

## CASE REPORT

### An unusual cause of haemoptysis and headache: Cryptococcosis

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#### Abstract

Pulmonary cryptococcosis can be clinically silent in non-HIV infected patients but can also present as nodules and masses on the chest radiograph, which can be mistaken for tuberculosis or lung cancer. Common symptoms include fever and cough, and uncommonly haemoptysis. This report illustrates a non-HIV infected patient whose main complaint was haemoptysis and headache. He was diagnosed with pulmonary cryptococcosis from biopsy of an endobronchial mass found on flexible bronchoscopy. Disseminated cryptococcal infection should be considered as a differential diagnosis in non-HIV infected patients presenting with haemoptysis and headache. Early recognition and administration of appropriate therapy will improve clinical outcome in these patients.

*Keywords:* cryptococcosis, haemoptysis, headache.

#### INTRODUCTION

With the rising incidence of AIDS each year, clinicians are faced with the unenviable task of managing fulminant opportunistic infections with life-threatening complications. One such infection is cryptococcosis which is spread by inhalation of airborne spores. Although patients who are immune-compromised are susceptible to the infection, healthy individuals can also be affected. In clinical practice, haemoptysis is a common respiratory symptom but haemoptysis associated with headache is uncommon. In a country with a high incidence of tuberculosis, disseminated tuberculosis needs to be excluded when a patient presents with headache and haemoptysis. Carcinoma of the lung with brain secondaries is a differential diagnosis in the elderly patient. We report a case of haemoptysis and mild headache due to disseminated cryptococcus infection.

#### CASE REPORT

A 30-year-old Malay gentleman was admitted with a month's history of cough with streaky haemoptysis. He also complained of occasional throbbing occipital headache and blurred vision after bouts of coughing. He also claimed to

have weight loss but there was no fever. Prior to this admission, he was seen twice by a general practitioner and on both occasions, he was prescribed a course of antibiotics. He worked with the Malaysian Air Force and had never smoked or taken alcohol. He denied any high risk behaviour or exposure to pigeons or contact with tuberculosis patients. Full systemic inquiries were unremarkable.

Clinical examination revealed he was afebrile. There was no clubbing and lung examination revealed crepitations over the left lung base. Fundoscopy was normal. Initial full blood count, urea and electrolytes, and liver function tests were normal. Blood, urine and sputum cultures were negative. Human Immunodeficiency Virus serology (HIV I and II) were both negative. The chest radiograph however showed left lower lobe consolidation (Fig 1). Erythrocyte sedimentation rate (ESR) was 100mm/hr. Fiberoptic bronchoscopy revealed an endobronchial mass at the posterior segment of the left lower lobe bronchus.

#### Pathology

Broncho-alveolar lavage and bronchial brushing showed numerous cryptococcal spores (Fig 2) in a background of numerous foamy macrophages, an



FIG. 1: Chest radiograph showed left lower lobe consolidation



FIG. 2: Broncho-alveolar lavage showed numerous cryptococcal spores with thick capsules.

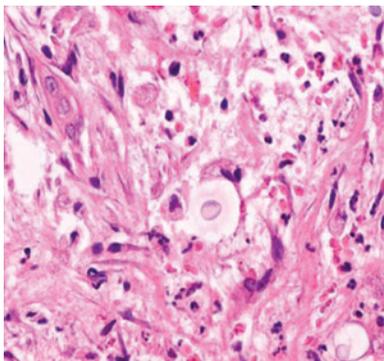


FIG. 3: Endobronchial biopsy showing cryptococcal spores with thick capsule associated with acute and chronic inflammation in the lung tissue.

occasional multinucleated giant cell and reactive respiratory cells. The yeast bodies were round spores with thick capsules. The endobronchial biopsy showed similar large spores with thick capsule in a background of acute and chronic inflammation in the lung tissue (Fig 3). The morphology and histochemical stains led to a diagnosis of cryptococcosis. In view of the histology results and occasional headache complained by the patient, contrast enhanced CT Brain was performed which turned out normal. Lumbar puncture was performed and the results are showed in Table 1 (1st sample).

#### Clinical course

The patient received intravenous amphotericin-B at 0.8mg/kg/day after a test dose and gradual dose increment. At day eleven, he felt much better and insisted on going home despite medical advice. He was then given oral fluconazole 200mg daily and a week follow-up appointment. He did not turn up for the appointment but presented two months later with bilateral blurring of vision. Fundoscopy showed bilateral papilloedema. He was readmitted and lumbar puncture showed positive fungal spores of cryptococci revealed by India Ink (Table 1, 2nd sample). Intravenous amphotericin-B and oral fluconazole 200mg daily was started but amphotericin-B was prematurely stopped due to worsening renal function. Hence only 160 mg amphotericin-B was administered during this admission. Instead intravenous fluconazole 400mg daily was commenced and later changed to oral fluconazole 400 mg daily when CSF showed negative India Ink findings. This was continued for a year. Repeated lumbar punctures (Table 1, 3rd to 4<sup>th</sup> samples) showed gradual improvement to normality and he has remained clinically well for over 2 years since hospital discharge except for reduced vision of both eyes due to optic atrophy.

