

Pulmonary Mucormycosis in the Setting of Chronic Obstructive Pulmonary Disease

A Case Report and Review of the Literature

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Key Words

Mucormycosis · COPD

Abstract

We describe the first case of pulmonary mucormycosis occurring in a patient with chronic obstructive pulmonary disease (COPD) maintained on chronic low dose oral steroids (10 mg/day). The diagnosis was made by direct histopathological examination and culturing of infected tissue obtained by fiberoptic bronchoscopy. Pulmonary mucormycosis is caused by infection with an opportunistic fungus of the order Mucorales and is an acute, rapidly developing and often fulminant process usually occurring in immunocompromised individuals. Risk factors include neutropenia, hematologic malignancies, uncontrolled diabetes mellitus, skin burns and deferoxamine therapy in dialysis patients. This case illustrates the importance of early suspicion of mucormycosis and immediate diagnostic bronchoscopic examination in cases of rapidly progressing pulmonary infiltrates in COPD patients on low doses of corticosteroids.

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Introduction

Pulmonary mucormycosis is an uncommon opportunistic fungal infection that occurs almost exclusively in immunocompromised patients [1]. The causative agents are fungi in the class Zygomycetes of the order Mucorales. Zygomycetes are thermotolerant inhabitants of decaying organic matter and are distributed worldwide. Risk factors for infection include uncontrolled diabetes mellitus, hematologic malignancies, neutropenia, skin burns, and deferoxamine therapy in dialysis patients [1].

Case Report

A 74-year-old male with chronic obstructive pulmonary disease (COPD) was admitted to hospital following a 3-day history of increasing dyspnea and a cough productive of yellow sputum. He did not have any chest pain, hemoptysis, fever, chills or night sweats. His past medical history was significant for COPD: coronary artery bypass surgery with placement of a DDI pacemaker 2 years prior to admission, type II diabetes mellitus and congestive heart failure. Medications included prednisone (Medirex; Pine Brook, N.J., USA) 10 mg/day for the last 24 months, albuterol (Ventolin; Glaxo-Wellcome, Research Triangle Park, N.C., USA) and ipratropium inhalers

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Fig. 1. Chest X-ray (AP view) on admission, revealing minimal increased markings at right lung base.

Fig. 2. Chest X-ray (AP view) on hospital day 7, revealing extensive infiltrate of the right middle and lower lung.

Fig. 3. Chest X-ray (AP view) on hospital day 14, revealing progression of the right-sided infiltrate to consolidation involving the entire right lung.

(Atrovent; Boehringer Ingelheim, Ridgefield, Conn., USA), digoxin (Lanoxicaps; Glaxo-Wellcome), isosorbide dinitrate (Isordil; Wyeth-Ayerst, Philadelphia, Pa., USA), diltiazem (Cardizem CD; Hoechst Marion Roussel, Kansas City, Mo., USA), and alendronate (Fosamax; Merck, West Point, Pa., USA). He was an ex-smoker with a 60-pack-year smoking history. He had no history of alcohol or intravenous drug use.

On physical examination, the vital signs were within normal limits except for a temperature of 100.5° F (38.06 °C), and an O₂ saturation of 87% on room air. The head and neck examination was unremarkable. The chest examination revealed inspiratory crackles over the right lower lung field without bronchial breathing sounds. There was moderate expiratory wheezing throughout. The cardiovascular examination revealed normal heart sounds without any rubs or

murmurs. The remainder of the physical examination was within normal limits.

A chest radiograph obtained on admission revealed evidence of coronary artery bypass surgery, the pacemaker, cardiomegaly, and a possible right lower lobe infiltrate (fig. 1). Arterial blood gas, obtained with the patient breathing oxygen (2 liters/min via nasal cannula), revealed a pH of 7.36, a pCO₂ of 39 mm Hg, and a pO₂ of 94 mm Hg. White blood cell count was $5.2 \times 10^3/\text{mm}^3$, hemoglobin 11.4 g/dl and platelet count was $133 \times 10^3/\text{mm}^3$. Electrolytes and liver function tests were within normal limits.

The patient was admitted to the medical ward and was treated for COPD exacerbation and possible pneumonia with albuterol and atrovent nebulizers, intravenous methylprednisolone (Solumedrol; Pharmacia Upjohn, Peapeck, N.J., USA), ceftriaxone (Rocephin;

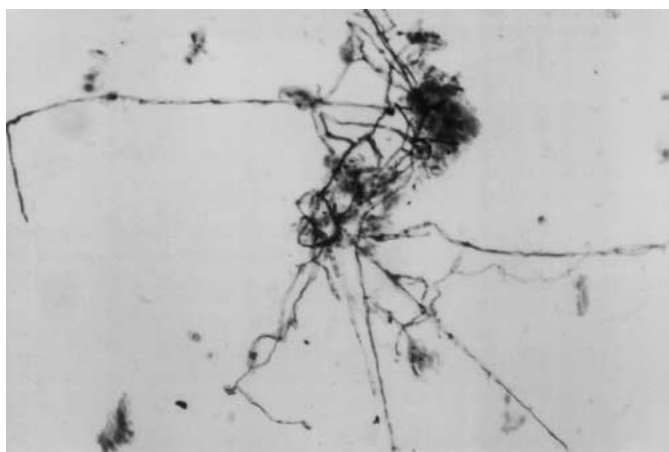


Fig. 4. Papanicolaou stain of the bronchial brush specimen showing the broad, twisted, ribbon-like, nonseptate hyphae of *Rhizopus arrhizus*. $\times 290$.

