An Adult With Acute Poststreptococcal Glomerulonephritis Complicated by Hemolytic Uremic Syndrome and Nephrotic Syndrome

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• **We report the case of a 47-year-old man with the simultaneous occurrence of clinical and laboratory features consistent with acute poststreptococcal glomerulonephritis (APSGN), hemolytic uremic syndrome (HUS), and nephrotic syndrome. Acute nephritic syndrome occurred 3 weeks after having pharyngeal pain and diarrhea. He presented with edema and hypertension on admission. Laboratory evaluation showed hemolytic anemia with fragmentation, thrombocytopenia, elevated lactic dehydrogenase level, low haptoglobin level, low complement C3 level, and elevated antistreptolysin-O titer. Serum creatinine level was 1.22 mg/dL (108 μmol/L), and urinalysis showed marked proteinuria, with protein of 8.7 g/d, and hematuria. The renal biopsy specimen was characteristic of APSGN, but not HUS. Moderate expansion of the mesangial matrix, moderate proliferation of epithelial and endothelial cells, and marked infiltration of neutrophils was seen by means of light microscopy, and many subepithelial humps were seen by means of electron microscopy. Neither fibrin deposition nor evidence of thrombotic microangiopathy was found. Complement C3 deposition along the capillary wall and tubules was seen in an immunofluorescence study. The patient was administered plasma infusion at 320 mL/d and antihypertensive drugs. Serum complement C3 and haptoglobin levels returned to normal within 3 weeks. This is a rare case of the simultaneous occurrence of APSGN, HUS, and nephrotic syndrome. *Am J Kidney Dis* 46:E59-E63.**

INDEX WORDS: Acute poststreptococcal glomerulonephritis; hemolytic uremic syndrome; nephrotic syndrome; nephritis-associated plasmin receptor.

ACUTE POSTSTREPTOCOCCAL glomerulonephritis (APSGN) is found mostly in children 2 to 12 years of age, but is more severe in adults. It is caused mainly by otopharyngeal or skin infection from group A β-hemolytic streptococci. APSGN generally is induced by the glomerular deposition of nephritogenic streptococcal antigen. Streptococcal proteins, such as nephritis strain–associated protein,[1] streptococcal pyrogenic exotoxin B,[2] and nephritis-associated plasmin receptor (NAPlr),[3] are nephritogenic antigens in patients with APSGN. The main clinical manifestation is acute nephritic syndrome characterized by gross hematuria, hypertension, azotemia, and edema. Proteinuria usually is mild, and the rate of APSGN-complicated nephrotic syndrome is less than 10%. Baldwin et al[4] reported that the rate of APSGN with nephrotic syndrome in adults was 20%.

Hemolytic uremic syndrome (HUS) is an acute disorder characterized by the triad of microangiopathic hemolytic anemia, nephropathy, and thrombocytopenia. The majority of patients are children, although adults can be affected. HUS in adults often is a complication of an autoimmune disease, hormonal imbalance, drugs, malignant hypertension, and transplant rejection. HUS-complicated APSGN is rare.

We report an adult with serological and pathological evidence of poststreptococcal glomerulonephritis complicated with hemolytic anemia, thrombocytopenia, and nephrotic syndrome.

CASE REPORT

A 47-year-old man had pharyngeal pain and diarrhea without bloody stool on October 20, 2003. After treatment with antibiotics, these symptoms improved. Three weeks later, he had hypertension and anasarca and a gain in body weight. Because urinary abnormalities and renal dysfunc-

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tion appeared, he was admitted to our hospital on November 9.

On admission, the patient's body temperature was 36.4°C, blood pressure was 182/100 mm Hg, and pulse rate was 60 beats/min. He had pretibial edema, but did not show skin lesions. Urinary protein excretion was 8.7 g/d, and many urinary red blood cells were seen in high-power fields. Hematologically, his white blood cell count was 12,700/μL, with 74% neutrophils. Hemoglobin level (10.6 g/dL [106 g/L]) and platelet count ($4.4 \times 10^4/\mu$L) were decreased, and a peripheral-blood smear showed fragmentation of red blood cells. Blood urea nitrogen level was 35 mg/dL (12.5 mmol/L), creatinine level was 1.22 mg/dL (108 μmol/L), and creatinine clearance was 67.8 mL/min (1.13 mL/s). Total protein level was 5.5 g/dL (55 g/L); albumin, 3.0 g/dL (30 g/L); aspartate aminotransferase, 27 IU/L; alanine aminotransferase, 18 IU/L; and lactate dehydrogenase, 629 IU/L (normal, 100 to 225 IU/L). The patient's prothrombin time index was 71.7%, and activated partial thromboplastin time was 26.9 seconds (control, 30.3 seconds). Fibrin/fibrinogen degradation products were 7 μg/mL (normal, <4 μg/mL); d-dimer, 14.8 μg/mL (normal, <1.0 μg/mL); von Willebrand factor activity, 163%; and haptoglobin, <10 mg/dL (<1.0 μmol/L). C-Reactive protein level was 1.4 mg/dL; immunoglobulin G, 1,280 mg/dL (12.8 g/L); immunoglobulin A, 224 mg/dL (2.24 g/L); and immunoglobulin M, 63 mg/dL (0.63 g/L). Also, complement C3 level was 12 mg/dL (0.12 g/L; normal, 60 to 116 mg/dL); C4, 26 mg/dL (0.26 g/L; normal, 15 to 44 mg/dL); and CH50, 21 U/mL (normal, 30 to 50 U/mL). Test results for antinuclear antibody, anti-DNA antibody, antineutrophil cytoplasmic antibody, and cryoglobulin were negative. Antistreptolysin-O titer was 791 IU/mL (normal, <166 IU/mL), and antistreptokinase titer was 20,480 (normal, <640).

