Diffuse Interstitial Pneumonitis and Fibrosis in Sarcoidosis*

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Interstitial pneumonitis in sarcoidosis is rare. When present, it is confined to areas of active granuloma formation. We report finding widespread interstitial pneumonitis and fibrosis in a patient with sarcoidosis. Due to the focal sampling of pulmonary tissue by transbronchial biopsy, a finding of interstitial pneumonitis does not exclude a diagnosis of sarcoidosis.

Sarcoidosis is a multisystem disorder of unknown etiology characterized pathologically by the formation of non-necrotizing granulomata in multiple sites in the body. Although the clinical and radiographic presentation of cases is quite characteristic, a histologic diagnosis is necessary before beginning treatment. Fiberoptic bronchoscopy with transbronchial lung biopsies is diagnostic in 60 to 95 percent of cases, depending upon the clinical stage of the disease.1,2 The diagnosis is established when non-necrotizing epithelioid granulomata with giant cells are found on biopsy and cultures are negative. While interstitial fibrosis and interstitial pneumonitis have been reported in sarcoidosis, they are usually localized to areas of extensive involvement with active granulomatous disease.3 We report a case of pulmonary sarcoidosis with extensive interstitial pneumonitis and fibrosis in regions without active granuloma formation.

Case Report

A previously healthy 27-year-old black woman presented to the emergency room at the University of Maryland Medical Systems complaining of dyspnea and a nonproductive cough for the past 12 months. Her exercise capacity had diminished to the point of severe dyspnea after walking one block. She recently noted arthralgias, and there was a 5.4-kg (12-lb) weight loss. There was a 14 pack-year history of smoking, but the patient had discontinued smoking cigarettes three months prior to admission. She had previously smoked marijuana for many years and recently began snorting cocaine. There was no occupational history of exposure to toxins.

Physical examination was remarkable only for the presence of fine end-inspiratory crackles on auscultation and digital clubbing. Admitting laboratory studies revealed a hematocrit reading of 47 percent and a white blood cell count of 6,100/μl, mm, with a normal differential. The serum calcium level was 9.6 mg/dl, and the alkaline phosphatase level was 366 units (normal, 95 to 300 units). An arterial blood specimen while breathing room air revealed a pH of 7.39, an arterial carbon dioxide tension of 35 mm Hg, and an arterial oxygen pressure of 72 mm Hg. The chest roentgenogram demonstrated bilateral paratracheal and perihilar lymphadenopathy with a diffuse, reticulonodular parenchymal infiltrate (Fig 1). There was no pleural thickening or effusion. The patient was unable to perform pulmonary function tests due to dyspnea and cough.

The patient underwent fiberoptic bronchoscopic examination, which showed a cobblestone pattern in the airways but no endobronchial lesions. Microscopic examination of the transbronchial biopsies revealed diffuse interstitial fibrosis and inflamma-

![Figure 1. Posteroanterior (left) and lateral (right) chest roentgenograms on admission. Bilateral para-tracheal and perihilar adenopathy is present. Reticulonodular infiltrates are present throughout the lung fields.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21579/ on 04/08/2017)
Diffuse interstitial pneumonitis and fibrosis in sarcoidosis (Atiser, Albin)

Interstitial pneumonitis in sarcoidosis is infrequently recognized. Katzenstein and Askin\(^4\) state that there is little, if any, interstitial pneumonitis surrounding the granulomata in the lung. Spencer\(^4\) makes no mention of interstitial pneumonitis in his discussion of the histopathologic findings in sarcoidosis. In contrast, Rosen and co-workers\(^5\) reported finding focal, nonspecific interstitial pneumonitis in 62 percent of 128 open lung biopsies performed for presumed sarcoidosis. All biopsies from their series demonstrated granulomata. Based upon their observation that several regions of pneumonitis were organizing into granulomata, Rosen et al\(^6\) suggested that interstitial pneumonitis represented the earliest phase of granuloma development. Our patient differed from their cases in two respects. First, the interstitial pneumonitis was diffuse, and, secondly, the patient had evidence of advanced sarcoidosis, with parenchymal honeycombing and fibrosis.

It appears that the interstitial pneumonitis and secondary fibrosis in our case occurred independent from active granuloma formation. This raises the question of whether a second disease or drug exposure could account for these changes. Although the transbronchial lung biopsies suggested desquamative interstitial pneumonitis, the open lung biopsy ruled this out. The major histopathologic findings in marijuana smokers from a recent postmortem series were alveolar infiltration with pigmented macrophages and varying degrees of monocytic and lymphocytic infiltration in the pulmonary interstitium.\(^7\) These findings were not present in this case. Similarly, a postmortem series involving cocaine abusers failed to demonstrate interstitial pneumonitis.\(^8\) Our patient abused no other drugs, had no evidence of a collagen-vascular disorder, and was not exposed to any toxic substances at her place of employment.

