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Sarcoidosis Masquerading as Eosinophilic Pneumonia

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A 29-year-old woman presented with progressive dyspnea, fever, cough, and weight loss. A chest roentgenogram revealed bilateral peripheral infiltrates suggestive of chronic eosinophilic pneumonia. Bronchoscopic evaluation, as well as a therapeutic trial of corticosteroids, was nondiagnostic. Open lung biopsy revealed findings consistent with a diagnosis of sarcoidosis. Roentgenographically, differentiating between sarcoidosis and chronic eosinophilic pneumonia can be difficult. A diagnostic approach, as well as the differential diagnosis of bilateral peripheral pulmonary infiltrates, is discussed.

(Key words: Sarcoidosis, eosinophilic pneumonia, pulmonary infiltrates)

Chronic eosinophilic pneumonia (CEP), as first described by Carrington and associates in 1969,[1] is associated with characteristic peripheral pulmonary infiltrates described as the "photographic negative" of pulmonary edema. It has been suggested that typical roentgenographic findings in combination with compatible clinical features and a rapid therapeutic response to corticosteroids may permit the diagnosis without biopsy.[1,2] We describe the clinical course of a patient with roentgenographic and clinical features compatible with CEP in whom a trial of corticosteroids did not support the diagnosis. Sarcoidosis was diagnosed by findings observed in tissue recovered at open lung biopsy.

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Report of case

A 29-year-old woman was hospitalized with a 1-month history of cough, progressive dyspnea, chest tightness, low-grade fevers, generalized malaise, and an associated 3-kg weight loss. The patient described her cough as initially nonproductive, changing to productive 2 weeks before admission. She reported no other significant symptoms.

The patient denied using any prescription medications. She said she had used an over-the-counter cold preparation on two occasions before admission. She reported 25 pack-years of tobacco use and the episodic use of free-base cocaine and marijuana. Her occupational history was unremarkable; the patient had previously been employed only as a waitress.

She had a temperature of 99.4°F and a respiratory rate of 24 per minute; chest examination revealed diffuse expiratory wheezing. The patient's admission chest roentgenogram is shown in *Figure 1*. Results of an intermediate-strength purified protein derivative skin test were negative; delayed hypersensitivity responses to candida and mumps antigens were intact.

The patient's complete blood cell count revealed a total white blood cell count of 5.9×10^3 cells/mm^3 with 4 eosinophils, 49 segmented neutrophils, 42 lymphocytes, 4 monocytes, and 1 basophil. Arterial blood gases on room air revealed a pH of 7.44, a $PaCO_2$ of 35 mm Hg, and a $PaCO_2$ of 90 mm Hg.

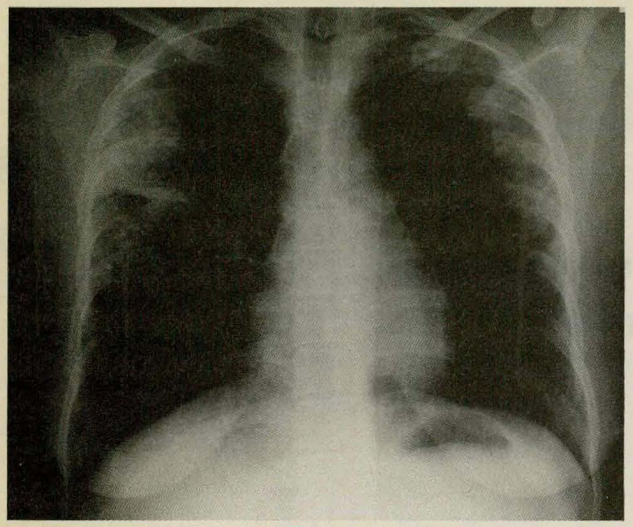

Figure 1. *Posteroanterior chest roentgenogram revealing bilateral peripheral infiltrates (with upper lobe predominance) in the absence of hilar or mediastinal adenopathy.*

The serum angiotensin-converting enzyme level was 48 U/L (normal, 8 to 53 U/L), and sputum examination failed to reveal typical or atypical pathogens. Results of pulmonary function studies were within normal limits, with the exception of a total lung capacity of 4.0 L (69% of predicted values) and a diffusion capacity for carbon monoxide of 55% of predicted values.

