Goodpasture's Syndrome Mimicking Idiopathic Pulmonary Hemosiderosis*

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ABSTRACT

A patient initially diagnosed by clinical findings and pulmonary biopsy as suffering from idiopathic hemosiderosis was subsequently proven by renal biopsy and serologic assay to have Goodpasture's syndrome with minimal renal alterations. The authors speculate on the relationship of these two complex disorders.

The causes of idiopathic pulmonary hemosiderosis, its pathogenesis, and its relationship to renal disease are unclear. It is known that the clinical picture seen in idiopathic pulmonary hemosiderosis may mimic the pulmonary manifestations of Goodpasture's syndrome.11 A case is presented initially diagnosed as idiopathic pulmonary hemosiderosis which was subsequently found to be Goodpasture's syndrome with normal renal function. Speculation is made on the relationship of these two complex disorders.

Case Report

A 29-year old Black female was admitted to Hahnemann University Hospital because of dyspnea, weakness on exertion for three weeks, and hemoptysis over a five day period. Physical examination upon admission showed the pulse to be 80 per minute. The blood pressure was 120/80 mmHg, and respirations were 20 and unlabored. The lungs had decreased breath sounds on the left with occasional crackles throughout both lung fields. The heart, breasts, abdomen, and extremities were normal. The chest roentgenogram showed diffuse interstitial infiltrates throughout the right lung with areas of possible consolidation and questionable diffuse infiltrate of the lower left lobe. The hematocrit was 20.9 percent, the white cell count was 9,400 per cmm, with 82 percent neutrophils, two percent bands, 13 percent lymphocytes, and the platelet count of 408,000 per ml. The prothrombin time and partial thromboplastin time were both normal. Serum electrolytes, blood area nitrogen, and serum creatinine were all within normal limits. Initial urinalysis was negative. On repeated urinalysis, trace protein, 10 to 20 red blood cells, 2 to 20 white blood cells, and occasional red blood cell casts were detected.

Three days after admission, the patient developed worsening dyspnea, and an open lung biopsy was performed. Light microscopic examination revealed marked intra-alveolar hemorrhage and large collections of hemosiderin-laden macrophages within the alveoli and small bronchi. The interstitium was widened by a focal lymphoreticular infiltrate, numerous hemosiderin-laden macrophages and focal fibrosis (figures 1 and 2). Immunofluorescence

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Figure 1. The lung biopsy specimen demonstrates hemosiderin laden macrophages, a focal lymphoctic inflammatory infiltrate, and focal fibrosis of the interstitium (hematoxylin and eosin: ×700).

Figure 2. Iron preparation of lung biopsy highlights the hemosiderin laden macrophages (Prussian blue; ×700).
FIGURE 3. By immuno­fluorescence microscopy, a portion of the lung stained for IgG, shows intermittent linear deposits of the antibody along the alveolar basement membrane (fluorescence labeled anti-IgG; ×400).

FIGURE 4. Ultrastructurally, the alveolar basement membrane is intact (uranyl acetate, lead citrate; ×10,000).
microscopy demonstrated intermittent linear deposits of IgG and C3 within the alveolar basement membranes (figure 3), and electron microscopy showed intact alveolar basement membranes (figure 4).

The patient was transfused with five units of packed red blood cells. Hematocrit stabilized thereafter with gradual normalization of pulmonic findings.

Based upon the slight abnormalities of the urinalysis, an open renal biopsy was performed three weeks after admission to evaluate the relationship of the pulmonary and renal lesions. By light microscopy, all 45 glomeruli were normal (figure 5). The interstitium exhibited negligible fibrosis. The tubules and vessels were unremarkable. Immunofluorescent microscopy demonstrated conspicuous linear deposits of IgG and C3 within all glomeruli (figure 6), and by electron microscopy sparse electron-lucencies in the glomerular basement membrane were noticed (figure 7).

Radioimmunoassay performed at the Scripps Clinic in La Jolla, California subsequently demonstrated a low titer of circulating antibodies to glomerular basement membrane.