While a second disease cannot be completely excluded, we believe that this case represents an unusual histopathologic presentation of sarcoidosis and demonstrates several important points. First, diffuse interstitial pneumonitis may be seen in advanced sarcoidosis. Secondly, interstitial pneumonitis and alveolar cell hyperplasia without closely associated granulomata or giant cells can be found in sarcoidosis. This may be especially important when evaluating small pieces of tissue from transbronchial lung biopsies. In this context, transbronchial lung biopsies which reveal these findings alone do not exclude the diagnosis of pulmonary sarcoidosis. Additional biopsy material should be obtained when sarcoidosis is suspected and the histologic findings reveal only interstitial pneumonitis or fibrosis.

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REFERENCES
1 Roethe RA, Fuller PB, Byrd RB, Hafermann DR. Transbronchoscopic lung biopsy in sarcoidosis: optimal number and sites for diagnosis. Chest 1980; 77:400-02
4 Spencer H. Pathology of the lung. New York: Pergamon Press,
Rhodococcus equi Pneumonia*
An Unusual Early Manifestation of the Acquired Immunodeficiency Syndrome (AIDS)

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Infection with Rhodococcus equi has been reported as an occasional cause of cavitary pneumonia in severely immunocompromised patients, including those with the acquired immunodeficiency syndrome (AIDS). We report two cases of R equi pneumonia presenting in one month in patients infected with human immunodeficiency virus (HIV) who had not previously had an opportunistic infection. The clinical and radiographic manifestations of the disease are distinctive and should suggest the diagnosis. R equi pneumonia in a person with HIV infection should be considered diagnostic of AIDS. Recognition of this entity is important since antibiotic therapy is different from that conventionally used in pneumonias in AIDS patients and must be prolonged.

Rhodococcus equi is an aerobic Gram-positive weakly acid-fast nonmotile nonsporeforming pleomorphic bacillus which has been identified as a source of cavitary pneumonia, pleural effusions, brain abscesses, and subcutaneous nodules in immunocompromised hosts. Initially recognized as a pathogen in animals, Rhodococcus equi (formerly known as Corynebacterium equi) was first reported as a human pathogen by Golub et al in 1967 in a patient with a lung abscess. In 1983, Van Etta et al summarized findings in the ten cases in the literature and added two of their own. Since then, four additional cases have been reported, two of which occurred in patients with the acquired immunodeficiency syndrome (AIDS). We report two additional cases of cavitary pneumonia with pleural effusion due to Rhodococcus equi presenting in one month to Parkland Memorial Hospital in patients infected with the human immunodeficiency virus (HIV). Recognition of this pathogen as a cause of pneumonia and/or pleural effusion in the growing population of patients with HIV-associated illness has important therapeutic implications regarding both choice and duration of antibiotic therapy. Because R equi very rarely infects normal hosts, we feel that this infection in patients positive for HIV should be regarded as sufficient for a diagnosis of AIDS.

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Case Reports

Case 1
A 29-year-old homosexual white man with a history of HIV infection presented to Parkland Memorial Hospital with a one-month history of fever, pleuritic chest pain, and cough productive of scant clear sputum not responsive to a course of trimethoprim-sulfamethoxazole and cefaclor. He gave an occupational history of commercial landscaping and ranch work with exposure to horses and a variety of livestock. On examination, he had a temperature of 36°C with a respiratory rate 14/minute. Chest auscultation was significant for the presence of a pleural rub over the left anterior chest wall. Chest radiographs demonstrated a cavitating infiltrate in the superior segment of the lingula, with a small left pleural effusion. Thoracentesis yielded 20 ml of bloody fluid with white blood cell count 20,500 × 10^6/L and red blood cell count 108,000 × 10^6/L. Bronchoscopic examination revealed mild erythema of the entire bronchial tree, but no localized abnormalities. Transbronchial biopsy revealed fibrosis and mild acute and chronic inflammation consistent with organizing pneumonia. Biopsy specimens, as well as brushings and washings, were negative for acid-fast bacilli, fungi, and Pneumocystis. A blood culture was reported as growing a "diphtheroid" which was regarded as a contaminant.

He returned several days following discharge with recurrent left pleuritic chest pain and cough, now with a temperature of 38.5°C. His white blood cell count had risen to 19.1 × 10^9/L. Chest radiographs showed enlargement of the left upper lobe infiltrate with a cavity containing an air-fluid level (Fig 1). The cultures of pleural fluid, bronchoscopic washings, and blood from the previous hospitalization, as well as blood and sputum from this hospitalization, all grew a Gram-positive aerobic bacillus identified as R equi. The isolates of R equi were very sensitive to erythromycin, gentamicin, and vancomycin, moderately sensitive to clindamycin and tetracycline, but resistant to ampicillin, cephalothin, and penicillin. Therapy with clindamycin alone had little effect, although the addition of erythromycin and later tetracycline resulted in clinical improvement for the next six months.

Case 2
A previously healthy 45-year-old homosexual white man first presented to another hospital with a four-day history of fever, chills, right pleuritic chest pain, and cough productive of gray blood-tinged sputum. Physical examination revealed a temperature of 40°C and respiratory rate of 28/minute. Rhonchi, egophony, and dullness were