CASE REPORT

Primary Pulmonary Cryptococcosis Presenting as Endobronchial Tumor with Left Upper Lobe Collapse

Ying-Shan Chang, Kuo-Chih Chou*, Po-Chien Wang, Hsiao-Bai Yang[1], Chung-Hwa Chen

Departments of Internal Medicine and [1]Pathology, Ton-Yen General Hospital, Chupei, Hsinchu, Taiwan, R.O.C.

Primary pulmonary cryptococcosis is difficult to diagnose because the symptoms and radiologic findings are non-specific. Further, pulmonary cryptococcal infections are extremely rare in individuals with normal immunity. This case report describes a case of primary pulmonary cryptococcosis in an immunocompetent individual who presented with left upper lobe collapse due to endobronchial occlusion. [*J Chin Med Assoc* 2005;68(1):33–36]

Key Words: Cryptococcosis, *Cryptococcus neoformans*, endobronchial tumor, lung collapse, primary pulmonary cryptococcosis

Introduction

Cryptococcosis is an infection caused by the yeast-like fungus *Cryptococcus neoformans*. The infection is thought to be acquired by inhalation of spores into the lungs. Patients are frequently asymptomatic and have a tendency towards spontaneous resolution. Radiographically, however, the infection may present as a spectrum ranging from the most common findings of a well or poorly marginated nodule or mass, and lobar or segmental parenchymal opacities, to the less common patterns of diffusely scattered nodules or reticulonodules. This case highlights a rare instance of primary pulmonary cryptococcosis presenting as left upper lobe collapse due to endobronchial occlusion.

Case Report

A 33-year-old man presented with a 6-month history of cough with chest discomfort. The patient was initially treated for upper respiratory tract infection, but failed to improve. A consultation was therefore arranged at the outpatient department of our hospital. Chest X-ray revealed left upper lobe collapse (Figure 1), and the

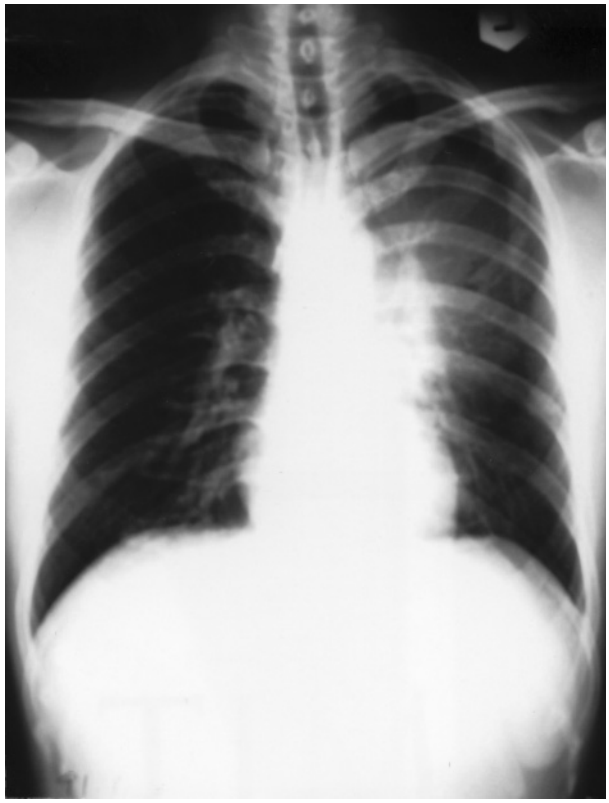

Figure 1. Chest X-ray (postero-anterior view) revealed left upper lobe collapse.

*Correspondence to: Dr. Kuo-Chih Chou, Department of Internal Medicine, Ton-Yen General Hospital, 69 Second Hsien-Chen Road, Chupei, Hsinchu 302, Taiwan, R.O.C.
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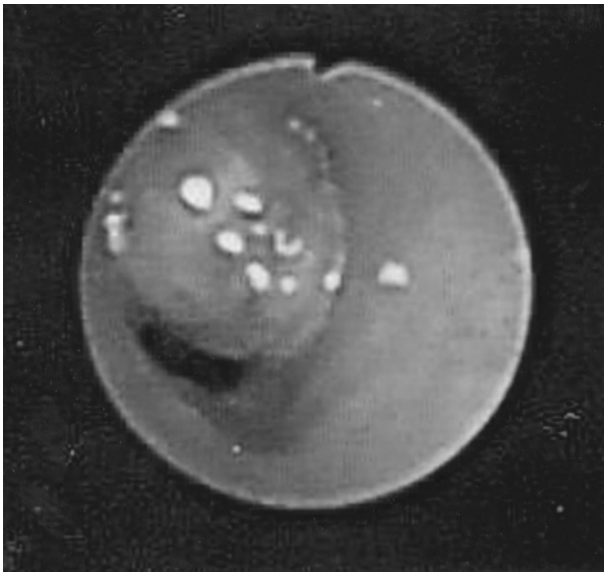

