Rapidly Progressive Glomerulonephritis following Hemolytic Crisis

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and impairment of the renal function progressed and on the third day after admission hemodialysis was begun. Renal biopsy was performed, showing on light microscopy, cellular crescent formation in 90% of glomeruli without necrotizing lesions (fig. 1). Tubules showed localized necroses, scanty tubular pigmented casts and mild interstitial inflammatory reaction. Immunofluorescence for IgG, IgA, IgM, fibrinogen and C3 was negative except for occasional and scanty deposits of C3 in the mesangium. No electron microscopic study was performed. Three intravenous boluses of methylprednisolone 1 g/day × 3 days followed by predni-

Dear Sir,

A 76-year-old man was admitted to the Hospital with a 2-day history of progressive malaise, dyspnea and orthopnea. Six years earlier he was investigated for anemia and found to have spherocytes in peripheral blood and a positive incubated osmotic fragility test. Familial search disclosed three first-degree relatives with the same findings. He was diagnosed as having hereditary spherocytosis and became transfusion-dependent because of progressive and severe anemia.

Physical examination revealed a blood pressure of 179/90 mm Hg and the pulse was 126 beats/min. He was tachypneic, pale and mildly jaundiced. A loud third heart sound and a low-grade systolic cardiac murmur were audible. Other findings were bibasilar rales and severe hepatosplenomegaly.

Laboratory data included: hematocrit 15% (0.15); hemoglobin 7.75 g/dl (77.5 g/l); WBC $2.3 \times 1,000/\text{mm}^3$; platelets $78 \times 10^3/\text{mm}^3$; urea 188 mg/dl (67 mmol/l) and serum creatinine was 5.4 mg/dl (477.3 $\mu\text{mol/l}$); serum LDH 1,764 U/l and serum bilirubin 4.44 mg/dl (76 $\mu\text{mol/l}$) (unconjugated 3.9 mg/dl). The Coombs test was negative and serum haptoglobin was < 5 mg/dl. Anti-nuclear antibodies, antineutrophil cytoplasmic antibodies (ANCA) and circulating anti-GBM antibodies were negative. Microscopic examination of the urine disclosed 50-60 red blood cells; hemoglobinuria was positive and urinary protein excretion was 2.6 g/24 h. Chest x-ray showed an enlarged cardiac silhouette, alveolar pulmonary edema and Kerley B lines.

Blood transfusion, vasodilators and diuretics were instituted. However, oliguria

Fig. 1. Renal biopsy demonstrates massive cellular crescent formation and tubular pigmented casts (arrow). PAS. $\times 108$.

sone 1 mg/kg/day were administered without improvement of renal function. The patient entered a chronic hemodialysis program. Because of recurrent hemolytic crises and repeated blood transfusions in spite of erythropoietin treatment, splenectomy was performed. After splenectomy, hemolytic crises did not recur and transfusions could be withheld.

Comments: Hereditary spherocytosis is an inherited hemolytic anemia characterized by spectrin-deficient red cells. The hallmarks of hereditary spherocytosis are anemia, jaundice and splenomegaly. Clinical severity can vary widely; in old age, when bone marrow

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becomes sluggish, patients may become dangerously anemic. The clinical course is interrupted in most patients by periodic hemolytic crises.

The exact factor causing crescent formation is unknown, but passage of blood components through glomerular capillary wall gaps and contact with Bowman's space has been incriminated. In particular, fibrin deposition and polymerization and macrophage activation appear to be important [1].

Some studies indicate that patients with mesangial IgA nephropathy have a high likelihood of focal and segmental proliferative changes with crescents on renal biopsy specimens during an acute episode of macroscopic hematuria [2, 3]. These clinical and histologic studies suggest that glomerular bleeding may result in focal breaks in the glomerular basement membrane, and that through them intravascular contents leak into Bowman's space and they are presumed to be the cause of crescent formation. These episodes of macroscopic hematuria are often associated with renal dysfunction which is frequent-

ly reversible. Similar to what occurs in IgA nephropathy, hemolytic crises in our patient could have induced extracapillary proliferation. The hemolytic episode was demonstrated by severe anemia, jaundice, reticulocytosis, elevated LDH levels and absent haptoglobin. It was followed immediately in time by the development of RPGN. This temporal relationship argues in favor of hemolysis being a cause of extracapillary proliferation. Moreover, other causes of RPGN such as anti-GBM nephritis and ANCA-associated vasculitis [4, 5] were ruled out, and no other known cause of it was apparent. The mechanism by which hemolysis could induce extracapillary proliferation is not known at the moment, but one can speculate about an increase in procoagulant activity associated with hemolysis or a toxic effect of red blood cell breakdown products like hemoglobin or altered red blood cell membrane components. We believe that regardless of the mechanism, severe hemolysis should be considered a potential cause of RPGN.

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