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Rapidly Progressive Glomerulonephritis Associated with Brucellosis: A Case Report

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Abstract

Crescentic glomerulonephritis is a nephrological emergency that may be associated with immune complexes, various types of vasculitis, anti-GBM disease and many infections however only a limited number of cases with Brucellosis-associated RPGN have been demonstrated despite it being one of the most common zoonotic infections. We report a case of Brucellosis-associated RPGN in an elderly male and challenges in management. A 67-year-old male patient presented to clinic with weight loss, progressive renal failure, shivering and fatigue; his urinalysis revealed hematuria. Common etiologies were investigated without determination of any possible source leading to further investigation of rare infectious causes. Patient was diagnosed with Brucellosis following positive Rose-Bengal and Wright agglutination tests and prescribed with doxycycline and rifampicin.

Introduction

Rapidly Progressive Glomerulonephritis (RPGN), also known as crescentic glomerulonephritis, is an emergency condition that may be fatal in weeks to months due to necrotizing extra capillary proliferative crescentic glomerulonephritis, thus, requiring proper diagnosis and treatment [1]. Five main types of RPGN including anti-glomerular basement membrane disease (type 1), immune-complex mediated (type 2) and pauci-immune with ANCA positive vasculitis (type 3), combination of type 1 and 3 (type 4), ANCA-negative, pauci-immune renal vasculitis (type 5) have been identified [1,2]. Despite RPGN being the second most common histopathological diagnosis on kidney biopsies after IgA nephropathy, only single case of Brucella-associated RPGN has been reported so far, despite Brucellosis being one of the most common zoonotic infection [3,4]. Although orchitis and epididymitis are the most common genitourinary presentations of Brucellosis, other types of kidney involvement including membranoproliferative glomerulonephritis, tubulointerstitial nephritis and IgA nephropathy have been reported in the course of Brucellosis [5-8]. In this case report, we present a rare case of RPGN caused by Brucellosis in an elderly male patient and its' clinical outcome.

Case Presentation

A 67-year-old male patient presented to our clinic with progressive renal failure, fatigue, weight loss and shivering. Past medical history was significant for hypertension controlled with three medications, ischemic heart disease that required cardiac stenting 5 years ago, aortofemoral bypass 3 years ago, and tuberculosis osteomyelitis 4 years ago treated with 12 months of combination therapy. Family history was significant for ischemic heart diseases. No history of smoking or alcohol consumption was present. The patient stated that he did not consume unpasteurized milk and dairy products. Physical examination and vitals of the patient were in normal range. Laboratory analysis revealed anemia (Hb: 8.1 g/dl, Hct: 26.4%), thrombocytopenia (110.000 cells/mm^3); elevated erythrocyte sedimentation rate (119 mm), C-Reactive Protein (68.6 mg/L), blood urea nitrogen (25 mg/dl), serum creatinine (2.58 mg/dl), PTH (118 pg/mL), potassium (5.2 mmol/L), and low estimated GFR (24.83 mL/min/1,73m^2). Liver and thyroid function tests, uric acid levels, and other electrolytes were all in normal range. Urinalysis demonstrated hematuria (71 RBC/HPF) without proteinuria. ANA, p-ANCA, c-ANCA, and anti-ds DNA were negative. Urinary ultrasonography and renal Doppler ultrasonography revealed no pathologies; both kidneys were in normal size and parenchymal thickness. Multiple blood and urine cultures were negative. Infection serologies for hepatitis B, hepatitis C and HIV were negative. Infectious causes of patient's symptoms including Brucella and tuberculosis were evaluated. Tests were positive for Brucella demonstrated by positive Rose Bengal agglutination test and 1/1280 antibody titer on Wright agglutination test (Table 1).

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Table 1: Blood work-up, urinalysis and infectious serology of the patient at initial diagnosis, during follow-ups and current status.

	Initial presentation	1-month follow-up	1-year follow-up	Current status
Blood work-up				
Hb (g/dl)	8.1	8.3	5.6	12.8
Hct (%)	26.4	25.5	17	38
WBC count (1000 cells/mm^3)	6	4.8	6.3	4.04
Platelet count (1000 cells/mm^3)	110	112	70	75
Sodium (mmol/L)	137	138	136	143
Potassium (mmol/L)	5.2	4.6	3.6	4.7
Bicarbonate	20.7	19.4	18.1	21.9
Calcium (mg/dL)	9.5	8.7	8.9	-
Phosphorus (mg/dL)	3.3	3.7	6.4	-
Parathyroid hormone (pg/ml)	118	-	-	-
Albumin (g/dL)	3.6	2.3	2.7	4.5
Serum creatinine (mg/dl)	2.58	4.1	7.6	1.78
BUN (mg/dl)	25	47	54	30
Estimated GFR (mL/min/1,73m^2)	24.83	29.14		38
CRP (mg/L)	68.6	40.2	79.9	31.5
ESR (mm)	119	74	67	-
ANA	Negative	-	-	-
Anti-dsDNA	Negative	-	-	-
Anti-GBM	Negative	-	-	-
p-ANCA	Negative	-	-	-
c-ANCA	Negative	-	-	-
C3c (mg/dl)	-	40	-	-
C4 (mg/dl)	-	25	-	-
Infection serologies				
Anti-HIV antibody	Negative	-	-	-
HbsAg	Negative	-	-	-
Anti-HBs antibody	Negative	-	-	-
Anti-HBc antibody	Negative	-	-	-
Anti-HCV antibody	Negative	-	-	-
Rose-Bengal	Positive	-	-	-
Wright agglutination	1/1280	-	-	-
Anti-Influenza A	Negative	-	-	-
Anti-Influenza B	Negative	-	-	-
QuantiFERON	Positive	-	-	-
Urinalysis				
Hematuria (RBC/HPF)	71	124	171	7
Proteinuria	Negative	Negative	Negative	Negative

