

RAPIDLY PROGRESSIVE PULMONARY CRYPTOCOCCOSIS WITH CAVITATION IN AN IMMUNOCOMPETENT WOMAN: A CASE REPORT AND LITERATURE REVIEW

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Abstract. Pulmonary cryptococcosis with pulmonary cavitation is rare, especially in immunocompetent cryptococcosis patients. We describe here a case of rapidly progressive pulmonary with cavitation in an immunocompetent woman. A 29-year-old woman had a routine chest X-ray as part of a routine examination. The chest X-ray showed pulmonary nodules. She was diagnosed as having bacterial pneumonia even though she had no symptoms and was treated with ampicillin orally. A chest X-ray was repeated 12 days later as follow-up which showed an increase in the nodules. She continued to be asymptomatic and had a normal lung examination. Her complete blood count revealed a normal white blood cell count and her anti-human immunodeficiency virus test was normal, as were her immunoglobulin levels and CD4 counts. She had a computed tomography (CT) scan of the lungs that showed two pulmonary nodules, one with cavitation. She then underwent a CT guided needle biopsy of the cavitory lesion which revealed pulmonary cryptococcosis. A serum latex cryptococcal antigen test revealed a titer of 1:32. She was treated with fluconazole 400 mg IV daily for 7 days, followed by oral fluconazole 200 mg daily for a year. The cavitory lesion gradually disappeared and the nodules decreased in size. A follow-up CT 1 year later was normal. Although rare, cryptococcosis of the lungs with pulmonary cavitation can occur in otherwise healthy patients, requiring long term treatment to improve.

Keywords: pulmonary cryptococcosis, cavitation, cryptococcal infection, immunocompetent patient

INTRODUCTION

Pulmonary cryptococcosis (PC) caused by *Cryptococcus neoformans* occurs more commonly among immunocompromised individuals (Woodring *et al*, 1996; Wu *et al*, 1999). Computed tomography (CT)

manifestations of PC consist mainly of pulmonary nodules or masses and focal areas of consolidation (Perfect and Casadevall, 2002). PC is most often found in patients without acquired immune deficiency syndrome (AIDS) and is slowly progressive (Song *et al*, 2010). PC with pulmonary cavitation is rare, especially in immunocompetent cases (Chang *et al*, 2006). We report a case of rapidly progressive pulmonary cryptococcosis with cavitation in an immunocompetent young woman.

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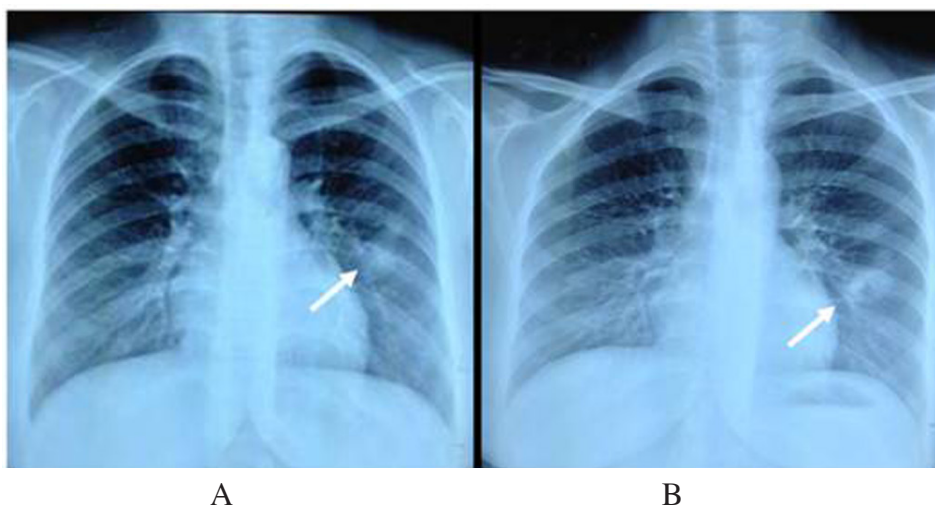


Fig 1—(A) A chest radiograph showing a round opacity in the left lower lobe of the lung; (B) a chest X-ray taken 12 days after X-ray (A) with an increase in pulmonary nodules.

