Pulmonary Infarct: An Unusual Manifestation of Fibrosing Mediastinitis*

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We have recently seen lung biopsy specimens showing pulmonary infarcts in two patients with fibrosing mediastinitis. The patients were young, and in each, the infarcts were the first manifestation of the underlying mediastinal fibrosis. The infarcts had several distinctive histologic features and may have been caused by constriction of major pulmonary veins by the fibrosis.

Fibrosing mediastinitis (FM) is an uncommon disease of uncertain etiology characterized by slowly progressive fibrosis and exuberant collagen formation within the mediastinum. Symptoms result from compression of mediastinal structures, especially the superior vena cava, pulmonary arteries and veins, and bronchii. Asymmetric mediastinal widening is the usual roentgenographic finding; reticulonodular interstitial infiltrates related either to interstitial fibrosis or to lymphatic or venous congestion are commonly associated changes in pulmonary parenchyma. We have seen lung biopsy specimens from two young patients with FM who presented with puzzling chest roentgenograms showing localized pulmonary infiltrates in addition to hilar enlargement. Biopsy specimen of the parenchymal infiltrates showed recent pulmonary infarcts, while mediastinal biopsy specimen was characteristic of FM.

Case Reports

Case 1

This 12-year-old black boy first became ill in January 1977 with cough and fever. A chest roentgenogram taken two weeks later showed a left upper lobe infiltrate. There was no response to therapy with penicillin or erythromycin, and the patient was admitted to St. Louis Children’s Hospital in March, 1977. The patient’s home was near St. Louis, and he had travelled to Tennessee and California. His father had recently developed a positive tuberculin skin test and a pulmonary infiltrate suggestive of tuberculosis. His three-year-old sister had a right middle lobe infiltrate of unknown etiology. On physical examination, the patient’s temperature was 38.5°C. His chest was clear. A repeat chest roentgenogram showed persistence of the left upper lobe infiltrate. A tuberculin skin test was negative while a mumps skin test was positive. Multiple sputum, gastric, and urine cultures were taken. The patient was discharged on a regimen of rifampin, isoniazid, and pyridoxine pending culture results with the presumptive diagnosis of tuberculosis. He continued to be febrile, however,

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FIGURE 1. Case 1. Posteroanterior chest roentgenogram showing left hilar mass, some narrowing of left mainstem bronchus, and wedge-shaped pleural-based area of consolidation in the superior segment of left lower lobe.
Figure 2. Tiny subpleural hemorrhagic infarct with surrounding viable parenchyma. Alveolar septa in the latter area are thickened by a chronic inflammatory cell infiltrate (hematoxylin-eosin, original magnification × 35).

Pathology

The first biopsy specimen from the left lower lobe consisted of a 1.5 × 1 cm fragment of dark red lung which microscopically contained hemorrhagic infarcts (Fig 2). The infarcts were tiny, usually located subpleurally and were separated by larger areas of viable parenchyma. As demonstrated by elastic stains, many of the infarcts were located near or around vessels, the lumina of which were occluded by cellular, and often edematous fibrous tissue (Fig 3). The lumina of a few small arteries also contained similar fibrous tissue and sometimes appeared to be recanalized. A layer of fibrin and erythrocytes covered the adjacent pleural surface. There was a striking proliferation of loose fibrous tissue combined with chronic inflammatory cells within the viable alveolar septa surrounding the infarcted areas, and prominent reactive type II pneumocytes lined the thickened septa. Those changes gave the appearance of an interstitial pneumonitis extending out from the infarcts. Intraalveolar hemorrhage was prominent in areas surrounding the infarcts. The secondary biopsy specimen from the left hilum showed dense fibrosis containing wide bands of collagen and scattered chronic inflammatory cells. The subaortic lymph node was partially destroyed by caseating granulomatous inflammation; however, no organisms could be demonstrated with special stains for acid-fast bacilli and fungi. The left lower lobe appeared unremarkable except for pleural fibrosis.

