Fibrosing Interstitial Pneumonitis in Ankylosing Spondylitis*

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A patient with ankylosing spondylitis developed bilateral upper lobe lesions which radiographically suggested active granulomatous disease. Lung tissue obtained by percutaneous needle biopsy demonstrated fibrosing interstitial pneumonitis. Recognition that this pulmonary disorder may appear during the course of ankylosing spondylitis can direct subsequent diagnostic studies.

A distinctive type of pulmonary fibrosis confined to the upper lobes in patients with ankylosing spondylitis (AS), although recognized in 1949 by Hamilton† and later characterized by Campbell and MacDonald‡ and Jessamine,§ has received little attention in publications dealing with the pulmonary manifestations of this disorder.¶ Moreover, the variability of the pulmonary histopathology in such patients is rarely illustrated or emphasized.

This report concerns a patient with AS in whom the cause for an active pulmonary disease remained obscure until microscopic examination of his percutaneous lung biopsy established the diagnosis of fibrosing interstitial pneumonitis (FIP).

CASE REPORT

A 72-year-old man entered Methodist Hospital in January 1970 for evaluation of pancytopenia and an abnormal chest roentgenogram. These findings, first appreciated three weeks earlier when he complained of fever and malaise, had remained essentially unchanged despite treatment with penicillin, corticosteroids and warfarin.

In 1947 the patient developed pain and restricted movement of the lumbosacral spine. Within two years complete fusion of his cervical, thoracic and lumbar spine occurred. Roentgenographic findings at that time confirmed AS. His treatment was symptomatic and did not include phenylbutazone or radiotherapy to the spine. In 1958 the diagnosis of pernicious anemia seemed likely based upon documentation of megaloblastic anemia associated with histamine-fast achlorhydria and return of his hematoctit value to normal following administration of vitamin B 12. Additionally, his father had died with pernicious anemia. The patient continued to receive monthly intramuscular injections of vitamin B 12 until the present admission.

On examination he appeared chronically ill. Blood pressure was 120/70 mm Hg; respirations, 36 per minute; pulse rate, 94 per minute; and oral temperature, 99°F. Pertinent findings included mild conjunctival pallor. He was kyphotic and had complete immobility of the cervical and thoracic spine without evidence of peripheral articular disease. Although the chest expanded minimally with deep inspiration, his breath sounds were normal.

Roentgenograms of the chest demonstrated that bilateral upper lobe infiltrates were evident since a previous examination (Fig 1); films of the cervical and thoracolumbar spine revealed extensive calcification of anterior and paraspinal ligaments. Both sacroiliac joints were obliterated. These findings confirmed AS roentgenographically. Electrocardiogram showed sinus tachycardia and nonspecific ST-T wave changes.

Hematoctit value was 31 percent and total leukocyte count, 3,200 per mm³. Differential cell count included 49 segmented neutrophils, 40 lymphocytes, 3 monocytes, 1 eosinophil and 7 myeloblasts. Direct platelet count was 130,000 per mm³ and reticulocyte count, 0.8 percent. Blood urea nitrogen was 20 mg percent and serum creatinine, 1.0 mg percent. Serum protein electrophoresis demonstrated a diffuse increase in the gamma globulin fraction. Arterial blood gases showed Po₂ 82 mm Hg and Paco₂ 32 mm Hg.

Films of a bone marrow aspirate revealed about 30 percent of the nucleated cells to be myeloblasts confirming acute myeloblastic leukemia and demonstrated a mild plasmacytosis. First stage Schillings test showed only 0.8 percent urinary excretion of the isotope. When he received intrinsic factor

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with radiolabeled vitamin B 12, 19 percent of the administered radioactivity appeared in his urine. These findings supported the diagnosis of pernicious anemia.

Multiple examinations of his sputum revealed no fungi or acid fast bacilli. Sputum cultures yielded no growth of pathogens. Results of skin tests for tuberculosis, histoplasmosis and coccidioidomycosis as well as fungal agglutinin titers were negative.

