

Dyspnea and bilateral interstitial pulmonary infiltrates in an intravenous drug user

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CASE PRESENTATION

BRADLEY S. JONES, MD: A 66-year-old man, a known intravenous heroin user for 45 years, presented to Baylor University Medical Center (BUMC) in May 2001 with a painful left upper arm after falling off a crate. A fractured left humerus was diagnosed, the arm was placed in a sling, and the patient was sent home. Upon reviewing the radiograph the following day, the attending radiologist noticed abnormal lung findings and called the patient, who reported a 1- to 2-month history of dyspnea on exertion. Several months earlier the patient was found to have an ejection fraction of 30% by echocardiogram, as well as severe chronic pulmonary obstructive disease. A partial gastrectomy had been performed many years previously, and a bypass operation had been done in one leg. He had no known allergies. The only medicine he was taking was a "water pill," although several medications had been prescribed after a recent hospital discharge. During his last admission, he had tested negative for HIV. He smoked one pack of cigarettes per day for 45 years, smoked crack at least once per week, and drank 4 to 6 beers 4 to 5 times a week.

On examination, he was cachectic but in no acute distress. His temperature was 98.0°F (36.6°C); heart rate, 80 beats per minute; respirations, 20 breaths per minute; and blood pressure, 130/80 mm Hg. He denied cough, orthopnea, hemoptysis, chills, night sweats, and recent weight loss. He had bilateral temporal wasting but no lymphadenopathy or bruits. In both lung fields, diffuse fine crackles were present throughout. He also had dullness to percussion in the bases a third of the way up bilaterally. A 3/6 systolic ejection murmur was heard at the apex. No abdominal abnormalities were noted. He had 2+ pitting edema in his ankles bilaterally. He was alert and oriented.

While breathing 2 L/min of oxygen, the patient's arterial blood gas values showed a pH of 7.45, a PCO_2 of 41, a PO_2 of 70, and an oxygen saturation of 96%. A urine toxicology screen disclosed the presence of opiates and cocaine. A pleurocentesis was performed, and the pleural fluid was clear and yellowish, with a red blood cell count of $170/mm^3$, white blood cell count of $48/mm^3$ (with 32% lymphocytes, 48% neutrophils, 12% monocytes, and 8% mesothelial cells), pH of 7.97, protein of 1.1 g/dL, lactate dehydrogenase of 44 U/L, and specific gravity of 1.011. Other laboratory results are in the *Table*.

The most recent chest radiograph showed bilateral interstitial infiltrates and bilateral pleural effusions (*Figure 1*). Films

Table. Laboratory values upon admission to Baylor University Medical Center

Glucose	208 mg/dL	Aspartate aminotransferase	29 U/L
Sodium	143 mEq/L	Alanine aminotransferase	9 U/L
Potassium	3.1 mEq/L	White blood cell count	$9.7 \times 10^3/\mu L$
Chloride	103 mEq/L	Differential:	18% lymphocytes
Bicarbonate	25 mEq/L		5% monocytes
Blood urea nitrogen	19 mg/dL		75% segmented neutrophils
Creatinine	0.8 mg/dL		3% eosinophils
Total protein	8.2 g/dL	Hemoglobin	11.4 g/dL
Albumin	3.3 g/dL	Hematocrit	37.3%
Total bilirubin	0.5 mg/dL	Mean corpuscular volume	85 fL
Alkaline phosphatase	279 U/L	Platelet count	$424 \times 10^3/\mu L$