There was no evidence of infection caused by Epstein-Barr virus; hepatitis A, B, or C virus; or human immunodeficiency virus, and stool and pharyngeal culture results also were negative. Chest radiograph showed pleural effusion without infiltrated shadow. Abdominal ultrasonography did not show abnormalities. His past medical history was unremarkable.

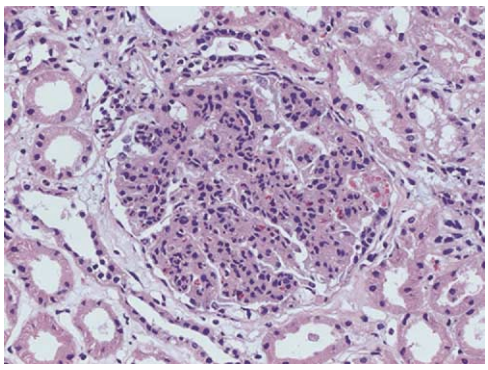

Fig 1. With light microscopy, endocapillary proliferative glomerular changes and marked infiltration of neutrophils were found. (Hematoxylin and eosin stain; original magnification ×400.)

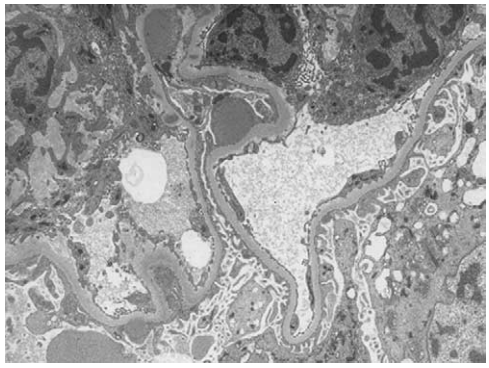

Fig 2. With electron microscopy, many subepithelial humps and endothelial and mesangial cell proliferation were seen. No fibrin deposition or evidence of thrombotic microangiopathy was found.

A percutaneous renal biopsy was performed on day 7. Light microscopy showed endocapillary proliferative glomerular changes and marked infiltration of neutrophils (Fig 1). One of 22 glomeruli showed global sclerosis, and 2 glomeruli showed fibrocellular crescent formation. Electron microscopy showed many subepithelial humps and endothelial and mesangial cell proliferation. However, there was no fibrin deposition or evidence of thrombotic microangiopathy (Fig 2).

In an immunofluorescence study, complement C3 deposition along the capillary wall was seen in a starry-sky type appearance (Fig 3), but immunoglobulin deposition was negative. We also examined NAPlr, which was isolated from group A streptococcus T types 1, 4, and 12 and M types 12 and 49 obtained from the pharynx of patients with APSGN. NAPlr is present mainly in kidney specimens from the early stage of APSGN.[3] NAPlr was positive along part of the capillary wall and mesangium (Fig 4). These findings are characteristic of APSGN.

Based on these results, we made the diagnosis of APSGN complicated with nephrotic syndrome and HUS,

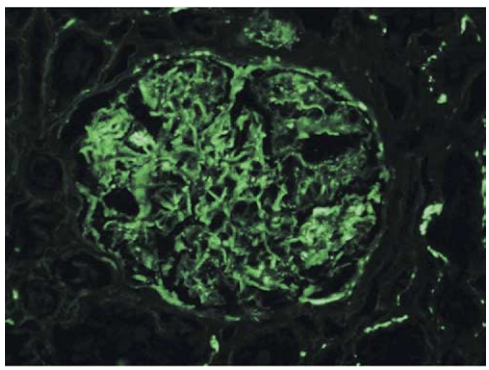

Fig 3. Immunofluorescence study showed the starry-sky type of complement C3 deposition along the capillary wall and tubules.