

Fatal Massive Hemoptysis in a Patient on Low-Dose Oral Prednisone: Chronic Necrotizing Pulmonary Aspergillosis

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We report a case of chronic necrotizing aspergillosis in a 74-year-old man with chronic lung disease, who was on low-dose oral prednisone. The patient was treated with various antibiotics but had no improvement. Samples obtained via bronchoscopy grew *Aspergillus*, and the patient was started on lipid formulation amphotericin B. Three days after admission the patient developed fatal massive hemoptysis, presumably secondary to acquired systemic-to-pulmonary vascular communication. This is an unusual presentation of a rare manifestation of pulmonary aspergillosis. A high index of suspicion is needed to diagnose this condition in susceptible patients. Key words: chronic necrotizing aspergillosis, hemoptysis, pulmonary mycosis. [Respir Care 2007;52(1):56–58. © 2007 Daedalus Enterprises]

Introduction

Chronic necrotizing pulmonary aspergillosis was first described in 1981 by Gefer et al,¹ who described 5 patients with locally invasive pulmonary aspergillosis. Gefer et al used the term “semi-invasive pulmonary aspergillosis” to differentiate this clinical entity from colonization of the respiratory tract and frank pulmonary invasive aspergillosis.¹ In 1982, Binder et al² cited 22 cases in the literature that were consistent with the diagnosis of chronic necrotizing pulmonary aspergillosis, and coined the term “chronic necrotizing aspergillosis.” Terms that were used to describe cases of chronic necrotizing pulmonary aspergillosis before 1982 were “primary pulmonary aspergillosis,” “pulmonary aspergillosis with cavitation,” and “symptomatic pulmonary aspergilloma.”²

Massive hemoptysis is a rare and potentially fatal complication of chronic necrotizing pulmonary aspergillosis. We describe a case of chronic necrotizing pulmonary aspergillosis that was misdiagnosed as bacterial pneumonia

for several months and led to massive hemoptysis, with a fatal consequence.

Case Summary

A 74-year-old African American man was admitted to the hospital for dyspnea, weight loss, and chronic cough. A chest radiograph and chest computed tomogram (Fig. 1) showed bilateral pulmonary consolidations. Review of a chest radiograph from 2 months before this presentation revealed progression of infiltrates in the left upper and left lower lobes. No cavitary lesions were seen. The patient had been treated with several courses of various antibiotics (azithromycin, levofloxacin, and doxycycline) during the several months before this presentation, but his fever, cough, and dyspnea progressed. His medical history was notable for chronic obstructive pulmonary disease (COPD), hypertension, diabetes mellitus, and gastroesophageal reflux disease. The COPD was diagnosed 5 years before this presentation. The patient reported frequent hospital admissions for COPD exacerbations. His last spirometry showed severe airway obstruction (forced expiratory volume in the first second 0.83 L). The patient was a smoker for 50 years. He also reported a tuberculosis exposure in the past, but his recent skin tuberculin test was nonreactive. He also had a substantial asbestos exposure when he worked at a Navy shipyard. His medications on presentation to us included metformin, lisinopril, aspirin, oral prednisone (10 mg/d for about 2 years, for COPD), and an as-needed bronchodilator.

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Fig. 1. Chest computed tomogram showing bilateral infiltrates.

Physical examination on admission showed a temperature of 38.0°C, blood pressure of 146/82 mm Hg, heart rate of 96 beats/min, respiratory rate of 20 breaths/min, and oxygen saturation of 87% on room air. He was in mild respiratory distress. Chest examination revealed bilateral crackles. The heart and abdominal examination was unremarkable. There was no peripheral edema or clubbing. Laboratory findings were: white-blood-cell count $8.5 \times 10^3/\mu\text{L}$, hemoglobin 8.6 g/L, and creatinine of 1.2 mg/dL. Bronchoalveolar lavage fluid collected during bronchoscopy grew *Aspergillus fumigatus*. The bronchoalveolar lavage fluid bacterial, viral, and mycobacterial cultures were negative. Chronic necrotizing pulmonary aspergillosis was suspected, and the patient was started on lipid formulation amphotericin B. Three days after presentation, the patient developed massive hemoptysis and died secondary to respiratory failure. The lungs at autopsy showed patchy pulmonary parenchymal invasion of fungal elements, with involvement of the bronchial wall, consistent with chronic necrotizing pulmonary aspergillosis (Fig. 2). There was no vascular invasion. Although there was pleural thickening and chronic inflammation, we found no *Aspergillus* invasion of the pleura, nor disseminated aspergillosis in other organs. The massive hemoptysis was thought to be secondary to acquired systemic-to-pulmonary vascular communications seen in chronic inflammatory and infectious diseases of the lung.