CASE REPORT

On 14 September 2012, a 29-year-old woman was seen at another hospital for a routine examination. A routine chest X-ray showed pulmonary nodules in the left mid-lung field (Fig 1A). She had no respiratory symptoms, such as cough, sputum or dyspnea. Her physical examination, electrocardiogram, and routine blood tests were normal. She had been in good health and had no history of diabetes, hypertension, autoimmune disease, alcohol or substance dependence. She was diagnosed as having bacterial pneumonia and was treated with ampicillin (United Lab, Hong Kong, China) 0.5 g orally every 6 hours for 7 days. Twelve days later, a follow-up chest X-ray showed the pulmonary nodules had increased (Fig 1B). She still had no symptoms.

On physical examination, she had a temperature of 36.3°C, a heart rate of 74 beats/minute, a blood pressure of 106/68 mmHg, and a respiratory rate of 18 breaths/minute. The lung examination

was normal. Laboratory investigations showed a normal white blood cell count and blood chemistry. Her anti-human immunodeficiency virus test was negative. Flow cytometry showed a CD4+ lymphocyte percentage of 34.1% and CD4+/CD8+ ratio of 1.19. The levels of immunoglobulins were normal. She had a chest computed tomography (CT) scan that showed two pulmonary nodules in the left lower lobe, one with cavitation (Fig 2A). She then underwent a CT guided needle biopsy of the cavitory lesion which revealed pulmonary cryptococcosis. A serum latex cryptococcal antigen (CrAg) test was positive with a titer of 1:32. To rule out cryptococcal meningitis and other diseases, a lumbar puncture was performed. The cerebrospinal fluid (CSF) testing for cryptococcal antigens (CrAS), India ink staining and fungal culture were all negative. A follow-up chest CT scan showed expansion of the lung nodule and cavitory lesion (Fig 2B). Pulmonary cryptococcosis was diagnosed. She was referred to our hospital for further treat-

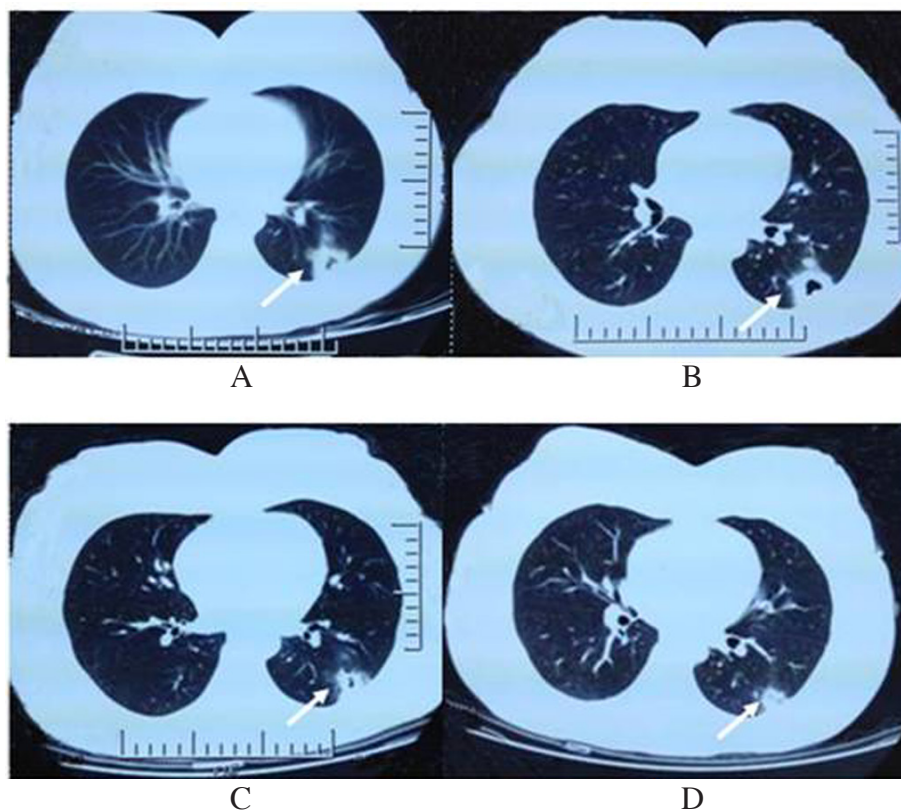


Fig 2—(A) The initial chest CT scan showing two pulmonary nodules, one with cavitation (white arrow). (B) A chest CT scan obtained 11 days after CT (A) showing expanded lung nodules and cavitation. (C) A chest CT scan taken 17 days after initiation of treatment for pulmonary cryptococcosis showing partial resolution of the cavitary pulmonary nodule (white arrow). (D) A chest CT scan taken 52 days after initiation of anti-cryptococcal therapy showing a decrease in the lung nodules and cavitation (white arrow).

ment. On presentation to our hospital, she appeared healthy and continued to be asymptomatic. Her physical examination was normal. She was treated with intravenous fluconazole (Pfizer, Beijing, China) at 400 mg daily for 7 days and followed by oral fluconazole (Pfizer, Beijing, China) at 200 mg daily for a year.

