Fever, Cough, Pleuritic Chest Pain, and Pleural Fluid Eosinophilia in a 30-Year-Old Man*

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A 30-year-old previously healthy Hispanic man presented to the emergency department with a 3-day history of fever (temperature to 39.3°C), nonproductive cough, and left pleuritic chest pain. He denied smoking, intravenous drug use, or tuberculosis. He drank beer daily. His father had been diagnosed with pulmonary tuberculosis 6 years previously, but the patient had never been skin-tested or given tuberculosis chemoprophylaxis. He had been born in, and had not traveled outside, Los Angeles.

Physical Examination

Vital signs: temperature, 38.5°C; pulse, 114/min; respirations, 16/min; BP, 120/80 mm Hg. General: in moderate discomfort due to chest pain and fever. Skin: no rash. Mouth: good oral hygiene. Lymph nodes: no adenopathy. Heart: normal heart sounds without gallops or murmurs. Lungs: egophony over the left midlung field with decreased fremitus and breath sounds over two thirds of the left side of the chest.

Laboratory Findings

WBC: 12,300/ml with 71 percent neutrophils, 13 percent lymphocytes, 5 percent monocytes, 8 percent eosinophils, 2 percent basophils. Hemoglobin: 15.7 g/dl. Hematocrit: 47 percent. Arterial blood gas values (room air): pH, 7.42; PaO₂, 40 mm Hg; PaCO₂, 7.7 mm Hg. Chest radiograph shows large left pleural effusion with contralateral mediastinal shift and hilar adenopathy.

Thoracentesis pleural fluid analysis: Appearance, serosanguineous; serum total protein, 4.9 g/dl (normal, 6.4 g/dl); lactate dehydrogenase, 589 U/L (normal, 137 U/L); nucleated cells, 16,950/ml; differential, 30 percent neutrophils, 29 percent lymphocytes, 13 percent monocytes, 20 percent eosinophils. RBC: 7,400/ml; glucose, 100 mg/dl (normal, 152 mg/dl); Gram stain, negative; culture: pending.

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What is the most likely diagnosis?
Diagnosis: Acute pulmonary coccidioidomycosis with pleural effusion

Pleural effusions have been reported to occur in 7 to 20 percent of symptomatic cases of acute primary infection with Coccidioides immitis. These effusions are usually small and left-sided, although large to massive (as seen in the present patient) and right-sided or bilateral effusions have been reported. In approximately half of the cases, a pulmonary infiltrate, which is contiguous to the pleural effusion, is noted initially. Mediastinal and hilar adenopathy (as seen in the present patient) is seen in up to 20 percent of cases. The effusion is thought to result from direct extension of the pulmonary parenchymal focus into the pleural space.

The presence of peripheral eosinophilia, particularly in a patient with a pulmonary infiltrate who resides in or has traveled to the southwestern United States, strongly suggests infection with C immitis. Moderate (10 to 20 percent) peripheral eosinophilia may occur in acute, primary, coccidioidal infection, peaking at the second or third week of illness. The peripheral WBC count may be normal or minimally elevated.

Pleural fluid eosinophilia, defined as more than 10 percent eosinophils in the pleural fluid nucleated cell differential, is most commonly associated with air or blood in the pleural space, and thus it is most frequent with pneumothorax, hemotorax, pulmonary infarction, and benign asbestos pleural effusion. Despite the high frequency of bloody effusions in malignancy, fewer than 10 percent of malignant effusions have pleural fluid eosinophilia. Similarly, tuberculous pleurisy is an uncommon cause of pleural fluid eosinophilia, probably related to the lack of pleural space hemorrhage. Pleural fluid eosinophilia is rare in acute coccidioidal pleural effusion, being reported in only 1 of 15 cases in one series, despite 40 percent of the patients having blood eosinophilia. The pleural fluid nucleated cell count is usually less than 10,000/ml with a predominance of mononuclear cells (usually lymphocytes). This exudative effusion has a glucose concentration that approximates that of serum.

The diagnosis of acute pulmonary coccidioidal infection is made by culture, serology, and/or skin testing. If a pleural effusion is present, culture of the pleural biopsy specimen is the most sensitive test, with yields approaching 100 percent. Pleural fluid cultures are positive in only about 20 percent of patients, similar to the rate in tuberculous pleurisy. Sputum culture is positive in fewer than 15 percent of cases.

Management of acute pulmonary coccidioidal infection is based on evaluation of clinical and serologic evidence of possible dissemination. Increases in the complement fixation IgG titer (to 1:16 to 1:32 or higher) or continued elevation of the latex agglutinin or tube precipitin IgM titer should prompt evaluation for dissemination, utilizing thorough physical examination, bone scan, and lumbar puncture.

The present patient initially had a C immitis serum complement fixation titer of 1:2 with positive latex agglutinin and immunodiffusion tests. His coccidioidin skin test (performed at 1:10 dilution) was markedly positive. Two months after admission, his pleural effusion had resolved; however, the complement fixation titer had risen to 1:32, with a positive IgM immunodiffusion titer. He remained asymptomatic and had a normal bone scan and lumbar puncture with a negative cerebrospinal fluid complement fixation titer. On the basis of the persistently high complement fixation titer (1:32) and positive IgM immunodiffusion titer, at 10 months he was placed on fluconazole, 400 mg daily. He has been treated for 4 months to date and remains asymptomatic.

CLINICAL PEARLS

1. The presence of peripheral eosinophilia in a patient who lives or has traveled in the southwestern United States and who has respiratory symptoms and fever should suggest infection with C immitis.

2. Pleural effusions are relatively uncommon in acute C immitis infection and are usually small, left-sided exudates with a predominance of mononuclear cells. Culture of the pleural biopsy specimen provides the best diagnostic yield.

3. Pleural fluid eosinophilia may be seen with C immitis infection but is more commonly associated with air or blood in the pleural space, as occurs with pneumothorax, hemotorax, benign asbestos pleural effusion, and pulmonary infarction.

SUGGESTED READING