Bronchoscopy with bronchoalveolar lavage and transbronchial biopsies was performed. The bronchoalveolar lavage was performed in the posterior segment of the right upper lobe with less than 25% return of instilled fluid. The bronchoalveolar lavage differential revealed 84% macrophages, 13% lymphocytes, and 3% eosinophils. Results of special stains for acid fast, fungal, and parasitic microorganisms (as subsequent culture results) were negative. The transbronchial biopsies were remarkable only for the finding of a single noncaseating granuloma.

Therapy was instituted with prednisone, 40 mg daily, and maintained for 3 weeks. The patient's symptoms and roentgenographic abnormalities persisted despite this therapy. The prednisone therapy was discontinued, and an open lung biopsy of the left upper lobe was performed. Grossly, diffuse parenchymal nodularity extending to the pleura was found. Histopathologic findings included multiple noncaseating granulomas, asteroid bodies, and interstitial fibrosis (*Figure 2*). These findings were consistent with a diagnosis of sarcoidosis.

At long term follow-up (36 months), the patient remained stable clinically and by pulmonary function testing.

Discussion

Since its description in 1969,[1] CEP has been considered diagnosable when the classic roentgenographic findings described as the "photographic negative" of pulmonary edema are seen in association with typical clinical features,[1-3] including fever, dyspnea, productive cough, and weight loss. Recent reviews, however, have suggested that the typical roentgenographic features of CEP may be present in only one fourth of the cases, and that, in fact, the chest roentgenogram may be entirely normal.[5]

The differential diagnosis of peripheral pulmonary infiltrates (in addition to CEP) includes Loeffler's syndrome, mycobacterial and fungal diseases, periarteritis nodosa, Churg-Strauss vasculitis, lymphoma, eosinophilic granuloma, desquamative interstitial pneumonitis, pneumonitis or fibrosis complicating axillary radiation, bronchiolitis obliterans organizing pneumonia (BOOP), and sarcoidosis.[1-3,6,7]

Common chest roentgenographic features of sarcoidosis have been described, including thoracic lymphadenopathy with or without parenchymal infiltrates.[8,9] Uncommonly, peripheral pulmonary infiltrates may be seen in sarcoidosis which resemble those seen typically in CEP.[7,10] Glazer and associates[7] delineated several roentgenographic features useful in distinguishing between these two diseases. These features include adenopathy and a nodular quality of the infiltrates, the presence of which is more suggestive of a diagnosis of sarcoidosis than of CEP.[7]

Our patient had clinical and roentgenographic features compatible with a diagnosis of CEP. Results of the transbronchial biopsies, which revealed a single noncaseating granuloma, and the lack of peripheral eosinophilia, did not initially dissuade us from this diagnosis because a lack of peripheral eosinophilia,[1,3,4] as well as the presence of noncaseating granulomas,[1,4] has been described in CEP.

In addition, the bronchoalveolar lavage differential was made suspect by the poor return

