Idiopathic Thrombocytopenic Purpura Occurring with Interstitial Pneumonitis

JOHN J. MAY, M.D.; MARVIN I. SCHWARZ, M.D.; and ROBERT B. DREISIN, M.D.

Veterans Administration Hospital; Denver, Colorado

INTERSTITIAL PNEUMONITIS occurs with connective tissue diseases and other disorders thought to be autoimmune in nature (Hashimoto's thyroiditis, chronic active hepatitis, pernicious anemia, autoimmune hemolytic anemia) (1, 2). The association of interstitial pneumonitis and idiopathic thrombocytopenic purpura has not previously been described. We present here a case documenting this association.

An 81-year-old man was admitted after 9 months of progressive dyspnea and a 7-kg weight loss. He had a cough, moderate sputum production, and increased bruising. His respiration rate was 20 and he had bibasilar rales. His pulmonic second sound was increased. He had no hepatosplenomegaly or clubbing; large ecchymoses, however, were present. Platelet count was 42 000/mm^3; complete blood count findings were normal. Review of chest roentgenograms for the past 3 years revealed a reduced lung volume, prominent pulmonary arteries, and a dense bibasilar interstitial pattern that had progressed in recent months. A bone marrow biopsy revealed adequate megakaryocytes. Liver-spleen scan was normal. The chromium-51 platelet half-life was 1.5 days (normal, 3.7 ± 0.03 days). Pulmonary function test findings showed a reduction in all lung volumes and a marked reduction in the diffusing capacity. Rheumatoid and antinuclear factors were absent. After platelet infusion, the patient underwent an uncomplicated open lung biopsy. Prednisone therapy, 60 mg/day, was begun postoperatively. The platelet count subsequently has stabilized at 225 000/mm^3, and the diffusing capacity has increased from 23% to 55% of predicted. Subjectively, his dyspnea is markedly improved, and chest radiograph indicates moderate improvement. He has continued to take the small amounts of indomethacin (< 25 mg/day) that he took preoperatively.

Microscopic examination revealed cellular infiltration of the alveolar walls by lymphocytes, plasma cells, and eosinophils. Fibrous tissue was present in alveoli adjacent to bronchioles. Many alveoli were lined by hyperplastic epithelium and filled with histiocytes. Increased numbers of lymphoid follicles were present (Figure 1A). Direct immunofluorescence as previously described (3) showed granular deposits of IgG, IgA, C_3, and fibrinogen along alveolar walls and vessels (Figure 1A). Immunoglobulin M and albumin stains were negative (Figure 1B). Antiplatelet antibody studies measuring platelet surface IgG were done by the complement lysis inhibition assay (4). This patient's platelet-bound IgG was significantly elevated at 18.6×10^{-15} g of IgG/platelet (normal, less than 10×10^{-15} g of IgG/platelet). Circulating immune complexes were measured by the Raji-cell radioimmune assay (5) and found to be markedly elevated at 400 μg/ml (normal, less than 12 μg/ml) in the pretreatment phase, fall-