On 24 October 2012, a CT scan demonstrated partial resolution of the cavitary lesion (Fig 2C). On 29 November 2012, a chest CT showed the lung nodule had decreased and the cavitation had disap-

peared (Fig 2D). Her serum CrAg test was negative at that time. On 27 April 2013, a follow-up chest CT scan was normal. During a follow-up period of 12 months after treatment withdrawal. She continued to have a normal life and to work. She had no evidence of recurrence.

DISCUSSION

Cryptococcosis is an opportunistic infection estimated to occur in 1 million people and cause at least 600,000 deaths

per year globally (Park *et al*, 2009). The most pathogenic species of *Cryptococcus* are *C. neoformans* and *C. gattii* (Kwon-Chung *et al*, 2014). *C. neoformans* infection is more commonly seen in immunocompromised patients, such as those with HIV infection, those who are post-transplant, tuberculosis patients and chronic users of corticosteroids and/or immunosuppressant drugs (Chayakulkeeree and Perfect, 2006). Cryptococcosis occurs uncommonly in immunocompetent patients (Jarvis and Harrison, 2008). Our presented patient is unusual.

The most common radiographic finding in PC among immunocompetent patients is non-calcified pulmonary nodules (Perfect and Casadevall, 2002). Other chest radiographic abnormalities found in PC include diffuse reticulonodular opacities, pleural effusion, hilar and mediastinal lymphadenopathy and rarely cavitations within cryptococcal nodules (Perfect and Casadevall, 2002). Cavitation in nodules and masses has previously been described as a radiographic feature limited to immunosuppressed patients (Zinck *et al*, 2002) but was seen in our patient. The mechanisms by which *C. neoformans* persists in an immunocompetent host are not well understood. Protection against cryptococcosis is mediated by CD4+T cell-mediated immunity (Buchanan and Doyle, 2000; Shoham and Levitz, 2005; Singh *et al*, 2008). This patient had a normal CD4+ lymphocyte percentage and a normal CD4+/CD8+ ratio but had PC with a cavitary pulmonary nodule. Protective responses to *C. neoformans* included classic macrophage activation and enhanced macrophage fungistasis of *C. neoformans* yeast (Hardison *et al*, 2012). In clinical practice, we cannot measure macrophage function, so this patient may have had poorly functioning or inadequate numbers of macrophages.

Pathological processes that can cavitate include suppurative necrosis, caseous necrosis, cystic dilatation of lung structures and malignant processes (Miura *et al*, 1998). The radiographic appearance of cavitary lesions is sometimes used to differentiate the etiology. Wall thickness has been used to classify cavitations, but some studies have found wall thickness is, at best, an imperfect tool for discriminating between malignant and non-malignant cases with pulmonary cavitary lesions (Park *et al*, 2007; Gadkowski and Stout, 2008). The location of lesions does not help differentiate malignant from non-malignant lesions (Gadkowski and Stout, 2008). The diagnosis of a cavitary lesion depends on the combination of clinical presentation, laboratory data, imaging and pathology.

Clinical practice guidelines for the management of PC in asymptomatic patients are close observation and no immediate systemic therapy (Perfect *et al*, 2010). Previous studies have found PC to be an indolent lung disease in patients without immune suppression and is slowly progressive without treatment (Song *et al*, 2010). In our patient, the PC progressed relatively rapidly but responded well to treatment. Cavitation indicates a long-term localized pulmonary abnormality (Wu *et al*, 1999). Patients with cavitary PC may have more severe disease and require more aggressive therapy (Chang *et al*, 2006).

In conclusion, PC with pulmonary cavitation can occur in immunocompetent patients and progress rapidly. Aggressive therapy should be given to even immunocompetent patients with cavitary PC.

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