Case 2

This 26-year-old white man was first evaluated at another hospital in September 1977 for left pleuritic chest pain and dry cough of two months' duration. The patient was a native of Chicago, but recently had lived in Champaign, Illinois where he attended college. A chest roentgenogram showed an enlarged left hilum and a left midlung infiltrate. He was treated with erythromycin and had symptomatic improvement. Gradual resolution of the pulmonary infiltrate was noted on follow-up films in October and November, although the hilar enlargement remained unchanged. Tomograms in November showed narrowing of the left mainstem bronchus. The patient remained relatively asymptomatic until July 1978, when he was admitted to Northwestern University Medical Center because of recurrent left-sided pleuritic chest pain, nonproductive cough, fever, and night sweats. On physical examination, the patient was febrile to 38.4°C. Coarse rhonchi were noted over the left hemithorax. A Histoplasma skin test was strongly positive while a tuberculin...
skin test was negative. A chest roentgenogram showed a left lower lobe infiltrate with left hilar lymph node enlargement and narrowing of the left main-stem bronchus (Fig 4). Fiberoptic bronchoscopy showed marked narrowing by external compression of the left main-stem bronchus; the scope could not be passed distal to the obstruction. At thoracotomy, consolidation of the superior segment of the left lower lobe was found, and there were dense adhesions of that lobe to the chest wall. The entire left hilum was involved in a mass of firm white tissue. No discrete lymph nodes or major vascular structures could be identified. Biopsy specimens of the involved portion of left lower lobe and the hilar tissue were taken. Postoperatively, the patient had gradual defervescence of his fever and decrease in chest pain and cough without specific therapy. Cultures of sputum, bronchial washings, and pulmonary tissue were negative. Serum titers to Histoplasma yeast were 1:16 and titers to mycelium were greater than 1:32, although these sera were drawn three weeks following skin testing. Pulmonary function tests performed subsequently were normal.

Pathology
The lung biopsy specimen consisted of a 2 × 1 cm piece of lung containing multiple microscopic infarcts which were often located near lobular septa (Fig 5). The infarcts were characterized by central bland necrosis containing acellular ghost-like remnants of alveolar septa. They were multifocal and were separated by large areas of viable parenchyma. Distinctive reactive appearing loose fibroblastic tissue containing a chronic inflammatory cell infiltrate was seen within alveolar spaces and alveolar septa surrounding the necrosis (Fig 6). Chronic inflammatory cells admixed with fibroblasts also thickened the alveolar septa in most of the remaining viable parenchyma; there was proliferation of granular pneumocytes in this area. The lumina of many pulmonary venules adjacent to the infarcts were obliterated by fibroblastic proliferation (Fig 5). The small hilar biopsy specimen showed the dense fibrosis of FM with prominent bands of collagen and a few chronic inflammatory cells.

Discussion
Fibrosing mediastinitis is known for its protean manifestations. While chest roentgenograms may occasionally show localized areas of consolidation, or rarely, cavitary infiltrates, there has been no report of a histologically documented infarct similar to our cases. Many cases of pulmonary arterial and venous narrowing or obstruction by the fibrosis have been described, but only one reported patient had an infiltrate clinically suggestive of an infarct. In the autopsy of one patient, necrosis of an entire lobe was found, while in another, there was a pulmonary infarct related to an arterial embolus. Absence of parenchymal necrosis in most cases with arterial or venous obstruction is explained by the presence of extensive collateral circulation.

Certain histologic features of the infarcts were unusual and suggested major pulmonary venous obstruction in their pathogenesis. The infarcts were microscopically multifocal and were often centered...
upon lobular septa or occluded venules. A similar distribution of infarcts has been described in pulmonary veno-occlusive disease.27 The intervening parenchyma between the infarcted areas showed marked interstitial thickening both by fibrosis and chronic inflammatory cells. Similar changes have been described in cases of FM with documented venous obstruction,1,9 and in cases of pulmonary venous hypertension due to a variety of other causes.26,27 Another explanation for these infarcts, although less likely, is that they were caused by pulmonary arterial occlusion in the presence of elevated pulmonary venous pressures. The distinctive loose fibroblastic matrix found within alveolar spaces and alveolar septa surrounding the necrotic areas likely represents a very reactive reparative response to the infarcts.

The exact etiology and pathogenesis of FM are uncertain. Some cases follow tuberculous or Histoplasma infections, and in such cases, the lesion is thought to represent an abnormal immune response to antigens shed from the organisms.1 Our case 2 may have been related to prior Histoplasma infection; case 1 is also likely to have been related to infection since a caseating granuloma was present in a hilar lymph node. However, no organisms could be found, and skin tests and serologic studies were negative.

Pulmonary infarction is a rare complication of FM and should be considered in the differential diagnosis of localized infiltrates in patients with this disease. Moreover, the diagnosis of FM should be considered in otherwise healthy young persons who develop pulmonary infarcts, especially when there is histologic evidence of venous obstruction. The multifocal nature of the infarcts, their distribution along lobular septa, their relation to occluded venules, and the interstitial thickening in the surrounding parenchyma form a distinctive morphologic pattern which should suggest the diagnosis of FM.

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