No sign of tuberculosis reactivation was determined. Patient was diagnosed as acute brucellosis and treated with doxycycline (2 mg/day × 100 mg/day) and rifampicin (2 mg/day × 300 mg/day) for 6 weeks.

At 3-month follow-up the patient was hospitalized due to worsening of fatigue, weight loss, decline in renal functions (SCr: 4.1 mg/dl), oliguria, and presence of hematuria (124 RBC/HPF). Other abnormal laboratory findings include elevated C-reactive protein (40.2 mg/L), alkaline phosphatase (190 U/L), blood urea nitrogen (47 mg/dl), decreased albumin (2.3 g/dL), complement C3c (40 mg/dL), and a normal complement C4 (25 mg/dl). Brucella (capture) was <1/80 negative. Patient underwent hemodialysis due to decline in kidney functions and oliguria. Percutaneous kidney biopsy revealed immune complex focal segmental necrotizing glomerulonephritis. Treatment plan at discharge included 64 mg/day oral prednisone, 6 cycles of cyclophosphamide (500 mg) for 6 months followed by oral azathioprine (2 mg/day × 50 mg/day) for 6 months.

Patient was non-compliant for his follow-ups. Patient was admitted to our clinic with dizziness, headache, night sweating, dry mouth, fatigue, and worsening in kidney function (SCr: 7.6 mg/dl) at 1-year follow-up. Some laboratory findings at admission were hemoglobin 5.7 g/dl, albumin 2.7 g/dL, CRP 79.9 mg/L, and BUN 54 mg/dl. Kidney biopsy was performed with the preliminary diagnosis of acute or chronic renal failure and biopsy revealed immune complex focal segmental necrotizing glomerulonephritis. And patient received corticosteroid and rituximab therapy. On that visit Brucella (capture) was >1/5250 positive. Doxycycline (2 mg/day × 100 mg/day) + rifampicin (1 mg/day × 600 mg/day) + ceftriaxone (2 g/day × 2 g/day) treatment was planned by the infectious disease department. Bone marrow biopsy was performed regarding the possibility of bone marrow aplasia in response to immunosuppressive treatment, though, no pathological finding had been determined. Patient was discharged after symptomatic relief and improvement in kidney function (SCr: 4.8 mg/dl) (Table 1). Two months later the patient presented to clinic for routine outpatient follow-up. He had no complaints and his kidney functions were improved (SCr: 1.44 mg/dl). Follow-up of the patient for 6 months was uneventful.

Discussion

Brucellosis is the most common zoonotic infection in Turkey, primarily affects bones, lymphatic tissues, and the heart. The genitourinary involvement rate of brucellosis is around 2% to 20%. Orchitis and epididymitis are the most common types of genitourinary involvement [9]. Symptomatic renal involvement is especially rare with limited number of cases including membranoproliferative glomerulonephritis, tubulointerstitial nephritis, IgA nephropathy, and a single case of RPGN [4-8]. Only one case of RPGN associated with Brucellosis reported by Ardalan and Shoja [4] which demonstrated RPGN in a young male patient which responded to rifampicin + doxycycline + corticosteroid treatment dramatically in 2 weeks [4], while we report RPGN case in an elderly male patient who required multiple hospitalizations during the course of treatment and became difficult to manage. Decline in kidney functions, hematuria, weight loss, requirement for RBC transfusions, multiple hospitalizations, morbidity and mortality are possible in the course of Brucellosis-associated RPGN especially, if it is not considered in the differential diagnosis or inappropriately treated. In addition, Brucellosis-associated kidney involvement may occur at any age despite most reported cases include young patients.

Furthermore, our case is significant by illustrating immune complex depositions which may be the primary mechanism of kidney involvement in the course of Brucellosis. Since immune complex depositions are frequently observed on kidney biopsies performed with the preliminary diagnosis of RPGN, it is important to consider Brucellosis, an infection, as a differential diagnosis of immune complex deposits especially in areas where it is endemic along with predominant causes, including systemic lupus erythematosus and

other immune complex ANCA-positive vasculitis.

Even though renal involvement rates are low and most cases report good prognosis and general status, it is important to point out the possibility of RPGN as a manifestation in which emergency cases may develop. Low rates of Brucellosis-associated kidney involvement may also be a consequence of not being considered in the differential diagnosis in most instances. Therefore, we recommend consideration of Brucellosis in the differential diagnosis of glomerulonephritis especially in the areas where Brucellosis is endemic or in patients with specific environmental or other risk factors. Also, it may be beneficial to evaluate Brucella serology in RPGN patients with unknown etiology after elimination of predominant causes which could become a cost-effective approach for patient evaluation.

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