Brucellosis With Kidney Failure

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Brucellosis is a multisystem disease that may present with a broad spectrum of clinical manifestations. The most frequent symptoms are constitutional symptoms. While involvement of the bones, joints, and liver is not rare, brucellosis may rarely involve the kidney. We present a case of brucellosis with hepatitis, pancytopenia, peripheral arthritis, and kidney failure.

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INTRODUCTION

Brucellosis has many faces and can involve various organs.[1] The most common urogenital presentation of brucellosis is epididymo-orchitis, which occurs in 20% of male patients.[2] Although *Brucella bacilli* has been found in urine of the patients, renal involvement is rare. So far, Interstitial nephritis, pyelonephritis, exudative glomerulonephritis, mixed cryoglobulinemia, kidney failure, and immunoglobulin A nephropathy have been reported.[2-4] Patients may present with hematuria, proteinuria, and different stages of kidney dysfunction. Renal involvement usually improves after antibiotic therapy. On kidney biopsy, mesangial proliferative, diffuse proliferative, rapidly progressive, and focal segmental glomerulonephritis have been described.[1,3,4]

We describe a patient who presented with acute kidney failure and involvement of multiple systems whose signs all disappeared following antibiotic therapy.

CASE REPORT

The patient was a 27-year-old married woman residing in Ardebil, Iran, with diffuse peripheral asymmetric arthritis with a diagnosis of rheumatiod arthritis who was receiving prednisolone, 10 mg/d, and chloroquin, 300 mg/d, since 1 year ago. Her joint pain had been first noticed in her left 4th proximal interpharyngial joint, progressing to the right 4th proximal interpharyngial joint, and then her left knee, right shoulder, and left ankle. She had also complained of photosensitivity and hair loss. During her first presentation, her kidney function and blood pressure were normal.

The patient was revisited by her physician because of deterioration of the pain in her joints. Laboratory tests revealed a serum creatinine level of 2.2 mg/dL and a blood urea nitrogen level of 30 mg/dL. Subsequently, the patient was referred to our center for further evaluation. She was experiencing epistaxis since a week ago and complaining of abdominal pain, nausea, vomiting, diarrhea, darkened urine, and light stool since the past 3 days. She did not have fever. Her urine output had decreased since a day before. She was on low-dose contraceptive pills during the past year.

On physical examination, the tilt sign was negative, and her respiratory rate was 17 per minute; pulse rate, 85 per minute; blood pressure, 120/80 mm Hg; and oral temperature, 37°C. Her conjunctiva was pale and her sclera was icteric. No lymphadenopathy was detected. A II/VI systolic heart murmur could be heard at the left sternal border. The spleen and the liver could be palpated 3 cm and 4 cm below the costal margin, respectively. The liver span was estimated to be 18 cm. No edema was found on the feet, but arthritis was detectable in the left ankle. The laboratory data during hospital stay are shown in the Table. In addition, urinalysis on admission revealed trace albuminuria (dipstick) and pyuria (leukocyte count,

Case Report

Results of Laboratory Tests During Hospital Stay and on Follow-up*

Blood Tests	Day 1	Day 9	Day 12	Day 15	Day 23	Day 32	Month 3
Serum creatinine, mg/dL	2.2	3.9	3.8	…	0.7	1	0.67
Blood urea nitrogen, mg/dL	30	73	74	…	17	16	13
Aspartate aminotransferase, U/L	…	511	…	…	40	29	20
Alanine aminotransaminase, U/L	…	291	…	…	56	17	17
Alkaline phosphatase, U/L	…	852	…	…	…	384	…
Total serum bilirubin, mg/dL	…	5.25	…	…	1.9	0.9	0.5
Direct serum bilirubin, mg/dL	…	4.59	…	…	1.15	0.4	0.1
Leukocyte count, × 10^9/L	…	2.3	2.4	…	3.6	5.1	6.9
Hemoglobin, g/dL	…	10.9	9.9	…	8.9	9.7	13.0
Platelet count, × 10^9/L	…	87	59	…	126	242	246
Erythrocyte sedimentation rate, mm/h	56	85	…	…	…	…	12
Lactate dehydrogenase, U/L	…	800	…	…	…	360	…
Creatine Phosphokinase, U/L	…	205	…	…	…	…	…
Wright agglutination titer	…	…	…	1/640	…	1/80	Negative
Two-mercaptoethanol agglutination titer	…	…	…	1/320	…	Negative	Negative

*Ellipses indicate not measured.

