Hemoptysis in Sarcoidosis*
Report of a Case
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Hemoptysis in sarcoidosis is infrequent, and massive pulmonary hemorrhage is rare. McCort and associates in 1947 reviewed 27 cases of sarcoidosis, and found only two had small pulmonary hemorrhages. In 1950, Oblath and Farber reviewed 40 cases and found that in four there were small bouts of hemoptysis. Riley, in a study of 52 cases of sarcoidosis seen at Bellevue Hospital between 1939 and 1949, found only ten patients who had complained of blood-streaked sputum. No pulmonary hemorrhages were encountered.

The first report of fatal pulmonary hemorrhage in a patient with sarcoidosis is that by Fischl and Freireich in 1948. The exact bleeding point could not be located microscopically; the pulmonary vessels were thick-walled, with prominent fibrosis. In 1954, Russakoff reported two additional cases of unexplained massive pulmonary hemorrhage, believed to be due to sarcoidosis. In 1956, Schourup and Vimtrup reported a sudden fatal hemorrhage in a 26-year-old woman with sarcoidosis. Microscopic examination of the lungs demonstrated noncaseating granulomas in the walls of pulmonary vessels. Talbot, Katz and Matthews in 1959 presented a case report of severe hemoptysis secondary to bronchiectatic changes resulting from sarcoidosis.

The case presented here has several unique features. First, there was a long duration of hemoptysis under repeated observation and second, there was a fatal pulmonary hemorrhage; finally, the characteristic lesions of sarcoidosis were found in bronchi and bronchioles and in the walls of the medium-sized pulmonary arteries.

CASE REPORT
The patient, a 36-year-old Negro man, was admitted to the Hines Veterans Administration Hospital in October, 1960. Twenty-four hours before admission he had begun to cough. The first few paroxysms produced no sputum, but within a short time he began to expectorate bright red blood. It was not mixed with sputum and no clots were seen. There were no other symptoms at that time. On admission, dry rales were heard throughout the lower lobes of both lungs and moist inspiratory rales in the area of the right lower lobe. The liver edge was palpated 2 cm. below the right costal margin. The hemoglobin was 7.7 gm./100 ml. A thoracic roentgenogram made with the patient in the dorsal recumbent position showed extensive nodular infiltrations in the upper two-thirds of both lungs. Many small cavities were seen in the same area. Hemoptysis persisted after admission, requiring four whole blood transfusions. The hemoptysis decreased in amount, but continued. Twenty-four hours after admission, the patient suddenly began to cough up large quantities of blood, had a convulsion, and died.

This man had first become ill in 1957, three months before his first hospital admission. He developed a dry, hacking, nonproductive cough. Two months later he developed hemoptysis and weakness, and was referred to the tuberculosis service of this hospital. At admission, findings on physical examination were entirely normal. Because of the appearance of the thoracic roentgenogram, the patient was thought to have active pulmonary tuberculosis. Smears and cultures of many specimens of sputum and gastric washings did not demonstrate tubercle bacilli. The first-strength PPD skin test was negative, but the second-strength test was two plus positive. The skin test for histoplasmosis, blastomycosis, and coccidioidomycosis were negative. The hemoglobin was 9.4 gm./100 ml., the serum calcium was 5.9 mEq./L., the serum albumin was 3.2 gm., and the serum globulin was 4.2 gm./100 ml. Complement fixation tests for blastomycosis and coccidioidomycosis were negative, but the complement fixation for histoplasmosis was positive in a titer of 1:16. Candida albicans was recovered on three occasions in sputum cultured for fungi, but ten

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attempts to find Histoplasma capsulatum failed. The thoracic roentgenogram (Fig. 1) at the time of admission showed extensive infiltration of the upper two-thirds of both lungs with discrete and conglomerate nodules. The hilar shadows were normal.

