Treatment of Coccidioidomycosis-associated Eosinophilic Pneumonia with Corticosteroids

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Abstract

Pulmonary coccidioidomycosis is a common cause of community-acquired pneumonia in endemic areas of the southwestern United States. The clinical spectrum of this disease ranges from an asymptomatic presentation to severe disease with ARDS and hypoxemic respiratory failure. Despite evidence supporting the use of corticosteroids for severe pulmonary disease in other fungal infections, there is currently no established role for this therapy in coccidioidomycosis infections. Peripheral eosinophilia is a common feature of coccidioidomycosis; however, pulmonary eosinophilia is rarely reported. In the setting of pulmonary eosinophilia of other etiologies, corticosteroid therapy has been demonstrated to have a role in reducing the inflammatory response and leading to a more rapid resolution of hypoxemic respiratory failure. We report a case of a patient with primary pulmonary coccidioidomycosis complicated by severe pulmonary eosinophilia that demonstrated rapid improvement after the initiation of corticosteroid therapy.

Case Report

A 71-year-old man presented to the emergency room in Tucson, Arizona with a one-week history of fever, cough, and malaise. The patient's symptoms began while returning from a trip to northern California. A chest radiograph ordered by the primary care physician demonstrated a right upper lobe consolidation (Figure 1) and azithromycin was prescribed. Fevers persisted along with worsening cough over the next three days, and the patient presented for further evaluation.