Figure 2. Bronchoscopy confirmed a whitish mass over the left upper lung orifice that caused total occlusion.

patient was subsequently admitted.

The patient, who worked as a supervisor in a glass company, was a carrier of hepatitis B virus, but denied any previous serious medical or surgical illness. Physical examination was near normal, without any meningeal signs, and vital signs were stable. No loss of body weight was noted. Hematologic and biologic parameters were within normal ranges. Sputum cytology and acid-fast stain revealed negative findings. Computed tomography (CT) scan of the chest revealed a suspicious soft tissue mass in the left upper lobe bronchus and left upper lung collapse. Bronchoscopy confirmed a whitish mass over the left upper lung orifice that caused total occlusion (Figure 2). A biopsy specimen was taken from the mass and showed cryptococcus infection (Figure 3); serum cryptococcus antigen was positive. Further work-ups included the following: negative HIV test; activated third component of complement (C3) = 106 mg/dL (normal, 90–180 mg/dL); activated fourth component of complement (C4) = 15 mg/dL (normal, 10–40 mg/dL); immunoglobulin G (IgG) = 1,610 mg/dL (normal, 680–1,530 mg/dL); IgA = 467 mg/dL (normal, 74.7–373.5 mg/dL); IgM = 83.7 mg/dL (normal, 40.2–167.5 mg/dL).

The patient was given oral fluconazole 200 mg once daily for 8 weeks. However, follow-up chest X-ray and bronchoscopy showed no improvement, so the patient was transferred to a medical center for lobectomy. The final biopsy report also revealed cryptococcosis. Microscopic findings of lung pathology from lobectomy of the left upper lobe showed sections of lung tissue with chronic granulomatous inflammation and multinucleate giant cells with areas of necrosis. There were numerous cryptococci, which appeared as small, pore-like, round-to-oval objects in the pulmonary parenchyma and giant cells. These microorganisms were positive for mucin and periodic acid-Schiff stains. Hilar lymph node biopsy showed reactive hyperplasia with no evidence of malignancy.

Discussion

The human pathogen *C. neoformans* is a common soil inhabitant and may be found throughout the world, particularly in areas where pigeon droppings contaminate the soil.[1] *C. neoformans* may occur as a saprophyte on the skin or mucous membranes, although most infections are initiated by inhalation of the microorganism. Pulmonary infections are rare in individuals with normal immunity, and more than 50% of reported cases are found in immunocompromised individuals.[2]

Cryptococcal infection limited to the lungs is defined as primary pulmonary cryptococcosis, which is difficult to diagnose because symptoms and radiologic findings are non-specific, and skin tests are insufficiently accurate. Serologic tests have an accuracy of 87% in patients with disseminated cryptococcosis, but only 30% in patients with pulmonary masses secondary to primary pulmonary cryptococcosis.[3] Active primary pulmonary cryptococcosis is considered if sputum Gram stains or cultures are positive for cryptococci, and if bilateral or multiple cavity lesions are noted radiographically.[3]

Cryptococcosis is thought to result in a subpleural focus of infection, with spreading to ipsilateral hilar

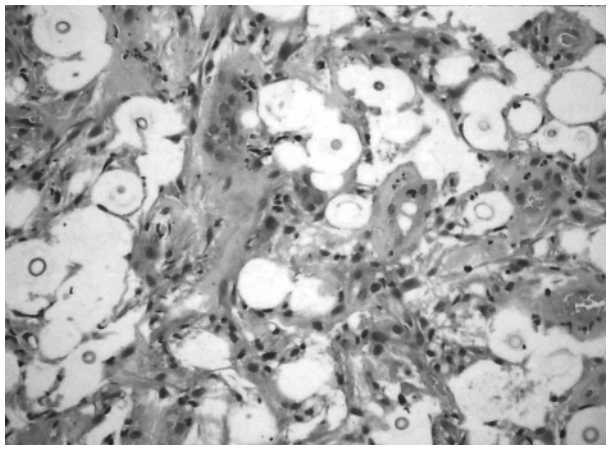

Figure 3. Pathologic features demonstrating several small grayish round or ovoid microorganisms (3–8 μm) in confluent rounded spaces surrounded by pneumocysts, fibrocytes and lymphocytes (hematoxylin & eosin, original magnification × 600).