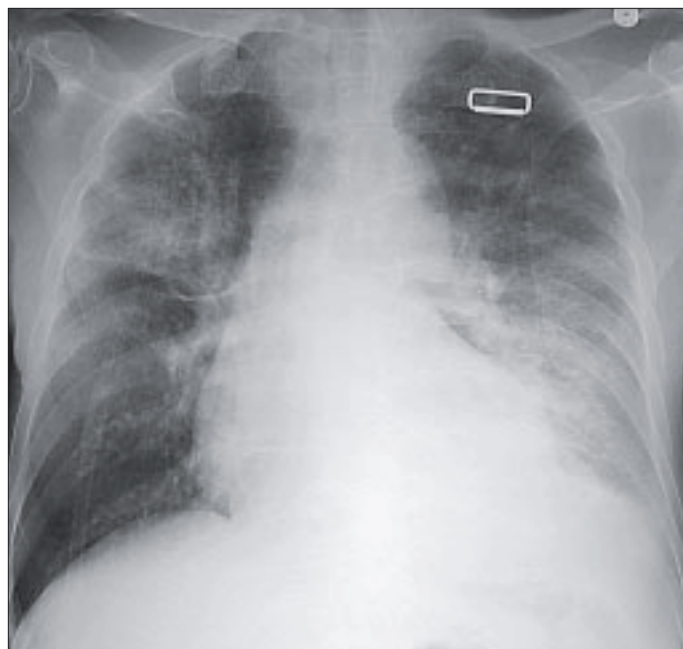


Figure 1. The chest radiograph taken of the patient after he was called back to the emergency department. Areas of consolidation are evident in the left lower lobe and right upper lobe. The pleural fluid was not significant in this image.

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taken a year and a half earlier showed a right lower lobe pneumonia with some infiltrates and relatively clear upper fields. Further, a computed tomography (CT) scan taken 3 months previously also showed bilateral interstitial fibrosis and pleural effusions with some consolidation on the right side.

DIFFERENTIAL DIAGNOSIS

FRANK A. BRANCACCIO, MD: When evaluating a patient with interstitial lung disease, a stepwise and systematic approach is required, as a myriad of conditions can be implicated: interstitial pneumonias, granulomatous disease, inherited disorders, inhalation of organic and inorganic dusts, collagen vascular disorders, and connective tissue diseases, as well as other conditions that may mimic interstitial lung disease, such as malignancy, infection, and heart failure. A careful history is crucial, focusing on smoking status; medications, particularly chemotherapeutic or antiarrhythmic drugs; occupation; and leisure activities. This patient had a long history of cigarette smoking. His symptoms were present for 1 to 2 months. He had a long history of intravenous drug use, which I believe is the most important clue to the diagnosis. There was no description of previous medication use. There was no comment on past employment that would suggest he was exposed to agents such as asbestos.

With the radiographic findings, it is somewhat surprising that the patient complained of dyspnea for only 2 months. He experienced no cough, fevers, sweats, or chills. The patient was described as cachectic, ill-appearing, and having bitemporal wasting, which suggests that he may have had more substantial weight loss than he admitted to; alternatively, he may have had the body habitus very common to career intravenous drug abusers. He had rales that were easily heard in both lung fields; dullness at the lung bases, which corresponded to the presence of bilateral effusions; a systolic precordial murmur but no gallop; and bilateral lower-extremity edema. He was HIV negative, had no evidence of renal disease, and had no eosinophilia on peripheral smear. The pleural effusion was consistent with a transudate, which I suspect is related to his known diagnosis of congestive heart failure.

Evaluation of the patient with interstitial lung disease involves routine laboratory tests, specific laboratory tests when indicated, a chest radiograph, and a CT scan. Often, these patients also undergo pulmonary function tests, although such a test was not described in this patient. Results of pulmonary function tests are variable, from normal to restrictive or obstructive lung volume. Also, diffusion capacity is often reduced. The pulmonary function tests may not provide diagnostic information, but they are important in clarifying the severity of the impairment, monitoring the progression of the disease, and watching for treatment-related improvement. If the diagnosis remains in question, as it often does, it's necessary to proceed with a lung tissue biopsy.

Based on the information available, I'll limit my differential diagnosis to the following. Any time a patient with a long smoking history has had weight loss and an abnormal chest radiograph, the possibility of *malignancy* must be considered. Based on this patient's radiographic findings, if he does have malignancy, he has lymphangitic spread. Cancer is highly unlikely considering the change in pattern seen in the radiograph as well as the chronicity of the radiographic abnormalities.

Idiopathic pulmonary fibrosis must be considered. Statistically, this is the most common diagnosis proven on biopsy in an older population with chronic interstitial infiltrates. Still, the CT findings, which tend to involve the lower lung zones and show a peripheral, subpleural distribution, are not characteristic of this disorder.

