Brucellosis Associated Post-Infectious Glomerulonephritis: A Case Report and Review of the Literature

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INTRODUCTION
Brucella are small gram-negative coccobacilli. The four species pathogenic to humans are: Brucella abortus, Brucella canis, Brucella melitensis, and Brucella suis.1 Brucella are resistant to phagocytic killing and thus can replicate and survive for long periods of time, which explains the infection's long course duration and frequent relapses.2 Stockbreeders, dairy farmers, and veterinarians can be occupationally exposed to Brucella.3 Brucella infection can also be acquired through consumption of unpasteurized dairy products, such as fresh cheese or cream butter.3 Brucellosis is endemic in Portugal, Spain, Greece, Turkey, France, Italy, the Middle East, as well as Central and South America, and Mexico.4 The majority of Brucellosis cases in the United States occur in California and Texas and are associated with travel to Mexico.1

An accurate diagnosis of Brucellosis is based on obtaining an adequate medical history and identifying the organism in blood cultures, however the organism is only isolated in 15-70% of the cases.5 The Labrisseau-Spink criteria can be used to make a diagnosis of chronic Brucellosis when the organism is not isolated in blood cultures.6 The Labrisseau-Spink criteria include known past exposure, clinical evidence of illness, positive Brucella agglutinins, and disease improvement with decreasing Brucella agglutinins after starting specific antibiotics.5,6 Brucella infection may manifest with a wide range of symptoms from back pain, myalgias, fatigue, weight loss, to fever and headache.6 Brucellosis is a systemic infection that can attack the body acutely or more insidiously taking up to 3 months after exposure to manifest disease symptoms.5 Renal involvement in Brucellosis is uncommon and biopsy-proven glomerulonephritis is exceedingly rare.4,5,8,9 In this report we discuss a case of post-infectious glomerulonephritis with concomitant endocarditis caused by Brucella melitensis and present a brief review of the literature.

CASE PRESENTATION
The patient is a 46-year-old Hispanic female who presented to the emergency department with a five month history of intermittent diarrhea. Four months prior, she was treated in Mexico with antibiotics (gentamicin & ciprofloxacin) and her symptoms improved. However, two weeks prior to admission, the patient’s watery diarrhea recurred this time with fever, chills, nausea, vomiting and gross hematuria. The patient was also experiencing generalized arthralgias and unintentional weight loss of 20 pounds during the past 2 months, which she attributed to decreased appetite. There was no known history of raw meat or unpasteurized milk consumption and no sick contacts were reported. Her only medications were over-the-counter anti-diarrheals. She denied any recent travel, except across the US-Mexico border into neighboring Ciudad Juarez, Chihuahua. The patient did not use tobacco products, alcohol or illegal drugs.

On physical examination, her temperature was 37.4°C, pulse 101, blood pressure 146/74mmHg. The oral mucosa were dry. A grade 2/6 holosystolic murmur on the mitral area with radiation to the axilla was noted. The patient had no lymphadenopathy, hepatosplenomegaly, or skin rash. The remainder of the physical examination was normal.

Laboratory studies upon admission: hemoglobin 9 g/dl, hematocrit 27%, mean corpuscular volume 77, leukocytes 5400/µl, with 30% bands; blood urea nitrogen (BUN) 81 mg/dl, and serum creatinine 6.3 mg/dl. Urine analysis showed: large blood, protein 100 mg/dl, and few granular casts. Her 24-hour protein excretion was 900mg. The chest radiograph and electrocardiogram were unremarkable. The brucella serum agglutination test was positive at a titer of 1/320 and the blood cultures grew Brucella melitensis.

Treatment with doxycycline, rifampin and ceftriaxone intravenously was started. A transthoracic echocardiogram showed a vegetation on the mitral valve. After four days of treatment, her symptoms improved, and she remained afebrile. The patient’s renal function continued to deteriorate and thus a renal biopsy was performed on hospital day 3.

Light microscopy revealed marked mesangial hypercellularity and endocapillary proliferation as well as extensive lymphocytic infiltration of the renal interstitium without granuloma formation. The immunofluorescence studies showed diffuse and global granular C3 mesangial and glomerular capillary deposits. IgG, IgA, IgM, and C1q were negative. The ultrastructural evaluation revealed the presence of electron dense deposits of the immune type located in the mesangial compartment. The renal biopsy was reported as being involved by an immune-mediated glomerulopathy consistent with post-infectious glomerulonephritis and a tubulointerstitial lymphocytic nephritis. (See figure 1).

The patient was started on hemodialysis preoperatively before undergoing mechanical mitral valve replacement. Four weeks later, she developed candidemia and multiorgan system failure. Shortly thereafter the patient passed away.

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DISCUSSION

Brucellosis is a cause of undulant fever with varied and nonspecific symptoms. Classic symptoms include: fever, sweats, malaise, headache and shivering. Due to its protean clinical presentation, Brucellosis is frequently missed or undertreated. Commonly involved sites include the bone, joints, the genitourinary tract, occasionally the central nervous system (meningitis, brain abscesses, and demyelinating syndromes) and rarely heart valves (endocarditis). While the liver is only involved in about 1 Notably, when patients diagnosed with renal brucellosis have concomitant endocarditis their risk of complications increases significantly.

Infected patients often lack clinical signs of genitourinary involvement, even though 4-50% of patients excrete the organisms in their urine. Brucella-associated nephritis is usually classified as three types: 1. acute interstitial nephritis or pyelonephritis during acute infection, 2. chronic involvement with granulomas, caseation and necrosis, and 3. renal involvement associated with Brucella endocarditis. Bakri et al. also suggest a fourth type: renal abscess. Different types of glomerulopathies include: IgA nephritis, membranous nephropathy, mesangiocapillary glomerulonephritis and end-stage renal disease (ESRD) as a result of brucellosis appears to be an extremely rare event, with only one of eleven reported cases of biopsy-proven Brucella-related glomerulonephritis resulting in ESRD.

The underlying pathogenetic mechanisms are either direct invasion by the bacteria (interstitial nephritis) or indirect glomerular involvement caused by circulating immune complexes (glomerulonephritis). Patients with Brucella glomerulonephritis almost always present with proteinuria, hematuria, and azotemia.

The coexistence of Brucella endocarditis and Brucella-associated nephritis portends a worsened prognosis as seen in our reported case, despite adequate antimicrobial therapy. Therefore, endocarditis and brucella nephritis should be suspected in patients with Brucellosis.

REFERENCES


Figure 1. Kidney biopsy. Light Microscopy showing mesangial and glomerular capillary loop endothelial cell proliferation.

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