#### DISCUSSION

This patient presented with the main symptom of haemoptysis. The headache was mild and not much attention was paid to it at the beginning. This is because he was young, so it was less likely to be a malignancy and chest X-ray was not suggestive of tuberculosis. During bronchoscopy, the nodule noted at the posterior segment of the left lower lobe mimicked endobronchial tumour but histology revealed cryptococcosis. *Cryptococcus neoformans* is a saprophytic encapsulated yeast with a worldwide

**TABLE 1: Progression of lumbar puncture results**

	1 <sup>st</sup> sample	2nd sample	3rd sample	4th sample
<b>Appearance</b>	Clear and colourless	Clear and colourless	Clear and colourless	Clear and colourless
<b>Cell count (numbers per mm<sup>3</sup>)</b>	40 [neutrophils 30%, lymphocytes 70%]	0	4 lymphocytes	0
<b>Glucose (mmol/L) (CSF/serum values)</b>	2.0/5.0	2.2/5.3	2.9/5.1	3.8/5.8
<b>Protein (mmol/L)</b>	1.85	0.426	0.320	0.7
<b>Gram Stain</b>	Negative	Negative	Negative	Negative
<b>AFB</b>	Negative	Negative	Negative	Negative
<b>Indian Ink</b>	Positive	Positive	Negative	Negative
<b>Latex</b>	Positive 1:1024	Positive 1:64	Negative (Positive 1:4 Dilution)	Negative (Positive 1:1 Dilution)
<b>CSF bacterial culture</b>	No Growth	No Growth	No Growth	No Growth

distribution in soil contaminated usually with avian excreta, mostly from pigeons.<sup>1</sup> Infection is acquired by inhalation of the organism and can be asymptomatic and limited to the lungs, especially in the immunocompetent host.<sup>2</sup> This patient could have been exposed to the airborne organism unawares under trivial circumstances, which he might not recall. Haematogenous dissemination, especially to the meninges, and fatal outcome occur in patients with impaired cell-mediated immunity secondary to a variety of conditions, particularly malignancy, diabetes mellitus, treatment with corticosteroids, and infection with the human immunodeficiency virus (HIV).<sup>3</sup>

Pulmonary cryptococcal disease can be clinically silent in 24-36% of HIV negative patients. In symptomatic patients, 61% develop cough, 29% fever and haemoptysis is not common (18%). It has a broad spectrum of radiographical manifestations e.g. diffuse interstitial opacities (70.5%), focal interstitial abnormalities, alveolar opacities, adenopathies and cavitory lesions especially in AIDS patients<sup>[4]</sup>. Nodules and pleural effusions are rare whereas nodules and masses are the predominant manifestations of pulmonary cryptococcosis in non-HIV infected patients.<sup>5</sup> We treated our patient with amphotericin-B but this was stopped

prematurely due to worsening renal function. He was instead commenced on fluconazole. Fluconazole has been shown to be efficacious especially in AIDS patients.<sup>6</sup>

Mortality in untreated cryptococcal meningitis reaches 86% as compared to 20% to 25% in patients treated with antifungal agents.<sup>7</sup> Although the combination of amphotericin-B and 5-flucytocine (5-FC) has been widely used, there is no conclusive evidence to show its superiority over using amphotericin-B alone.<sup>8</sup> In patients with AIDS, the use of 5-FC is not advisable due to possible exacerbation of bone marrow suppression. In addition, maintenance therapy with a single weekly dose of amphotericin-B (80 mg to 100 mg IV) is needed in these patients to avoid relapse.<sup>9</sup> Despite the high toxicity of the currently used drugs, none of the tried alternatives such as ketoconazole<sup>10</sup> or fluconazole<sup>11</sup> have been recommended for the initial treatment of cryptococcal meningitis at this stage. However, both itraconazole and fluconazole seem promising in therapy failure and maintenance therapy of AIDS patients with cryptococcal meningitis.<sup>6</sup>

In addition to antifungal therapy, surgery can be a helpful adjunct in the treatment of cases with intracerebral lesions or those with combined pulmonary and neural cryptococcosis.<sup>12</sup> Despite

the 75% to 80% cure rate in treated patients, 40% to 50% of the cured suffer neurological sequelae including visual loss as in our patient, cranial nerve palsy, significant motor dysfunction and impairment of mental status.<sup>13</sup>

The prognosis of cryptococcal meningitis is variable and depends on several factors.<sup>14</sup> Favourable outcome is observed with decreasing antigen titers in CSF and serum specimens. Unfavourable outcome has been associated with CSF elevated opening pressure, positive India ink, low leukocytes (<20x10<sup>9</sup>/L), no decrease in CSF or serum antigen during therapy, positive extraneural cultures, daily dose of >20 mg prednisone and patients with organ transplants or AIDS.<sup>15</sup> In our patient, repeated CSF examinations over the follow-up period of 2 years were reassuring. During the last clinic review in May 2007, the patient remained well and had since stopped fluconazole therapy.

This case is a reminder that disseminated cryptococcal infection must be considered when investigating patients with haemoptysis and headache.

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