Pulmonary Hemorrhage in Systemic Necrotizing Vasculitis Associated with Hepatitis B*

T. S. Bocanegra, M.D.; † L. R. Espinoza, M.D.; ‡ F. B. Vasey, M.D.; § and B. F. Germain, M.D.||

Reported here is the first case of massive intrapulmonary hemorrhage emerging in the setting of systemic necrotizing vasculitis associated with hepatitis B surface antigen (HBsAg)—positive viral hepatitis. Demonstration of circulating immune complexes, cryoglobulins containing both HBsAg and HBsAb, and resolution of the symptoms following immunosuppressive therapy suggest an immune complex mediated tissue injury for this unusual complication.

Although the systemic necrotizing vasculitides are diseases that can affect any organ of the body, the lungs are characteristically spared except in the granulomatous variants. Recently, however, the development of diffuse intrapulmonary hemorrhage in the course of nongranulomatous systemic necrotizing vasculitis has been documented. We report here the occurrence of pulmonary hemorrhage in a patient with hepatitis B associated vasculitis during a period of active disease.

CASE REPORT

A 48-year-old man was admitted with a four-week history of malaise, anorexia, and arthritis. Physical examination showed an acutely ill and icteric patient, tender hepatomegaly, and symmetrical generalized polyarthritis. Laboratory examination revealed the following values: hemoglobin, 13.7 g/100 ml; hematocrit, 40 percent; WBC count, 8,200/cu mm; 10 percent eosinophils; SGOT, 905 IU/100 ml; SGPT, 1,360 IU/100 ml; positive serum HBsAg; creatinine, 1.0 mg/100 ml; normal urinalysis; and normal chest roentgenogram. In the following weeks, the liver enzymes and eosinophil count returned to normal, but the patient developed fever, epididymitis, and mononeuritis multiplex. A gastrocnemius muscle biopsy specimen demonstrated necrotizing vasculitis in medium-sized arteries without eosinophils or granulomas. Treatment with prednisone, 40 mg/day, was initiated and because of the lack of clinical response, the dose was increased to 70 mg/day. Two weeks later, the patient developed cough and shortness of breath followed by massive painless hemoptysis with a fall in the hematocrit to 20 percent. On examination, blood pressure was 146/80, respirations, 24 per minute, and pulse rate, 108 beats per minute. Diffuse and bilateral pulmonary rales were heard but no murmurs or gallop. Platelet count, coagulation profile, and serial determinations of SGOT, CPK, LDH, and ECGs were within normal limits while the chest

*From the Division of Rheumatology, Department of Medicine, College of Medicine, University of South Florida, Tampa, FL.
†Fellow in Rheumatology.
‡Associate Professor of Medicine.
§Assistant Professor of Medicine.
||Director, Division of Rheumatology.
Reprint requests: Dr. Espinoza, Box 19, USF Medical Center, Tampa 33612

102 BOCANEGRA ET AL

FIGURE 1. Diffuse bilateral alveolar infiltrates with normal cardiac silhouette was present at time of massive episode of hemoptysis.

x-ray film showed normal cardiac silhouette and diffuse bilateral alveolar infiltrates (Fig 1). Repeated smears for acid-fast bacilli were negative. The Raji cell assay showed 325 µg/ml of immune complex reactive material (N<8-µg/ml). Serum cryoglobulin level was 39 µg/ml (N<10-µg/ml). The cryoglobulin contained both HBsAg and HBsAb demonstrated by radioimmunoassay. Bronchoscopy was not performed because of the critical condition of the patient. Treatment with intravenous methylprednisolone, 160 mg/day; azathioprine, 100 mg/day; diuretics; and oxygen, 6 L/min by face mask, was given to the patient.

Gradual improvement in the clinical status and chest roentgenogram (Fig 2) was observed over the following eight days. Administration of steroids was tapered to 20 mg over the next two weeks. However, the patient died of septicemia four weeks later. Autopsy was not performed.