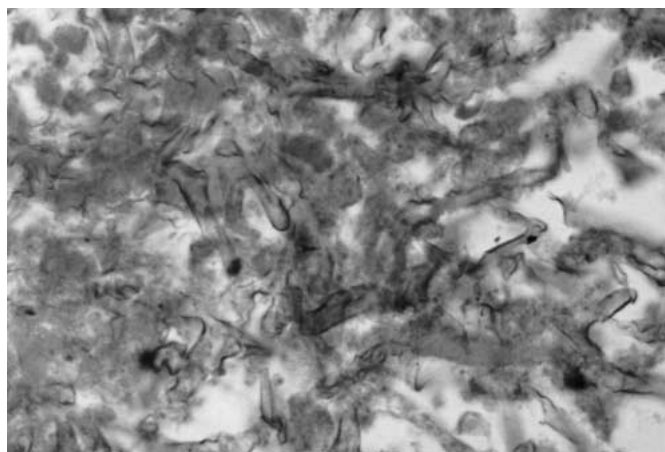


Fig. 5. HE stain of the transbronchoscopic lung biopsy specimen showing hyphae of *R. arrhizus* and associated necrosis. $\times 290$.

Roche, Nutley, N.J., USA) and clarithromycin (Biaxin; Abbott, Abbott Park, Ill., USA). Over the next 6 days his respiratory status deteriorated, leading to intubation and admission to the intensive care unit (ICU) on day 7. At that time, a chest radiograph revealed a worsening right-sided infiltrate involving most of the right lung (fig. 2). Sputum and blood cultures from admission were negative. The patient's antibiotic therapy was switched to cefipime (Maxipime; Bristol-Meyers-Squibb, Princeton, N.J., USA), vancomycin (Lilly, Indianapolis, Ind., USA) and metronidazole (Flagyl; SCS, Chicago, Ill., USA). His oxygenation continued to worsen and a representative chest film 1 week later revealed a total consolidation of the right lung (fig. 3).

Fiberoptic bronchoscopy was performed on hospital day 17. Erythematous bronchial mucosa with purulent secretions were seen, involving the entire right lung. Bronchial brushings and endobronchial biopsy both revealed mucormycosis (fig. 4, 5). Cultures of the endobronchial brushing grew *Rhizopus arrhizus* species. Amphotericin B (Abelcet; Liposome, Princeton, N.J., USA) therapy was initiated directly after the bronchoscopy, once the Gram stain results were known, but the patient continued to decline and expired on hospital day 20. A postmortem examination was not performed.

Discussion

This is the first report of a COPD patient on chronic oral steroids developing pulmonary mucormycosis. It is unclear whether our patient entered the hospital with this infection already present due to a COPD exacerbation, or whether mucor was selected by our initial use of antibiotics. The fungus was not present on initial sputum cultures obtained at admission. We suspect that the chronic use of

oral steroids may have increased the patient's susceptibility to this opportunistic fungus. Corticosteroids inhibit macrophage function, a key component of the immune system responsible for controlling spore germination [2].

Steroids are unlikely to be the sole reason for our patient acquiring this rare infection. Our patient's underlying diabetic condition, despite the fact that it was well controlled, may have played a synergistic immunosuppressive role by inhibiting neutrophil chemotaxis [3]. However, Lee et al. [4] could find no clear underlying immune defect in 11 of 87 patients with isolated pulmonary mucormycosis. Given that mucormycosis is ubiquitous in nature, and that Zygomycetous fungi grow very rapidly and release large numbers of spores, exposure to this agent is widespread in the population. The efficacy of the intact human immune system is evident by the fact that mucormycosis rarely produces infection.

A definitive diagnosis of mucormycosis can only be made by direct histopathological examination and culturing of infected tissue. Bronchoscopy is the most common method used to obtain tissue; about 40% of patients with this condition will have visible endobronchial lesions which may be biopsied [4]. Histopathological examination of infected tissue will reveal broad nonseptate hyphae with right angle branching that is more sensitive than culture (sensitivity of 93 vs. 49%) [4]. As mucorales may be a contaminant, the clinical significance of isolating the organism from sputum and bronchoalveolar lavage is problematic [5].

Treatment involves a combination of amphotericin B (1mg/kg/day), surgical debridement of infected tissue and reversal of the underlying medical condition [1]. The overall outcome is poor, with overall survival about 44% [4]. When diagnosed early, there may be a higher potential

for cure. This case illustrates the importance of early suspicion of mucormycosis and immediate diagnostic bronchoscopic examination, especially in the setting of steroid-dependent, diabetic COPD patients with pulmonary infiltrates that progress despite antibiotic therapy.

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