Tuberculosis is a condition that I would certainly want to exclude. While HIV infection is by far the most important risk factor for reactivation of latent disease, the patient is still at an increased risk because of his intravenous drug abuse. He lacks, however, the symptoms expected in a patient with extensive pulmonary disease, such as cough, fever, night sweats, and hemoptysis. If bronchoscopy results showed acid-fast bacteria and caseating granulomas, the diagnosis of tuberculosis would be secured.

Sarcoid should be considered in any patient with dyspnea and interstitial pulmonary infiltrates. These patients tend to present with a cough and hilar adenopathy. This patient could easily have stage 3 or stage 4 sarcoidosis: stage 1 being the most common presentation, which is purely bilateral hilar adenopathy; stage 2 being pulmonary infiltrates associated with hilar adenopathy; stage 3 being pulmonary infiltrates without adenopathy; and stage 4 being advanced fibrotic disease. The infiltrates of sarcoid can be interstitial, nodular, or both and tend to involve the upper lobe distribution. On biopsy, I would expect to find non-caseating granulomas that stain negatively for fungus and acid-fast bacteria.

I've also included *amiodarone toxicity* in the differential diagnosis for a number of reasons: the ambiguity about the exact drugs the patient has received, the fact that he had been in the hospital just a few months earlier, and the fact that he has a history of congestive heart failure. The drug and alcohol use and congestive heart failure put him at risk of atrial fibrillation, for which amiodarone is a frequent treatment. Pulmonary toxicity occurs in about 5% of patients receiving amiodarone. It is usually a dose-dependent response, with the risk being increased with a dosage of >400 mg/d or use of >2 months' duration. Patients with amiodarone toxicity usually have nonproductive cough or dyspnea, which often makes it difficult to distinguish from their underlying condition. Infiltrates are focal or diffuse and interstitial, and on biopsy alveolar septa are fibrotic and inflamed. Foamy macrophages also are usually present, but they do not equate with pulmonary toxicity, as nearly all patients taking amiodarone have them if a lung biopsy or lavage specimen is obtained. The treatment is to discontinue amiodarone. Most patients with amiodarone toxicity are treated with a corticosteroid, although there are no studies to suggest that it is effective.

Finally, I include what I believe this patient has: *foreign body granulomatosis*. This condition is found exclusively in the intravenous drug-abusing population, and it occurs because users unknowingly inject contaminants such as magnesium silicate (talc) or methylcellulose into their veins along with the drugs. These particular contaminants are often used to cut street heroin; they are also used as fillers in pills meant for oral consumption that drug users crush, dissolve, and inject.

Patients with foreign body granulomatosis may be asymptomatic or may present with progressive dyspnea. The radiograph would demonstrate a nodular interstitial infiltrate, and these

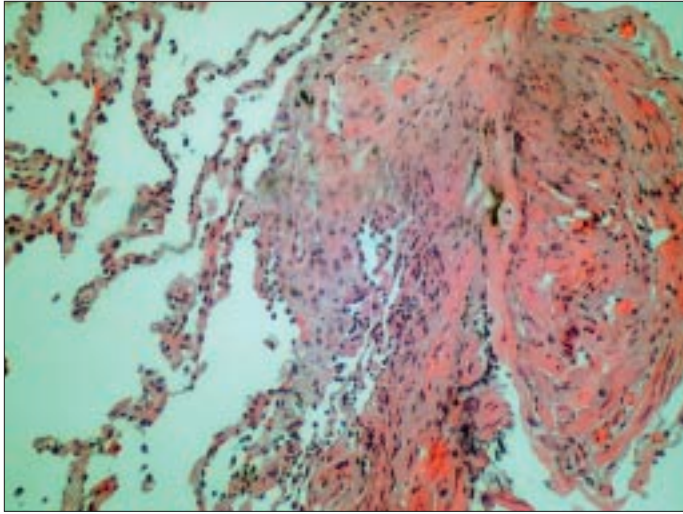


Figure 2. The biopsy of the lung tissue with marked scarring, septal fibrosis, and thickening. Hematoxylin-eosin stain, $\times 100$.

nodules can coalesce over time to form scarlike infiltrates. On biopsy, one might expect to find noncaseating granulomas, which contain talc particles. No effective treatment of this condition is available. Case reports have been published describing patients who have had dramatic improvement with steroids, but for the most part steroids are not successful.