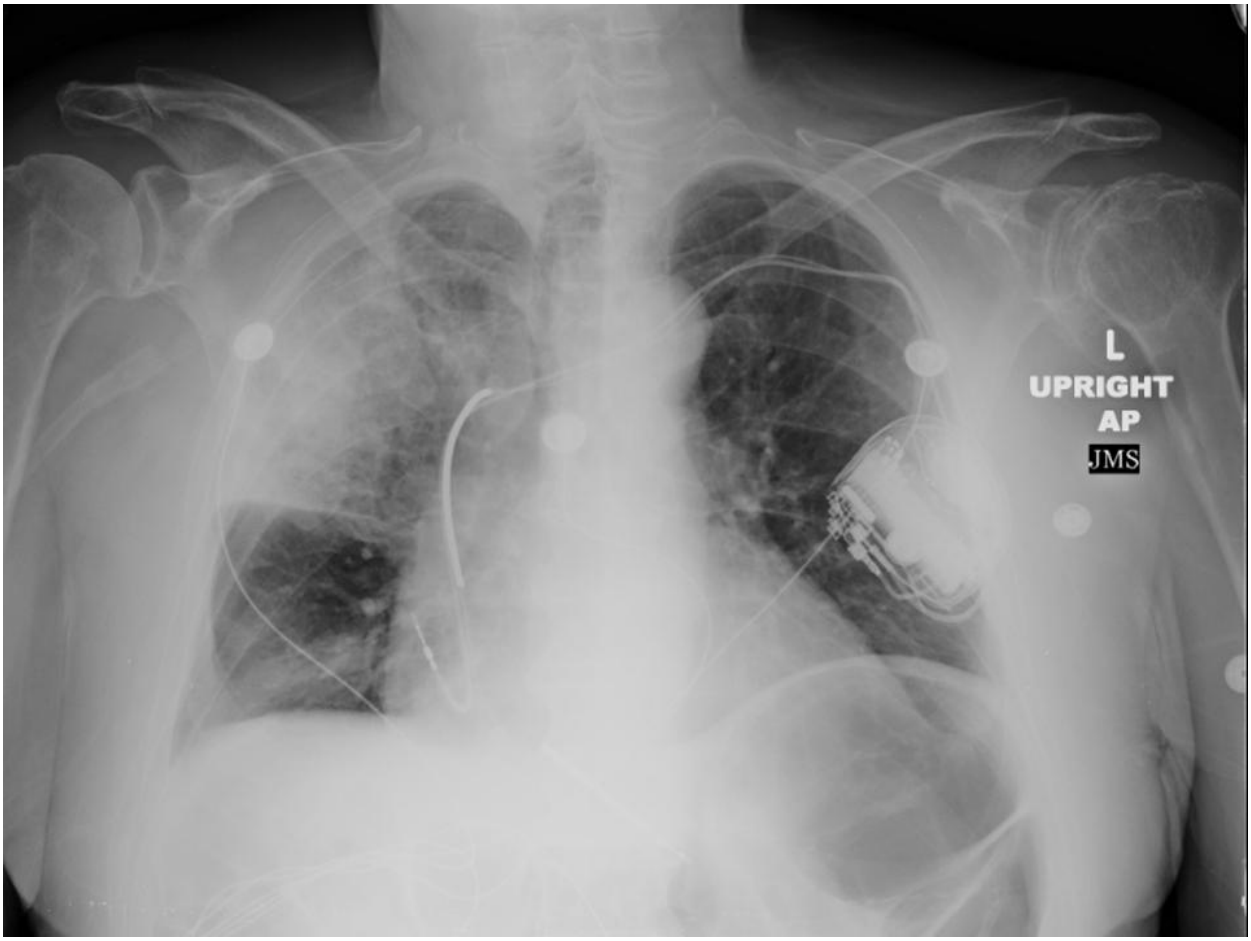

Figure 1. Admission radiograph demonstrating right upper lobe airspace disease.

Medical history was remarkable for viral cardiomyopathy requiring placement of an ICD after an episode of sudden cardiac death in 2006. An episode of *S. bovis* bacteremia occurred 4 months prior to the current presentation and was treated with a course of cefazolin. There is no known personal or family history of atopic disease. There is no history of tobacco use or significant occupational exposures. The patient had been living in Arizona during the preceding year and had no other recent travel history, dust, or environmental exposures.

On physical exam, temperature was 38.8°C and pulse oximetry saturation was 90 percent on room air. The patient was in moderate respiratory distress with rales auscultated in the right upper lung zone. Subsequent laboratory examination revealed a PaO2 of 69 mmHg on 4 liters-per-minute of oxygen via nasal cannula. A metabolic panel showed elevated transaminases and his initial leukocyte count was 11.8 x $10^3/\mu L$ with differential including 5% eosinophils.

The patient was admitted to the medical ward and treated with vancomycin, cefepime, and moxifloxacin for pneumonia caused by a potentially resistant organism. Fluconazole was started on the third hospital day for empiric treatment of primary pulmonary

coccidioidomycosis. A CT angiogram of the chest showed bilateral multilobar pneumonia (Figure 2).