20 to 25 per high-power field). Urine culture was negative for microorganisms. Urine protein was 1664 mg per 24 hours.

On the first few days of admission, she was oliguric with a 24-hour urine volume of 200 mL on average. She repeatedly experienced epistaxis. Serologic tests for systemic lupus erythematous, collagen-vascular diseases, vasculitis, and hepatitis were negative. Because of thrombocytopenia, kidney biopsy was not performed. Bone marrow aspiration and bone marrow biopsy revealed hyperplasia of the erythroid line and slightly elevated number of megakariocytes with pleomorphic nuclei. Echocardiography showed no evidence of subacute bacterial endocarditis. The renal arteries were normal on Doppler ultrasonography. Abdominal ultrasonography showed hepatosplenoomagaly without ascitis; however, both kidneys were normal. Abdominal computed tomography revealed fine lymphadenopathy around the celiac tree as well as hepatosplenomegaly.

Five days after admission, the patient developed fever (39.5°C). On the 2nd week of hospitalization, results of the Wright 2ME test were positive for brucellosis (Table). Thus, intramuscular streptomycin, 1 g/d, doxycycline, 100 mg twice a day were started on. Nine days after the beginning antibiotics, the patient's fever subsided, serum creatinine level decreased to 0.9 mg/dL, and blood urea nitrogen was 17 mg/dL. The liver test results partially improved, and leukopenia and thrombocytopenia gradually subsided during the following 2 weeks (Table). The patient was discharged from hospital with doxycycline, 100 mg twice a day, for two months and streptomycin, 1 g/d, for 1 month.

One month and a half later on, no symptoms were remained and hepatosplenomegaly was subsided. The kidney function tests, urinalysis, 24-hour urine protein level, complete blood count, and liver function tests were all in their reference ranges. Serologic tests for systemic lupus erythematous and brucellosis were negative.

DISCUSSION

Brucella, the organism causing brucellosis, is a gram-negative coccobacillus. Although the disease has been well-controlled in developed countries, it is a serious health hazard in the developing world. It is known as a thousand-face disease, has a wide spectrum of signs, and has asymptomatic as well as fatal forms.[1] Renal involvement in the form of acute kidney failure is rare, but acute interstitial nephritis which results from direct invasion of the organism is the most common form.[5-8] Deposition of circulating immune complex can involve the glomeruli. Kidney disease accompanying brucellosis has been reported in the forms of membranoproliferative glomerulonephritis, diffuse proliferative glomerulonephritis, rapidly progressive glomerulonephritis, rhabdomyolysis, focal segmental glomerolusclerosis and immunoglobulin A nephropathy.[7-9] Hemolytic uremic syndrome has also been mentioned in some case reports.[3,4]

In the context of brucellosis, kidney disease presents as hematuria, proteinuria (in nephrotic

range sometimes), and various degrees of kidney dysfunction. After antibiotic therapy these signs improve, but histologic findings, proteinuria, and hypertension may persist.[8] In general, regarding acute kidney failure, sterile pyuria, and proteinuria at the level of 1665 mg/d, our patient seemingly had developed acute interstitial nephritis by brucellosis; however, kidney biopsy was avoided due to thrombocytopenia, and consequently the pathologic feature of the disease remained obscure.

Mild jaundice and slightly elevated liver function, which are anticipated in brucellosis,[1,2] were relatively severe in our patient. Hepatosplenomegaly was another notable finding, which is reported in 15% to 20% of patients.[1] Hematologic changes have been seen in about 16% of cases which are in from of anemia, relative leucopenia, lymphopenia, and sometimes, thrombocytopenia. Pancytopenia occurs in 5% to 20% of cases.[1] Although it could secondarily arise due to hemophagocytosis, its etiology is multifactorial.[1] Presence of granuloma in the bone marrow, which is sometimes small and indistinct, as well as hypersplenism and hemophagocytosis with histiocytes in the bone marrow might be the etiology of pancypentia.[1]

Currently, the treatment of choice for brucellosis is administration of doxycycline aminoglycosides like streptomycin. Then, the patient should be followed up clinically and serologically every 3 to 6 months for 2 years.[1] Our patient responded to this classic treatment and no further treatment of kidney dysfunction was required. On the follow-up, we observed no sign of sequela on the kidneys.

In conclusion, acute *Brucella* infection should be considered in the differential diagnosis of acute kidney failure when accompanied by symptoms such as arthritis, particularly in areas where brucellosis is endemic.

CONFLICT OF INTEREST

None declared.

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