Pulmonary Alveolar Phospholipoproteinosis Associated with Amyloidosis

To the Editor:

Pulmonary alveolar phospholipoproteinosis (PAP) is a rare disorder characterized by deposition of lipoprotein material in the alveoli. The disease has been associated with a variety of infections, hematologic malignancies, and exposure to certain dusts and chemicals. In the case presented here, pathologic features characteristic of PAP have been documented in a patient with renal amyloidosis. To our knowledge, this association has never been reported before.

A 37-year-old man was admitted to the hospital because of severe abdominal pain of acute onset in the right upper quadrant, fever, chills, and asthenia of three days duration. The abdominal pain radiated to the anterior costal area and increased with cough and inspiratory movements. Forty-five days pre-admission, the patient had a short episode of fever accompanied by ankle edema that resolved with nonspecific therapy. Temperature was 39°C. On admission, an x-ray film of the chest showed consolidation in the middle and inferior right lobes and lower left lobe. Urinalysis revealed heavy proteinuria (5.5 g per day). Escherichia coli was consistently isolated in repeated blood cultures taken at 12-h intervals. Liver function tests disclosed normal aminotransferase levels and HBsAg-positive serum; anti-HBc antibodies were detected. Fever subsided after four days of antibiotic therapy with cephalosporins and aminoglycosides. Three months later, images of pulmonary consolidation persisted. Descending urography was normal. Proteinuria ranged from 2.8 to 4.7 g per day. Tuberculin skin test (5 and 10 TU of PPD-T) was negative. Acid-fast bacilli in sputum smears were not identified. A percutaneous liver biopsy showed auromine-negative granulomas without caseous necrosis. Because chest roentgenograms did not reveal changes, a thoracotomy/lung biopsy was performed. The most characteristic microscopic feature was the filling of large groups of alveoli with a granular and proteinaceous material that yielded a positive periodic acid-Schiff reaction, but negative to stain with alcin blue. A diagnosis of PAP was established. Renal biopsy included ten glomeruli infiltrated with eosinophilic, amorphous deposits which were positive with Congo red stain and revealed apple-green birefringence under polarized light. Deposition of amyloid, particularly in the vascular pole, mesangium, and in some capillary loops was found in all glomeruli. Similar depositions were also observed in the subintima of arterial vessels. The diagnosis of AA-type amyloidosis was made. Neither the liver nor lung parenchyma showed amyloid deposits. The patient underwent four therapeutic bronchoalveolar lavages, but the lung infiltrates did not tend to disappear. Lavages were discontinued upon the patient's request. The nephrotic syndrome improved progressively; ten months after admission there was a proteinuria <1 g per day. Corticosteroids were not given. The chest roentgenogram abnormalities vanished in a parallel manner. Complete roentgenographic resolution was evident six years after diagnosis of PAP. At present (eight years after admission), the patient has normal pulmonary and renal function.

The pathogenesis of PAP remains obscure. Defective macrophage function is a major feature of PAP. It has been suggested that impaired phagocytic activity of pulmonary macrophages may result from altered cell-mediated immunity. The clinical spectrum of the disorder varies between lack of symptoms and major restrictive pulmonary dysfunction. Patients with PAP may show spontaneous resolution, response to therapeutic lavage, or may die as a result of progressive respiratory failure or opportunistic infections. The case presented here illustrates an interesting occurrence of PAP and renal amyloidosis. Apparently the patient showed no response to therapeutic lavage and continued to have evidence of chronic interstitial infiltrates for several years; spontaneous resolution was noticed in the eighth follow-up year. Both amyloid disease and PAP have common disturbances in immunoregulatory mechanisms as an important step in the pathogenesis. Whether the intra-alveolar accumulation of phospholipids is a nonspecific response to a wide range of factors or represents an unknown type of immune disorder is open to question.

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