Discussion

Chronic necrotizing pulmonary aspergillosis is defined as an indolent but destructive inflammatory lung infection by invasive *Aspergillus* species (usually *A. fumigatus*), and is characterized by local invasion of lung tissue by fungal

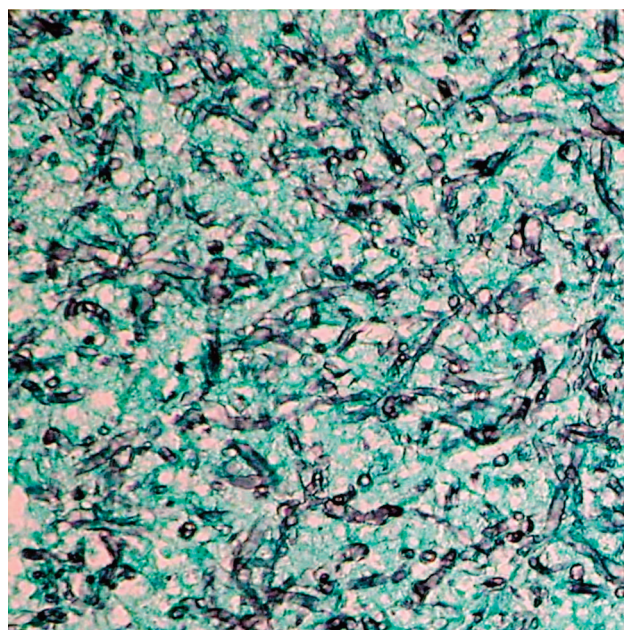


Fig. 2. Fungal elements, showing the 45° branching that is consistent with *Aspergillus* species ($\times 200$ silver stain).

elements, but absence of vascular invasion. Although chronic necrotizing aspergillosis is progressive over several months, there is no dissemination to other organs.^{3,4}

Chronic necrotizing pulmonary aspergillosis is usually seen in middle-age and elderly patients. Symptoms are nonspecific and include fever, cough, hemoptysis, and weight loss of 1–6 months duration.⁴ Most patients with chronic necrotizing pulmonary aspergillosis have either underlying chronic lung diseases or systemic diseases that predispose them to the disease. In one study, 9% of patients had no reported risk factors and 37% of patients had multiple risk factors. The pulmonary risk factors include COPD, interstitial lung disease, previous mycobacterial infections, asthma, cystic fibrosis, previous lung resection, sarcoidosis, and pneumoconiosis.^{3–8} The systemic risk factors are diabetes mellitus, low-dose corticosteroids, rheumatoid arthritis, ankylosing spondylitis, and malnutrition.^{1,3,4} Other rare clinical manifestations are pneumothorax,⁹ immune reconstitution syndrome in patients infected with human immunodeficiency virus who are on antiretroviral therapy,⁶ pulmonary infiltrates following cryptococcal infection,¹⁰ and Pancoast syndrome.¹¹ Radiographic findings include an infiltrative process in the upper lobes or superior segment of the lower lobes, and cavitory lesions, with adjacent pleural thickening. A mycetoma (fungus ball) can be seen in about 50% of patients with cavitory lesions. Histologic examination of the lung parenchyma shows necrotizing granulomas, invasion and destruction of lung tissue by mycetoma, or primary bronchiolar infection.^{3,4}

Diagnosing chronic necrotizing pulmonary aspergillosis can be challenging. Diagnosis may be helped by histologic evidence of tissue invasion by fungus, clinical and radiographic features consistent with the diagnosis, and isolation of *Aspergillus* from sputum or bronchoscopic samples after exclusion of other conditions. Delayed diagnosis is common and can contribute to morbidity and mortality. In one study, the average delay in diagnosis ranged from 3 months to 7 months. Treatment options include antifungal therapy with amphotericin B, itraconazole, or voriconazole. Although voriconazole is equal or superior to amphotericin B for invasive aspergillosis, there are few data on chronic necrotizing aspergillosis. Surgical resection is limited to a small subset of patients with local infection, adequate pulmonary reserve, and acceptable surgical risk.^{3,4}

Chronic necrotizing pulmonary aspergillosis should be included in the differential diagnosis of pulmonary infiltrates in a patient with pulmonary or systemic risk factors and fever, cough, dyspnea, and weight loss. Massive hemoptysis is a potentially fatal complication of chronic necrotizing pulmonary aspergillosis.

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