalization showing areas in the lateral, descending, and sigmoid colon with edematous mucosa, multiple petechiae, and exulcerations.
nosis of *B. melitensis* infection was made on the basis of blood cultures, and *Brucella*-associated ileitis was resolving completely after appropriate antibiotic treatment. A case of enterocolitis-like symptoms in a premature infant was described in which *B. melitensis* was isolated after three episodes of enterocolitis symptoms; proper antibiotic treatment led to recovery.

Mesenteric lymphadenitis or inflammation and ulceration of Peyer’s patches have been suggested as the possible mechanism for abdominal pain and bloody diarrhea in patients with *Brucella*-associated ileocolitis. In 1934, Sharp reviewed the literature on postmortem examinations of patients with brucellosis, mentioned a few cases with necrosis and ulcerations in Peyer’s patches. Although almost all cases were characterized by patchy intestinal hyperemia, ulceration occurred only rarely in the colonic mucosa. It is remarkable that these lesions were noted on autopsy, but the gastrointestinal symptoms or manifestations of these patients were unknown.

The diagnosis of brucellosis in our patient was based initially on the detection of specific antibodies at significant titers in serum, compatible with the clinical findings; titers ≥1:160 in a standard tube agglutination test are determined as significant. Our diagnosis was established by isolating *B. melitensis* from blood using the BACTEC 9240 automated blood culture system. Although several factors affect the growth and detection of *Brucella* spp. in blood cultures, the BACTEC system can isolate *Brucella* spp. in a fast and efficient way in approximately 80% or 95% of cases. Medical history, physical examination, blood and stool laboratory tests, and colonoscopic and histopathologic examinations excluded other possible known causes of inflammatory diarrhea and colitis, such as other infectious agents, tuberculosis of the gastrointestinal tract, inflammatory bowel disease (Crohn’s disease, ulcerative colitis), pseudomembranous colitis or antibiotic-associated diarrhea, ischemic colitis, and colon cancer or tumors.

In conclusion, brucellosis is a preventable and readily treatable condition that must be considered in the differential diagnosis of patients with “prolonged fever and colitis” in *Brucella*-endemic regions. Also, the risk of food-borne brucellosis must be underlined to military personnel, particularly when they travel in areas where brucellosis occurs in livestock.

**REFERENCES**