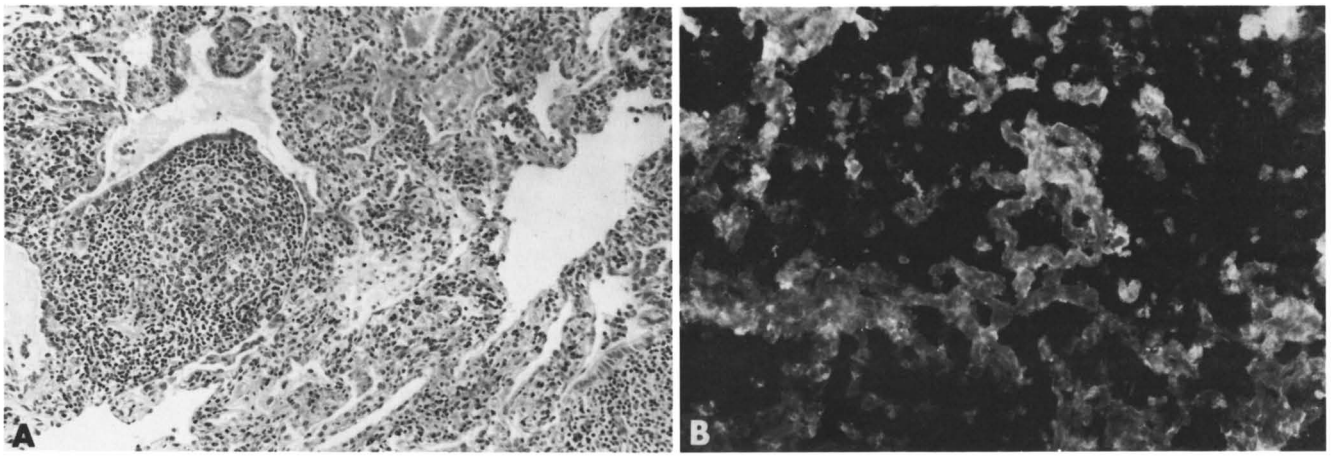

Figure 1A. Open lung biopsy showing thickening of alveolar walls with a dense cellular infiltrate of lymphocytes and monocytes. Additionally, there is some hyperplasia of alveolar lining cells and intra-alveolar collections of macrophages. (Hematoxylin and eosin stain; original magnification, × 164.) **B.** Immunofluorescent stain of lung biopsy showing IgG deposits in a granular pattern within alveolar walls and blood vessels. (Original magnification, × 40.)

ing to 80 μg/ml 13 days after the start of prednisone therapy.

Dreisin and associates (6) recently reported a high prevalence of circulating immune complexes in patients with a predominantly cellular idiopathic interstitial pneumonitis. The presence of circulating immune complexes correlated highly with immune complexes in lung tissue in an immunofluorescent pattern similar to that described in our patient. Our patient's favorable response to prednisone reflects the experience in other patients with high circulating immune complex levels (6).

Our patient's idiopathic thrombocytopenic purpura is documented by thrombocytopenia in the presence of a normal-sized spleen, adequate megakaryocytes, and shortened platelet survival. This disorder may occur with indomethacin; however, it is very unlikely that the small doses used by this patient could explain his thrombocytopenia, particularly since he continued to take it on an intermittent basis after discharge. Immune-complex-induced platelet aggregation, as proposed by Myllyla and colleagues (7) in postrubella thrombocytopenia, appears to be a possible mechanism of the thrombocytopenia noted in this patient with very high levels of circulating immune complexes. Thus, the elevated levels of platelet-bound IgG in our patient could indicate circulating immune complexes are bound to the platelet rather than that the antiplatelet membrane IgG is present. The latter appears to be more common in adults with idiopathic thrombocytopenic purpura (4, 8).

The concurrence of idiopathic thrombocytopenic purpura and interstitial pneumonitis has not previously been noted. It is not unexpected in view of the association of interstitial disease with other autoimmune disorders.

Scadding (2) described two cases of interstitial pneumonitis with autoimmune hemolytic anemia. He speculated that trapping of antibody-complement coated erythrocytes in the lung might lead to inflammation of the alveolar walls. A similar phenomenon involving deposits of coated platelet aggregates in the alveolar walls may be present in this patient. The idiopathic thrombocytopenic purpura and interstitial pneumonitis may have interacted in one of two ways. The platelet aggregates of primary idiopathic thrombocytopenic purpura may have collected in the lung, with subsequent inflammation and interstitial pneumonitis. A more likely relationship is that the circulating immune complexes associated with interstitial pneumonitis reached such high levels that platelet aggregation began to occur. Pulmonary deposits of platelet aggregates may have then contributed to the progression of the pneumonitis that preceded his admission. This is supported by experimental models in which release of vasoactive substances from platelets increases vascular permeability and allows trapping of larger immune complexes along vascular membranes, accelerating the inflammatory process (9).

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