A Rare Clinical Entity: Staphylococcus-Related Glomerulonephritis

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Abstract

Staphylococcus aureus is a rare cause of postinfectious glomerulonephritis, and Staphylococcus-related glomerulonephritis primarily occurs in middle-aged or elderly patients. Patients with Staphylococcus-related glomerulonephritis also present with hematuria, proteinuria of varying degrees, rising serum creatinine levels, and/or edema. The severity of renal insufficiency is proportional to the degree of proliferation and crescent formation. Here, we present a diabetic patient admitted with a history of 1 week of left elbow pain. Laboratory results revealed that erythrocyte sedimentation rate was 110 mm/hour, serum creatinine level was 1 mg/dL, C-reactive protein level was 150 mg/L, and magnetic resonance imaging showed signal changes in favor of osteomyelitis at the olecranon level, with diffuse edematous appearance in the elbow skin tissue and increased intra-articular effusion. After diagnosis of osteomyelitis, ampicillin/sulbactam and teicoplanin were administered. After day 7 of admission, the patient developed acute kidney injury requiring hemodialysis under antibiotic treatment. Kidney biopsy was performed to determine the underlying cause, which showed Staphylococcus-related glomerulonephritis. Recovery of renal functions was observed after antibiotic and supportive treatment.

Key words: Osteomyelitis, Postinfectious glomerulonephritis, Staphylococcus aureus

Introduction

Postinfectious glomerulonephritis can occur after bacterial, viral, parasitic, and fungal infections; it most commonly affects children. Staphylococcus aureus is a rare cause of postinfectious glomerulonephritis, and Staphylococcus-related glomerulonephritis most commonly occurs in middle-aged or elderly patients. Staphylococcus-related glomerulonephritis is an immune complex-related disease in which the antigen component of the immune complex is derived from the infective agent. These antigens are planted in the glomeruli and cause activation of T cells, resulting in polyclonal B-cell activation and production of polyclonal immunoglobulin (Ig) A, IgG, and IgM and also causing complement activation. Staphylococcus-related glomerulonephritis usually develops after Staphylococcal infections such as endocarditis, ventriculoatrial shunt infections, pneumonia, visceral abscesses, and rarely osteomyelitis. Patients with Staphylococcus-related glomerulonephritis also present with hematuria, proteinuria of varying degrees, rising serum creatinine levels, and/or edema. The severity of renal insufficiency is proportional to the degree of proliferation and crescent formation.

At least 2 of the following criteria must be present for diagnosis of Staphylococcus-related glomerulonephritis: hypocomplementemia, endocapillary proliferation and exudation glomerulonephritis on light microscopy, and immunoglobulin A (IgA) dominant or codominant glomerular staining on immunofluorescence microscopy and hump-shaped subepithelial deposits on electron microscopy. Treatment of the disease in adults should focus on eradicating the infection, relieving symptoms, and controlling hypertension and edema. Here, we describe an episode of biopsy-proven diffuse proliferative glomerulonephritis occurring after osteomyelitis.

Case Report

A 58-year-old man with a history of type 2 diabetes mellitus and hypertension was admitted to the clinic with symptoms of 1 week of left elbow pain. On
physical examination, the patient was afebrile, hemodynamically stable, and showing hyperemia and warmth and limited movement in the left elbow. Laboratory results revealed that erythrocyte sedimentation rate was 110 mm/hour, serum creatinine level was 1 mg/dL, hemoglobin level was 11 g/dL, C-reactive protein level was 150 mg/L, and liver function tests and blood electrolyte levels were normal. Urine albumin (0.01 g/24 hours) and protein levels (0.1 g/24 hours) were also within normal ranges, and urinary analysis showed one leukocyte and erythrocyte.

Radiographic imaging was performed with preliminary diagnosis of osteomyelitis. Magnetic resonance imaging showed signal changes in favor of osteomyelitis at the olecranon level, with diffuse edematous appearance in the elbow skin tissue and increased intra-articular effusion. Blood cultures were positive for *Staphylococcus aureus*. After diagnosis of osteomyelitis, ampicillin/sulbactam (3 g/day) and teicoplanin (400 mg every 4 days) were administered.