Pulmonary tuberculosis remained a prime consideration because of the roentgenographic findings and the patient received isoniazid and streptomycin. Seeking a specific diagnosis, we performed a percutaneous biopsy of the upper right lung. Histologic sections of tissue obtained demonstrated interstitial pneumonitis and fibrinous alveolitis (Fig 2). Methenamine-silver and Ziehl-Neelsen stains did not allow identification of organisms within the specimen.

The patient became progressively weaker and had increasing difficulty in clearing his bronchopulmonary secretions. He developed bilateral lower lobe pneumonia and died three weeks after entering the hospital. Hematologic findings just prior to death remained essentially unchanged from those on his admission.

GROSS AND MICROSCOPIC PATHOLOGY

Microscopic examination of the lung biopsy specimen (Fig 2) revealed an uneven widening of alveolar septa resulting from an inflammatory infiltrate consisting primarily of lymphocytes but also containing a few mononuclear and occasional plasma cells. Fibroblasts were evident and Masson trichrome stain verified a focal increase in interstitial collagen. Some alveolar spaces contained patchy deposits of fibrin and occasional phagocytic pneumocytes.

At autopsy, the lungs weighed 740 gm (right) and 620 gm (left); their pleural surfaces were normal. Both lungs manifested an increased consistency, especially in the upper lobes. Their cut surfaces seemed coarsened and showed reduced porosity with ill defined tan zones of opacity. No cavities or discrete lesions could be identified in the pulmonary parenchyma.

The upper lobes contained areas of interstitial fibrosis with foci of dense collagen deposits (Fig 3). Fibrin filled many alveolar spaces which remained free of inflammatory infiltrate. In some areas of the lung fibroblasts surrounded and extended into the fibrin masses. These upper lobe changes appeared irregularly throughout the lobules; some areas of lung parenchyma were normal. There was neither granulo-
matous inflammation nor vasculitis. In contrast, histologic sections of the lower lobes showed only focal interstitial edema and inflammation without a fibrinous exudate in the alveolar spaces. This pattern of transbronchial and peribronchial acute inflammation was quite distinct from the upper lobe histopathology described above.

The heart weighed 350 gm. Right ventricular thickness was 3 mm and there was an old posterior wall subendocardial infarct. Leukemic cells appeared throughout the bone marrow and within the sinusoids of the spleen. The gastric mucosa was markedly atrophic.

COMMENT

The roentgenographic appearance of FIP in patients with AS initially appears as a diffuse apical infiltrate, usually bilateral. In 13 such patients clinical evidence of spondylitis preceded the pulmonary abnormality by an average of 19 years. Fibrosis and retraction of both upper lobes then progressed over an additional several years. The location and appearance of the pulmonary lesion led to a provisional diagnosis of pulmonary tuberculosis in six of seven patients described by Jessamine, and in our patient.

Interstitial and intra-alveolar fibrosis is the predominant morphologic pulmonary alteration in AS and is accompanied by focal chronic inflammatory infiltrates mainly within alveolar septa. Although distinctive, this histopathology is not specific and is similar to pulmonary abnormalities in patients with rheumatoid arthritis. The typical rheumatoid nodule has not been described in the lungs of patients with AS.

The prevalence of FIP in association with AS remains uncertain. Possibly in some patients this lesion is unrecognized or confused with granulomatous pulmonary diseases. Hamilton theorized that recurrent upper lobe pneumonitis was the cause for the pulmonary fibrosis. Zorab, however, found no evidence of an increased incidence of pulmonary infections in patients with AS.

Familiarity with the entity of FIP in patients with AS may avoid prolonged diagnostic pursuit of suspected active granulomatous disease. Moreover, application of percutaneous lung biopsy techniques may not only allow confirmation of FIP but provide additional information on the evolution and response to therapy of this poorly understood pulmonary disorder.

The appearance of acute myeloid leukemia in a patient with pernicious anemia and AS deserves brief comment. Pernicious anemia and possibly AS are disorders which seem to be associated with an increased statistical incidence of myeloid leukemia. More commonly acute leukemia has followed radiotherapy to the spine in patients with AS; our patient could not recall submitting to such treatment.

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REFERENCES


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