After three weeks of hospitalization, hemoptysis ceased. Following two months of hospitalization, antituberculosis chemotherapy consisting of streptomycin, isonicotinylhydrazine and para-aminosalicylic acid was begun. Two months later, the thoracic roentgenograms were unchanged. Because of the lack of response to chemotherapy, a scalene node was excised and bronchoscopic examination done. Microsections of the lymph node showed a noncaseating granuloma compatible with sarcoidosis. The bronchoscopist noted that the tracheobronchial mucosa was inflamed, friable and bled on touch. Because of the histologic characteristics of the lymph node, the many sterile sputum cultures and the lack of response to antituberculosis chemotherapy, the diagnosis of tuberculosis was abandoned in favor of sarcoidosis. He was treated with 40 mg. of prednisone and 300 mg. of isonicotinylhydrazine daily. Serial roentgenograms of the chest made after treatment with prednisone was begun showed slow resolution of the nodular infiltrations of both upper lobes. Roentgenograms of the hands and feet showed no abnormalities. At the end of ten months, the patient was discharged on 10 mg. of prednisone daily.

Following hospitalization, he continued to have recurrent episodes of paroxysmal cough and expectoration of unclotted blood. These bouts lasted from three days to several weeks. Bronchoscopic examination at another institution did not reveal significant abnormalities.

Six days before the second admission in December, 1959, the patient again had hemoptysis which increased in amount until the time of admission. He had had no other symptom and had gained 20 pounds. Between periods of hospitalization, he had continued to take 10 mg. of prednisone daily. The physical findings at admission were entirely normal, except for a small bleeding ulcer on the posterior aspect of the left side of the nasal septum to which pressure was applied. The hemoptysis promptly ceased. Bronchoscopy was performed, and the tracheobronchial tree was entirely normal.

The hemoglobin levels ranged between 6.3 and 13.6 gm./100 ml. The platelet count was 436,000 and the reticulocyte count was 5.4 per cent. The serum calcium was 4.5 mEq.; the serum phosphorus was 2.4 mEq. The serum albumin was 2.5 gm. and the globulin was 3.2 gm./100 ml. Smears and cultures for tubercle bacilli were negative on 11 occasions. Candida albicans was recovered on two occasions from cultures for fungi. Complement fixation tests for histoplasmosis, blastomycosis and coccidioidomycosis were all negative. Bone marrow aspiration showed reticuloendothelial reactive changes and early signs of iron deficiency. The thoracic roentgenograms showed dense linear and nodular shadows in the upper two-thirds of both lungs and scattered nodular densities in the lower thirds. In the right upper lobe there were several radiolucencies of various sizes. After one month of bed rest and prednisone therapy, the patient was discharged.

In August, 1960, the patient was admitted for the third time because of severe hemoptysis of a week's duration. At this time, the patient had had exertional dyspnea for one year. Findings on physical examination were normal, except for expiratory dry rales throughout both lungs. Hemoptysis continued for two weeks, requiring two blood transfusions and finally pneumoperitoneum. The hemoglobin level varied between 7.3 gm. and 10 gm./100 ml. The thoracic roentgenograms made during this admission showed essentially no change. After seven weeks, the patient was discharged. Sixteen days later, he was admitted for the last time.

 Necropsy Findings: Most of the significant abnormalities were in the chest. There were dense fibrous adhesions over the apices of both lungs and the diaphragm bilaterally. No fluid was present in the pleural cavities. In the mediastinum, multiple enlarged discrete lymph nodes were found that measured up to 1.5 cm. in diameter. The cut surface of each of these nodes was pink.

**Figure 1:** Admission chest x-ray film of November 8, 1957.
ish-gray and the follicular architecture was obliterated. The heart weighed 310 grams, and was not greatly enlarged; yet, the right ventricular wall was 5 mm. in thickness. The lungs were slightly heavier than normal, the right weighing 600 gm. and the left 450 gm. The visceral pleura was thickened over both apices. When the tracheobronchial tree was opened, liquid and clotted blood filled all visible bronchi. In addition tubular bronchiectasis was found throughout both lungs. No source of the hemorrhage could be found. The pulmonary and bronchial arterial systems were grossly normal. The parenchyma of the lungs was firm and some areas were indurated. The gastrointestinal tract was filled with dark liquid and clotted blood. A superficial ulcer measuring 1.5 cm. in diameter was found in the posterior wall of the first portion of the duodenum. No eroded blood vessel was found in the ulcer crater, suggesting that the blood in the gastrointestinal tract had been swallowed during the terminal pulmonary hemorrhage. Numerous enlarged and indurated peripancreatic, periaortic and mesenteric lymph nodes were found. The appearance of the cut sections of these lymph nodes was similar to that seen in the mediastinum.

