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Pathological Case of the Month

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A 16-YEAR-OLD BOY complained of puffiness of the face and legs that was especially noticable in the morning and had persisted for 2 to 3 months, as well as nausea, vomiting, a cough, and hemoptysis that had lasted for 2 to 3 days. He had had a tonsillectomy 5 years before and had been smoking nearly 30 cigarettes a day for 3 years. He was the child of first cousins. A physical examination showed a blood pressure reading of 120/80 mm Hg, a heart rate of 80/min, and a respiratory rate of 22/min. He was pale and weak and had marked edema in his eyelids and lower extremities. Decreased sounds could be heard at the base of the lungs. Laboratory investigations revealed a urinary pH of 5, a urine-specific gravity of 1015, proteinuria (4+), numerous erythrocytes, and a few leukocytes in the urine sediment. The hemoglobin level was 10.3 g/dL, and the white blood cell count was 7300/µL; all of the cells were normal on a peripheral blood smear. The erythrocyte sedimentation rate was 50 mm/h. Biochemical findings showed the following concentrations: urea, 148 mg/dL; creatinine, 4.9 mg/dL (433 µmol/L); sodium, 141 mEq/L; total protein, 3.9 g/dL; albumin, 1.8 g/dL; calcium, 7.1 mg/dL; phosphorus, 9 mg/dL (2.91 mmol/L); alkaline phosphatase, 86 U/L; triglycerides, 234 mg/dL (2.64 mmol/L); and cholesterol, 215 mg/dL (5.56 mmol/L). The creatinine clearance was 11 mL/min (0.18 mL/s)/1.73 m^2. Test results were negative for antinuclear antibody and anti-DNA. Serum complement 3 (C3) and C4, serum iron and serum iron binding capacity, ferritin, prothrombin time, and partial thromboplastin time were all within normal limits. A plain chest x-ray film showed perihilar infiltration. Both of the kidneys were larger than normal with grade 2 echogenity on abdominal ultrasonography. A sputum examination was negative for hemosiderin-laden macrophages. A test for plasma anti–glomerular basement membrane (anti-GBM) antibody was positive. The kidney biopsy specimen showed glomerular epithelial crescents on light microscopy (**Figure 1**) and inflammatory infiltrate (**Figure 2**). A linear stain was seen along the GBM for IgG and C3 and to a lesser extent for IgM on an immunofluorescent examination. Treatment was started with prednisolone and furosemide. The patient's clinical condition gradually worsened with decreasing urine output, hypertension, and increasing blood urea and creatinine levels. He was given hemodialysis 3 times weekly and continued with prednisolone therapy, but unfortunately he did not respond and died.

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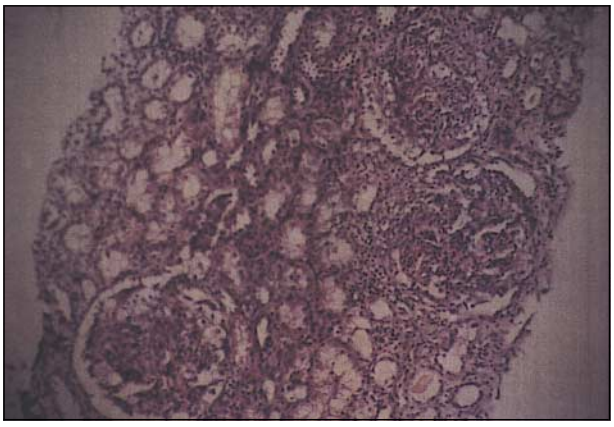

Figure 1.

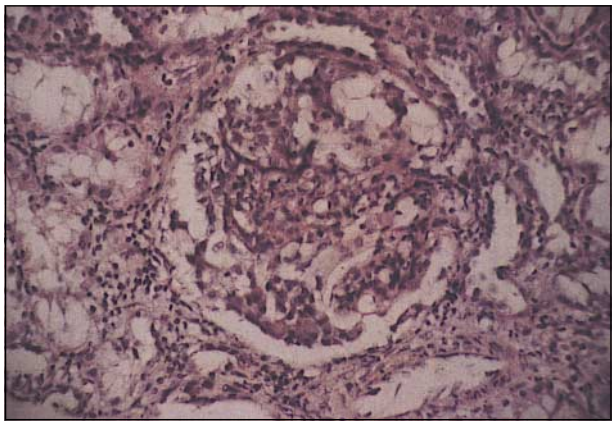

Figure 2.

Diagnosis and Discussion

Goodpasture Disease

Figure 1. Marked crescent formation of polymorphonuclear leukocytes associated with generalized edema and fibrotic expansions (hematoxylin-eosin, original magnification × 20).

Figure 2. Inflammatory infiltration of polymorphonclear leukocytes (hematoxylin-eosin, original magnification × 40).

The association of rapidly progressive glomerulonephritis and pulmonary hemorrhage is classically known as Goodpasture syndrome (GPS). In the presence of autoantibodies directed against glomerular and alveolar basement membranes, it is called Goodpasture disease (GPD) or anti-GBM disease. Goodpasture disease accounts for 20% to 40% of cases of GPS. The rest are caused by systemic vasculitis: most commonly by Wegener granulomatosis, microscopic polyarteritis, and systemic lupus erythematosus and less commonly by Churg-Strauss syndrome, Henoch-Schönlein purpura, Behçet disease, essential mixed cryoglobulinemia, rheumatoid vasculitis, and drugs such as penicillamine and hydralazine hydrochloride.[1]

Whereas some patients may manifest glomerulonephritis and pulmonary hemorrhage in isolation, others may have either severe pulmonary and renal involvement or proteinuria and hematuria along with normal renal and pulmonary functions.[1-3] The presence of pulmonary hemorrhage is closely related to that of pulmonary irritants, especially cigarette smoking as in our patient.[2,4-6] Pulmonary hemorrhage is extremely rare in nonsmokers.[1]

The most common laboratory abnormality in GPD is a positive result for anti-GBM antibodies in 90% of patients. The kidney biopsy finding of crescent formation may involve 80% to 100% of glomeruli. Diffuse linear immunoglobulin G deposition is seen along the GBM on an immunofluorescent examination.[1,2,4] The biopsy findings and the presence of anti-GBM antibodies in our patient were consistent with GPD.

Rapidly progressive glomerulonephritis and such factors as systemic lupus erythematosus, polyarteritis nodosa, Henoch-Schönlein purpura, hypersensitivity angiitis, mixed connective tissue disease, Wegener granulomatosis, and a drug reaction that may cause pulmonary-renal syndrome should be considered in the differential diagnosis.[1] The clinical and laboratory findings in our patient were inconsistent with these disorders.

Most patients with GPS progress rapidly to end-stage renal disease. Increased creatinine levels, oligoanuria, and the severity of renal lesions indicate a poor prognosis.[4]

New therapeutic approaches such as plasmapheresis and treatment with cyclosporine, cyclophosphamide, and prednisolone may be effective in 80% of patients.[1,7] However, patients with end-stage renal failure and those who require dialysis rarely improve.[1,2]

Accepted for publication May 23, 2000.

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