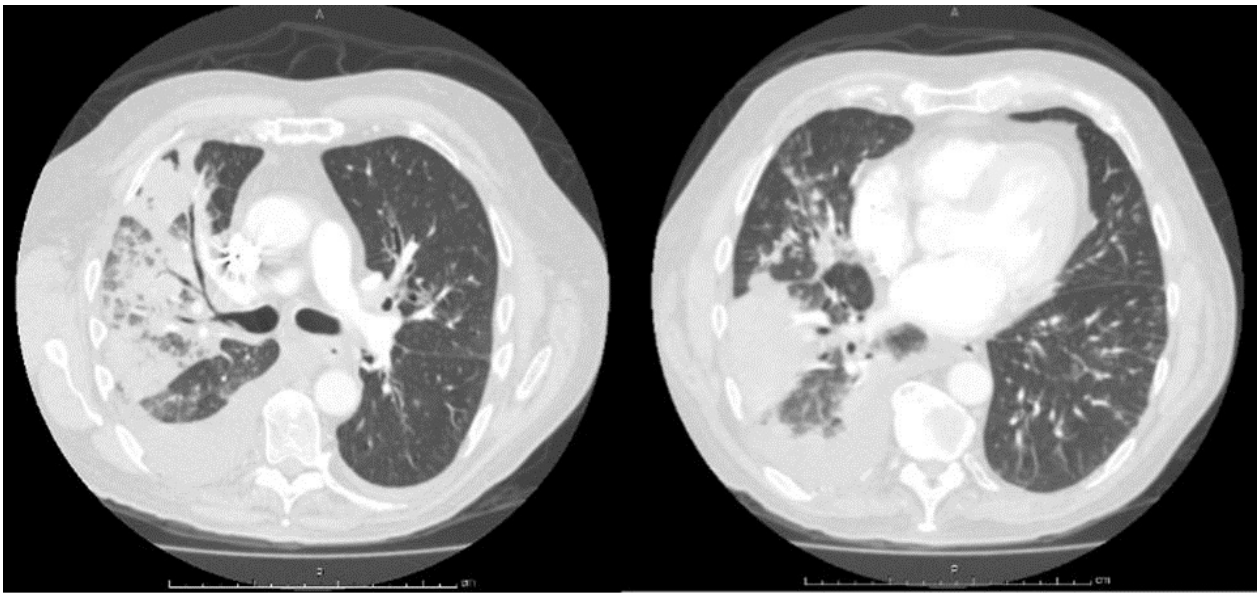

Figure 2. CT angiogram of the chest demonstrating multilobar consolidation of the right lung.

The patient deteriorated and required intubation for severe hypoxemia two days later. A bronchoalveolar lavage revealed *Coccidioides* spherules on cytological examination. Liposomal amphotericin B was initiated, which led to the development of oliguric renal failure necessitating hemodialysis. Initial *Coccidioides* serology was negative, however sputum and BAL cultures demonstrated *C. immitis*. Despite antifungal therapy his pulmonary status worsened with progressive bilateral pulmonary infiltrates and worsening hypoxemic respiratory failure (Figure 3).