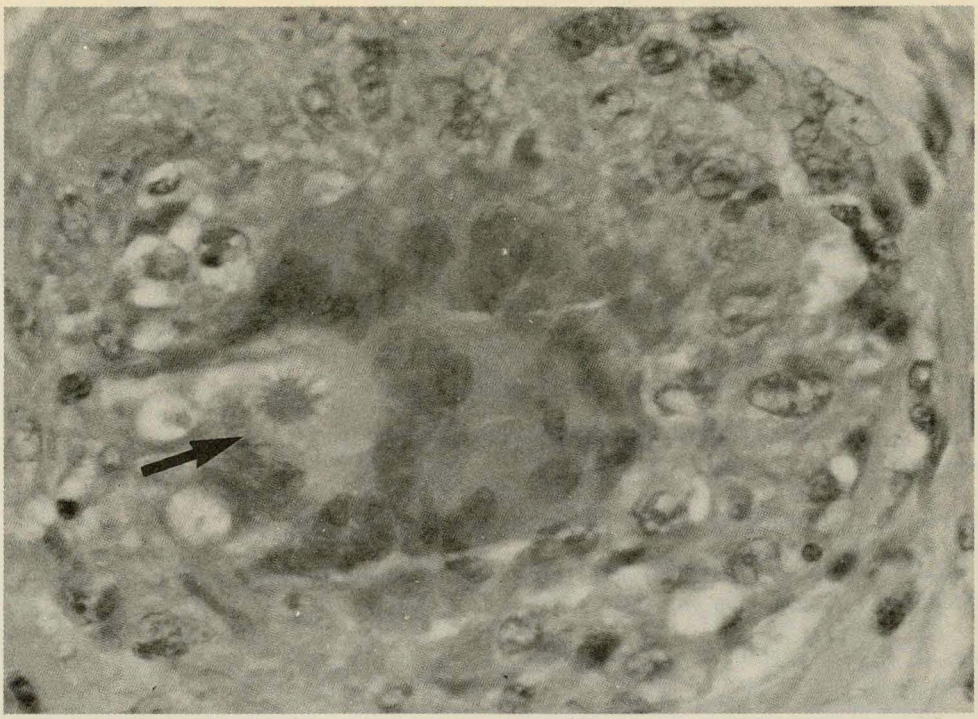

Figure 2. *Open lung biopsy specimen revealing a noncaseating granuloma and an asteroid body* (arrow), *consistent with a diagnosis of sarcoidosis (original magnification* × *1000).*

of instilled fluid. The absence of adenopathy and the nodularity of the infiltrates seen on chest roentgenogram also suggested a diagnosis of CEP as opposed to sarcoidosis when Glazer's criteria were used.[7] The absence of a response to corticosteroids led us to perform an open lung biopsy; hence, a diagnosis of sarcoidosis was confirmed.

The use of free-base cocaine has been associated with significant respiratory complications and has been the subject of a recent review.[11] Hypersensitivity pneumonitis has been reported as a complication of this form of substance abuse[12]; typical features include fever, transient pulmonary infiltrates, eosinophilia, and bronchospasm temporally linked to the inhalation of cocaine. In addition, BOOP has been associated with free-base cocaine use. As previously indicated, BOOP has also been reported to exhibit peripheral pulmonary infiltrates.[6] It is unlikely, however, that either of these reported complications was a factor in this case because the clinical and pathologic findings are not supportive of either diagnosis.

The utility of bronchoscopy and, in particular, bronchoalveolar lavage in diagnosing CEP has been described.[13,14] Bronchoalveolar lavage eosinophil counts in five untreated CEP patients ranged from 14% to 75% as reported by Dejaegher and Demedts.[14] In sarcoidosis, bronchoalveolar lavage findings are extremely variable and are dependent on both the activity and stage of the disease.[15] Bronchoalveolar lavage differentials from patients with sarcoidosis, as opposed to those from patients with CEP, rarely include significant numbers of eosinophils.

Certainly, when bronchoalveolar lavage or transbronchial biopsy or both are nondiagnostic for CEP or when the disease course does not respond to a trial of corticosteroids, open lung biopsy is indicated to rule out other pathologic entities that may require alternative modes of therapy. Additional information provided by open lung biopsy is often related to the larger tissue sampling available from grossly abnormal regions of lung parenchyma, as opposed to the random small samples retrieved by transbronchial biopsy.

Comment

As illustrated by this case, the absence of ade-

nopathy or a nodular quality of the peripheral infiltrates may not mitigate against the diagnosis of sarcoidosis in favor of CEP as has been suggested. Although these criteria may be useful clinically, they should not be regarded as all-inclusive.

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