Discussion

The patient presented herein, initially diagnosed by clinical and pathological methods as having idiopathic pulmonary hemosiderosis, was subsequently found to have Goodpasture's syndrome with normal renal function. The latter diagnosis is based upon the positive immunofluorescent microscopic studies of both the lung and kidney and upon positive assay for circulating antibodies to glomerular basement membrane.

The initiator(s) of idiopathic pulmonary hemosiderosis is largely unknown; however, it has been postulated that idiopathic pulmonary hemosiderosis involves an abnormality of alveolar epithelial growth and function which results in alveolar capillary bleeding.6,11 Also as noted by Donlan,5 there may be focal deposition of collagen and elastic fibers in the interstitium. The bleeding may be produced by breaks in the capillary basement membrane as seen in ultrastructural studies that are similar to those noted in Goodpasture's syndrome.6,8 Ultrastructural studies have also revealed the presence of osmiophilic amorphous deposits within the basement membrane, between the endothelium and the basement membrane, or just external to the basement membrane.6 The deposits may indicate that an immunopathogenic mechanism is involved in idiopathic pulmonary hemosiderosis. Donald4 suggests that there may be different mechanisms of tissue injury allowing distinction between the diseases based on ultrastructural evidence. He speculates that in Goodpasture's syndrome the findings are of primary vascular injury while in idiopathic pulmonary hemosiderosis there are focal rupture and progressive collagenization of the basement membrane with abnormalities to the pneumocytes. However, our patient exhibited focal fibrosis as well as hyperplasia of pneumocytes.

The data are scant concerning pulmonary deposition of antibody in idiopathic pulmonary hemosiderosis. Of seven reported cases of idiopathic pulmonary hemosiderosis in which immunofluorescence was mentioned, five were negative; in two cases, no immunofluorescence studies were performed.3,4,6,10 By contrast, in cases of Goodpasture’s syndrome in which pulmonary clinical and pathological manifestations closely resemble those of idiopathic pulmonary hemosiderosis, there may be positive linear staining for IgG in the alveolar basement membranes as well as the glomerular basement membranes. However, Donald4 records a case of Goodpasture's syndrome where immunofluorescent staining of the lung was negative while there was linear staining for IgG along the glomerular basement membranes.

The classical Goodpasture's syndrome presents a rapidly progressive crescentic glomerulonephritis. In the case presented herein, renal function was normal. Rarely, other authors have noted normal renal function in cases of Goodpasture's syndrome.9 It is of interest that articles concerning Goodpasture's syn-
Figure 5. By light microscopy, the glomeruli are normal (hematoxylin and eosin; ×600).

Figure 6. By immunofluorescence microscopy, the renal biopsy specimen shows linear deposition of IgG along the glomerular basement membranes (fluorescence labeled anti-IgG; ×250).
GOODPASTURE’S SYNDROME

Figure 7. Ultrastructural electron-lucencies of the glomerular basement membrane are noticed (uranyl acetate, lead citrate; x 40,000).

drome typically describe pulmonary manifestations consistent with idiopathic pulmonary hemosiderosis but tend to ignore pathophysiologic relationships between the two entities.

The case presented herein underscores the fact that some cases diagnosed as idiopathic pulmonary hemosiderosis may, in fact, be Goodpasture’s syndrome with minimal or early renal alterations. Gonzalez-Cusse proposes a spectrum of kidney-lung syndromes emerging from Goodpasture’s observations and raises the possibility that idiopathic pulmonary hemosiderosis may represent a stage of evolution of a broader pathoanatomic entity. Patients suspected of suffering from idiopathic pulmonary hemosiderosis should undergo a careful renal evaluation, and, if a lung biopsy is performed, immunofluorescence to detect antibodies to alveolar basement membrane seems warranted as well as electron microscopic studies. A thorough prospective clinicopathologic study of patients who suffer from idiopathic pulmonary hemosiderosis would further define the relationship between that
entity and Goodpasture's syndrome, but the major difficulty of such inquiry is that both conditions are uncommon.

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