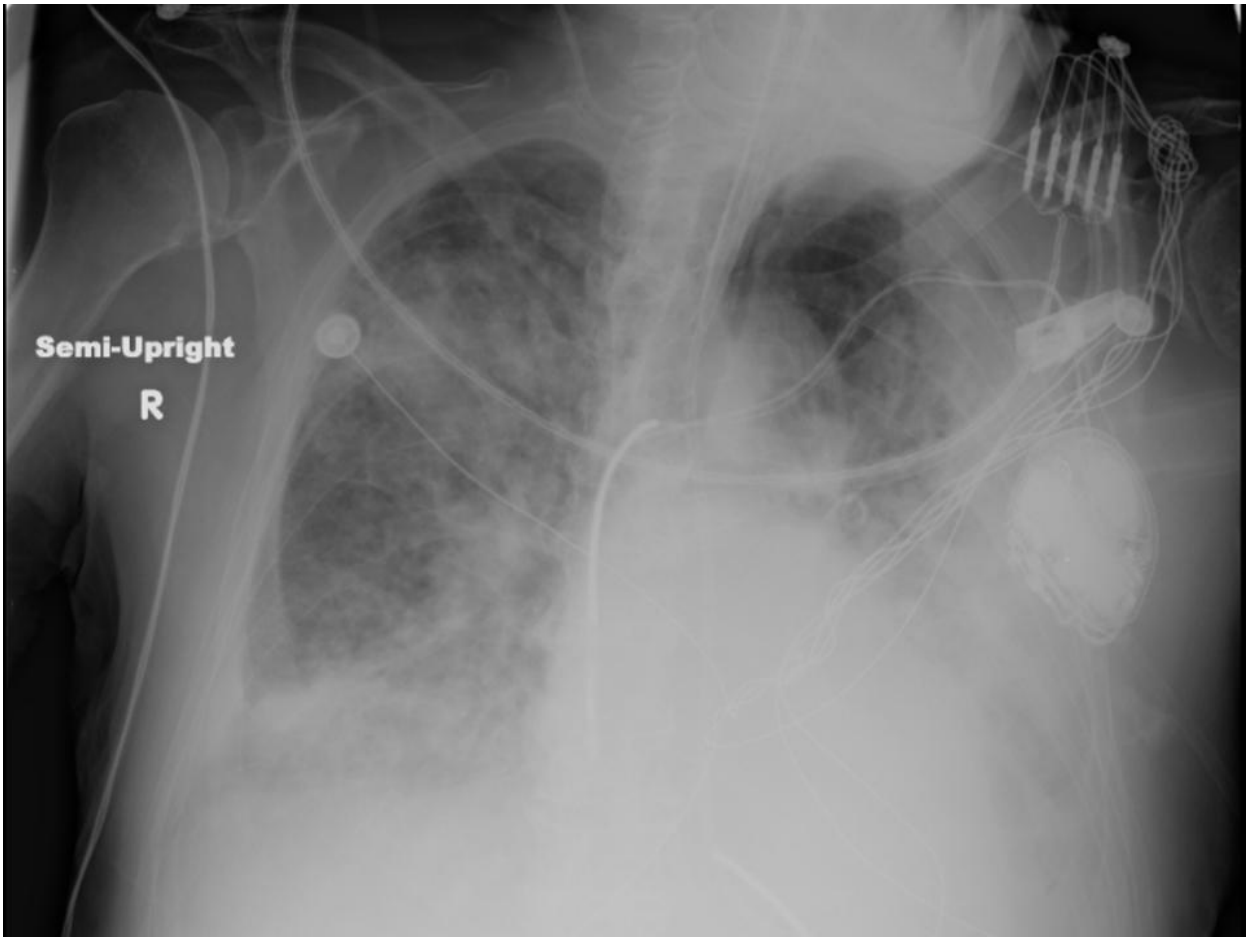

Figure 3. CXR demonstrating progressive bilateral alveolar opacities consistent with ARDS

In addition, he had a steadily increasing peripheral eosinophilia reaching a maximum of 40 percent with a leukocyte count of 14.8 x $10^3/\mu L$ despite the absence of any signs of disseminated coccidioidomycosis. A repeat BAL again showed *Coccidioides* spherules and eosinophils of 40 and 56 percent from the right middle lobe and lingula, respectively. Methylprednisolone 40mg IV three times daily was started with a decline in blood eosinophils to one percent within 24 hours. Chest radiographs and A-a gradient rapidly improved over the next 3 days leading to successful extubation. The patient was transitioned to oral fluconazole and prednisone and discharged from the hospital in good condition two weeks later.

At the follow-up six weeks after initial presentation, he remains on fluconazole and prednisone 15mg daily with no signs of disseminated coccidioidomycosis and is continuing a gradual reduction of prednisone dosage.

Discussion

Coccidioidomycosis is caused by either of 2 species of the dimorphic fungus *Coccidioides*. Endemic regions are present in North and South America, with the

majority of cases within the United States arising in Arizona and California. Although peripheral eosinophilia is a commonly reported finding (1), pulmonary eosinophilia has rarely been described.

Acute eosinophilic pneumonias may be idiopathic or a secondary inflammatory response to various infections or environmental exposures. In regions where endemic fungal infections are common, differentiating between eosinophilic pneumonias of idiopathic versus infectious etiology is vital in order to avoid inappropriate therapy and its adverse consequences. A review of the literature concerning pulmonary coccidioidomycosis and concurrent pulmonary eosinophilia demonstrates only 9 prior case reports. Corticosteroid therapy was used for treatment of the pulmonary eosinophilia in only 3 of these cases, 2 of which resulted in death from disseminated coccidioidal infection (1-3). One case ended in spontaneous resolution of disease without antifungals or corticosteroids leading the authors to suggest a conservative approach with corticosteroids due to the risk for dissemination (4).

In our case, there was progressive clinical deterioration despite ten days of treatment with appropriate antifungal regimen, leading to our decision to treat with corticosteroids. The immediate decrease in peripheral eosinophilia in conjunction with the rapid clinical improvement leads us to the conclusion that corticosteroids were beneficial in the resolution of his acute respiratory failure. The clinical response observed is similar to that expected in idiopathic acute eosinophilic pneumonia which supports the notion that the eosinophilic response, as opposed to the primary infection, was primarily responsible for our patient's severe hypoxemia.

There remains a risk for disseminated disease. In the cases cited in which patients died of dissemination, antifungal therapy preceding corticosteroid therapy was not described. Due to the risk of underlying pulmonary coccidioidomycosis in endemic regions, corticosteroid therapy for eosinophilic pneumonia should only be considered in the setting of severe hypoxemic respiratory failure and once adequate antifungal therapy has been initiated.

According to recent guidelines there is no role for corticosteroid therapy in the treatment of coccidioidomycosis due to a lack of convincing data for efficacy and safety (5). There is precedent for treating severe pulmonary disease caused by other fungal infections, such as histoplasmosis and blastomycosis, with corticosteroids. We suggest that there is a role for the use of corticosteroid therapy in the setting of progressive respiratory failure due to coccidioidomycosis with associated pulmonary eosinophilia that has failed conventional antifungal therapy.

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The authors report no conflicts of interest

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