lymph nodes.[4] Healing occurs in most cases, but dissemination of infection may occur in immunocompromised and, occasionally, in immunocompetent individuals.[4] Cryptococcosis may spread to the central nervous system, where it most commonly presents as meningitis. However, pulmonary infection frequently remains subclinical,[4] in which case there are no chest X-ray abnormalities because the lung lesions have healed.

Radiologically, primary pulmonary cryptococcosis is typically seen as a single, well-defined mass, often pleurally based, with multiple nodules or ill-defined consolidation.[5] The infection often mimics primary or metastatic malignancy, or 1 or more pulmonary mass lesions.[5]

Review of the literature on the radiologic manifestations of pulmonary cryptococcosis showed only a few cases presenting as lung volume reduction or collapse.[6] There was only 1 report of consolidation with minor volume loss, and radiologic evidence of bronchial occlusion due to an intrabronchial gelatinous cryptococcal mass.[6] A case of right middle lobe consolidation was also reported, with an obstructive defect later noted on spirometry, and a granulomatous cryptococcal lesion within the carina, partially obstructing both the right and left main bronchi, seen at bronchoscopy.[7] There was also a report of an anterior mediastinal toruloma, compressing and infiltrating the trachea, right and left main bronchi, and adjacent mediastinal and hilar structures.[8] Cavitation, a miliary pattern, pleural effusion, and hilar or mediastinal lymphadenopathy are also uncommon radiologic features, mostly seen in immunocompromised patients.[9] Furthermore, there is only 1 reported case of cryptococcosis presenting as complete lung collapse and mimicking pulmonary carcinoma clinically, radiographically and bronchoscopically.[10] Collapse or volume reduction is therefore an extremely rare manifestation of pulmonary cryptococcosis. It may be secondary to extrinsic bronchial compression or to the presence of an intrabronchial cryptococcal mass, as in this case and that described by Carter et al.[10]

A retrospective study of nine documented cases of pulmonary cryptococcosis, with nodules or infiltrates on chest X-ray, concluded that cryptococcal lesions tend to be subpleural and identifiable by ultrasound, and that diagnosis can be made by ultrasound-guided percutaneous aspiration.[11]

The management of pulmonary cryptococcosis has traditionally been based on the widely held belief that infection resolves spontaneously in most patients, especially immunocompetent individuals.[12] However, some patients have prominent and disabling symptoms, and infection may occasionally spread. Some researchers have suggested that selected, otherwise healthy individuals with primary pulmonary cryptococcosis, especially patients with very prominent or disabling symptoms, or those potentially at risk for the development of severe disease, might benefit from directed therapy.[2,13] These researchers assert that morbidity and mortality from pulmonary cryptococcosis can be reduced if treatment is started before dissemination and meningeal involvement occur.[2,13]

Nunez et al described four cases of primary pulmonary cryptococcosis, in otherwise healthy individuals, treated with oral fluconazole 400 mg/d for 6–8 weeks.[14] A literature review of other cases also reveals that fluconazole may be an appropriate choice of treatment for primary pulmonary cryptococcosis in immunocompetent individuals.[14] Indeed, fluconazole is active against *C. neoformans*, is easily administered, and has an excellent safety profile. However, additional studies are needed to precisely define the role of fluconazole in this setting and to determine the optimal dosage and duration of therapy.

Cases of primary pulmonary cryptococcosis diagnosed non-operatively are best treated with antifungal agents, such as fluconazole, and by resection of residual disease in patients with a good prognosis.[15] Thus, our case is reported to show that primary pulmonary cryptococcosis can present clinically and radiographically as left upper lobe collapse due to endobronchial occlusion; treatment can be initiated with antifungal agents such as fluconazole, and followed by resection of residual lesions in patients with a good prognosis.

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