PATHOLOGY REPORT

GABRIEL A. RODRIGUEZ, MD: Two small fragments of lung tissue obtained by transbronchial biopsy were submitted, measuring 0.3×0.2 cm in total aggregate. Multiple levels of tissue were examined and showed marked scarring with focal septal fibrosis and thickening (*Figure 2*). Polarization of the specimen showed refractile objects consistent with foreign material (*Figure 3*), but the particular type of foreign body could not be conclusively identified based on architecture. Pertinent negatives were lack of granulomas and foreign body giant cells; however, this may have been due to sampling error.

FURTHER DISCUSSION

BRADLEY S. JONES, MD: The pathological reports confirmed Dr. Brancaccio's diagnosis of foreign body emboli with reactive interstitial fibrosis. We don't know exactly what the foreign body was, but we suspect cotton wool. After we spoke with the patient, he indicated that he filtered his heroin through cotton balls. Other cases of cotton as the foreign body have been reported (1, 2). As Dr. Brancaccio indicated, talc and cellulose can also cause foreign body granulomatosis. Talc wasn't suspected here, since the biopsy showed a linear fragment and talc appears more crystalline. Starch—another possible contaminant—also forms more crystalline structures and doesn't cause fibrosis as much as it does thrombosis (3).

The exact mechanism leading to the fibrosis is not well understood. Most reports appeared in the 1970s. The initial damage is believed to be alveolitis, which progresses to fibrosis,

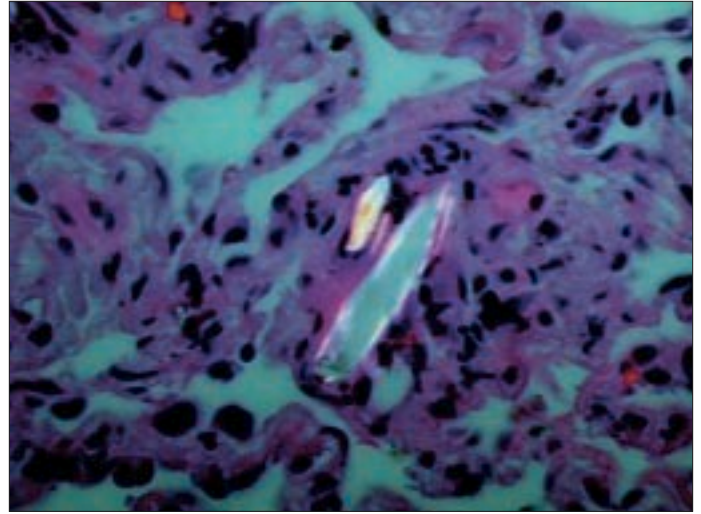


Figure 3. Polarization of foreign material in the lung tissue. Hematoxylin-eosin stain, $\times 400$.

perhaps through a delayed hypersensitivity reaction (3). Dyspnea, dry cough, low-grade fever, weight loss, and chest pain are the usual symptoms (1–6).

Pulmonary function tests usually show an almost universal decrease in the diffusing capacity of the lung for carbon dioxide. Lung volumes may be restrictive or obstructive but tend to be normal (3).

The consequences of this condition include angiothrombosis in the pulmonary vasculature, pulmonary hypertension, and cor pulmonale. This patient's peak systolic pulmonary pressure by echocardiogram was mildly elevated (36 to 38 mm Hg). Biopsy results usually show granulomatosis, micronodularity, and fibrosis. The biopsy specimen in this case was small, so the lack of granulomas and micronodularity may have been due to sampling error.

The patient was seen at BUMC for 18 months and during that period was admitted multiple times for dyspnea, pneumonia, and exacerbations. His most recent admission was in early 2002. He stayed several weeks, was sent to rehabilitation, and died at home 2 months later.

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