FIGURE 2. After one week and following corticosteroids and immunosuppressive therapy, there was marked improvement with almost complete resolution of bilateral alveolar infiltrates.
DISCUSSION

The development of pulmonary hemorrhage is a rare but recognized event in the course of diseases mediated by immune complex deposition. Although the same mechanism accounts for the tissue injury in the systemic necrotizing vasculitides, lung involvement is usually absent except in the granulomatous variants. In a recent report, however, Tomashow et al have documented the occurrence of this complication in a patient with non-granulomatous necrotizing vasculitis.

In our patient, the vasculitic syndrome was associated with hepatitis B infection. Although no histologic examination was performed to confirm the presence of immune complex deposits in the lungs, the development of the pulmonary complication in the setting of active disease coexisting with circulating immune complexes, demonstrated by the Raji cell assay and the presence of cryoglobulins, and the resolution of the symptoms after immunosuppressive therapy, are highly suggestive of an immune-complex-mediated tissue injury. This mechanism accounts also for the high prevalence of pulmonary involvement observed in essential mixed cryoglobulinemia, another syndrome frequently associated with hepatitis B infection. Although life-threatening, this complication, like the other manifestations of systemic necrotizing vasculitis, may respond to aggressive treatment with high-dose corticosteroids and immunosuppressive agents, of which cyclophosphamide seems to be the agent of choice.

The occurrence of pulmonary hemorrhage in HBsAg associated with vasculitis demonstrates the protean and frequently overlapping clinical manifestations of this disease, and suggests that systemic necrotizing vasculitis can rarely be associated with what may be immune-complex-mediated lung damage leading to massive intra-alveolar hemorrhage clinically similar to that seen in Goodpasture's syndrome.

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REFERENCES


Cardio-selective Beta-adrenergic Therapy in a Patient with Asthma and Hypertrophic Obstructive Cardiomyopathy*

Sidney C. Smith, Jr, M.D., F.C.C.P., and Sheldon L. Specter, M.D., F.C.C.P.

A patient is described with the unusual combination of severe asthma and hypertrophic obstructive cardiomyopathy. Cardioselective $\beta$-adrenergic therapy was instituted using the $\beta$-1 antagonist pindolol and the $\beta$-2 agonist albuterol. Pindolol proved effective as a $\beta$-1 antagonist; however, its use was precluded by deterioration in pulmonary function demonstrating moderate $\beta$-2 antagonistic properties. Albuterol was an effective $\beta$-2 agonist producing sustained bronchodilation without inducing symptoms related to the hypertrophic obstructive cardiomyopathy.

Beta adrenergic therapy with propranolol is the therapy of choice in the treatment of hypertrophic obstructive cardiomyopathy. However, it is contraindicated in the presence of severe asthma. Recently a cardio-selective $\beta$-1 adrenergic antagonist, pindolol, or 4-(2-hydroxy-3-isopropylaminopropoxy) indole has been developed with a potency equal to or greater than that of propranolol. Specific $\beta$-2 adrenergic agonists also are available for use in patients with asthma. Their effects on the cardiovascular system are minimal.

We recently encountered a patient with severe asthma and hypertrophic obstructive cardiomyopathy in whom it was desirable to use cardio-selective adrenergic therapy. The combined use of these agents has not previously been reported, and the combination of these disease states in a single patient is relatively rare. The present study was undertaken to establish the effectiveness and specificity of the $\beta$-1 adrenergic antagonist pindolol and the $\beta$-2 adrenergic agonist albuterol.

CASE REPORT

A 22-year-old man with steroid-dependent asthma since childhood was referred for evaluation of a systolic heart murmur. For three months before admission he experienced episodes of tachycardia, dyspnea, and dull precordial chest pain. These symptoms usually occurred following exertion

*From the Division of Cardiology, and Division of Allergy and Clinical Immunology, Department of Medicine, University of Colorado Medical Center and the National Jewish Hospital and Research Center, Denver.
Reprint requests: Dr. Smith, 7901 Fost Street, San Diego 92133

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CARDDO-SELECTIVE BETA-ADRENERGIC THERAPY 103

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