The important microscopic findings were in the lungs and lymph nodes. Numerous noncaseating granulomas were observed in the pulmonary parenchyma, the walls of large and small blood vessels, the walls of bronchi and bronchioles and replacing the follicles of lymph nodes. The granulomas were characterized by the presence of many multinucleated giant cells, principally of the Langhans type, epithelioid cells, numerous mononuclear cells and the absence of caseation necrosis; the appearance of these granulomas was compatible with the clinical diagnosis of sarcoidosis. Staining of the lymph nodes and sections made from the lung with the Fite stain failed to demonstrate acid-fast bacilli. The most striking feature was the presence of granulomas in the walls of blood vessels, bronchi, and bronchioles. The sarcoid lesions within the bronchial and bronchiolar walls probably produced the bronchiectatic cavities. The destruction of the bronchial wall was so marked in areas that entire granulomas lined by respiratory mucosa could be found within the bronchial lumen (Fig. 2). Adjacent to one such bronchus was a small artery with a portion of the wall completely replaced by a large noncaseating granuloma. This vessel had ruptured and produced a bronchovascular communication and exsanguinating hemorrhage (Fig. 3). The walls of many other arteries and veins in the lungs contained similar granulomas, so that it is possible that similar occurrences in the past had resulted in bouts of hemoptysis. No other organs demonstrated similar vascular changes. The pathologic changes in the lymph nodes were characterized by the complete loss of follicular architecture and replacement by noncaseating granulomas identical to those described in the lung. One important diagnostic feature was found in the lymph nodes which was not seen in the pulmonary lesions; within a number of multinucleated giant cells asteroid bodies were found with the characteristic stellate forms occupying a prominent position in the mid-portion of the cytoplasm (Fig. 4). No Schaumann bodies were identified, although in a few giant cells small anisotropic inclusions were seen.

**Figure 2** (upper): Microsection of lung showing noncaseating granuloma bulging into lumen of small bronchus. x100. **Figure 3** (center): Microsection of lung showing infiltration and replacement of wall of middle-sized artery by granuloma. x100. **Figure 4** (lower): Microsection of lymph node showing typical asteroid body within multinucleated giant cell.
DISCUSSION

Hemoptysis is unusual in sarcoidosis and is usually attributed to a concurrent disease or to a complication of sarcoidosis, such as bronchiectasis. There are only four previously reported cases in the literature in which the death of the patient was attributed to massive pulmonary hemorrhage believed to be due to sarcoidosis. In none of these cases was the site of bleeding demonstrated. Michaels and his group\(^1\) reported two cases in which similar noncaseating tuberculoid granulomas were found invading blood vessels in a manner almost identical with that in our case. In their cases the media of the vessels was the most conspicuous portion involved, although intimal changes were also noted. The adventitia was unaffected. No extrapulmonary vessel had similar granulomas.

The presence of the bronchiectasis in sarcoidosis and other granulomatous diseases of the lungs is described, although it is usually associated with severe pulmonary fibrosis following a protracted course. In our case, very little fibrosis was seen and the lesions within the bronchial walls are assumed to be the cause of the bronchiectasis. Another unusual feature of this case is the finding of endobronchial noncaseating granulomas lined by tall columnar respiratory epithelium. It is possible that these endobronchial lesions resulted from an outfolding of the bronchial wall following the initial granulomatous change. Bottcher\(^1\) described a case of disseminated sarcoidosis in which similar granulomas were found in the walls of arteries and veins. In her case, the pulmonary vessels showed the greatest involvement, but the endocardium and arteries in the mesentery and kidney also had granulomatous infiltrates. The adventitia in some vessels was involved, as well as the media and intima. In most areas fibrosis was extensive, probably accounting for the absence of rupture of any vessel. In the case described by Schourup and Vimtrup,\(^1\) granulomas were seen in the walls of large bronchi and the walls of small veins. None was seen in the walls of large vessels. The granulomas protruded into the lumen and in some areas only the endothelium and some strands of connective tissue separated the lesions from the vascular lumen. In the present case, granulomas were seen only in the walls of the pulmonary vessels. Here, too, all layers of the vascular walls were involved, particularly in the small artery which ruptured into the adjacent bronchiectatic cavity. Except for the area of rupture, the remainder of the vessel wall was entirely normal.

REFERENCES