After day 7 of admission, the patient developed acute kidney injury requiring hemodialysis, with decreased urine output and nephrotic-range proteinuria (5.33 g/24 hours). Laboratory results showed acute renal failure (creatinine level of 6.5 mg/dL, uric acid of 9.0 mg/dL, sodium of 143 mmol/L, calcium of 8.4 mg/dL, phosphorus of 7.5 mg/dL, and erythrocyte sedimentation rate of 95 mm/hour); urinary analysis showed 140 erythrocytes and 44 leukocytes. In addition, tests for antinuclear antibodies, cytoplasmic antineutrophil cytoplasmic antibodies, and perinuclear antineutrophil cytoplasmic antibodies were negative, and blood C3 and C4 levels were within normal range. The patient underwent a kidney biopsy for determination of the underlying cause, and hemodialysis was applied 2 times. Kidney biopsy analysis showed mesangial hypercellularity, segmental endocapillary hypercellularity, subepithelial deposits, and focal sclerosis in 10% of glomeruli. Immunoperoxidase staining showed strong granular deposits of immunoglobulin IgA and IgG and weak deposits of C3 within the glomerular mesangium.

After 14 days of admission, an increase in urine volume and a decrease in serum creatinine levels were observed, and dialysis treatment was terminated due to recovery of renal functions. Antibiotic treatment was continued for 4 weeks, and laboratory results showed that serum creatinine (0.8 mg/dL), urine albumin (0.02 g/24 hours), and protein levels (0.1 g/24 hours) were within normal ranges; urinary analysis showed no erythrocytes or leukocytes after antibiotic treatment. The patient has continued follow-up routine visits to our clinic.

**Discussion**

*Staphylococcus aureus* is the most common causative organism in acute osteomyelitis; however, it rarely causes postinfectious glomerulonephritis. Many affected adults have a predisposition to staphylococcal infection, such as those with diabetes, alcoholism, cancer, or intravenous drug addiction. The renal disease can occur 5 days to 4 weeks following the staphylococcal infection, and all of these patients have a strong chance for renal recovery under eradication of the underlying infection. In our case, glomerulonephritis developed after the first week of treatment, and recovery of renal function occurred due to successful treatment of osteomyelitis.

Staphylococcal antigens may activate T cells and polyclonal B cells and cause activation and production of polyclonal IgA, IgG, and IgM. Immunoglobulin A may react with staphylococcal antigens. This may explain, in part, why glomerular immune deposits in patients with *Staphylococcus*-related glomerulonephritis usually show heavy IgA deposits that are dominant or codominant with IgG.

Also, there was a similarity between C3 glomerulopathy and postinfectious glomerulonephritis. Activation of an alternative complement pathway causes development of postinfectious glomerulonephritis. Complement proteins and breakdown products in the glomeruli are the pathognomonic features of bright C3 staining on immunoperoxidase microscopy in the kidney biopsy. Kidney biopsy in postinfectious glomerulonephritis showed proliferative glomerulonephritis and subepithelial deposits on light microscopy and bright glomerular C3 staining with or without immunoglobulins on immunoperoxidase staining. These dome-shaped deposits are characteristic findings that locate under the effaced epithelium, particularly in the mesangial notch or waist regions. One indirect indication of the role of the alternative complement pathway is persistently low C3 levels noted in a small percentage of patients.
with postinfectious glomerulonephritis, although C3 titers typically normalize within 8 weeks of resolution of the infection. In our case, there was mesangial hypercellularity, segmental endocapillary hypercellularity, and subepithelial deposits on light microscopy. On immunofluorescence microscopy, there was IgA-dominant immunoglobulin staining with weak C3 staining.

In conclusion, we present a patient with osteomyelitis who developed acute kidney injury under antibiotic treatment, with kidney biopsy showing staphylococcus-related glomerulonephritis. Recovery of renal functions was observed after successful treatment.

References