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Case report

Pulmonary cryptococcal infection presenting with multiple lung nodules

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ABSTRACT

Pulmonary infections from the environmental fungus *Cryptococcus gattii* (*C. gattii*) are notable for cryptococcomas, which are usually solitary and can be very large. As with infections with *Cryptococcus neoformans (C. neoformans)* patients can have concomitant cryptococcal meningitis; however, unlike for *C. neoformans,* infections with *C. gattii* often occur in immunocompetent patients. The highest published incidence of *C. gattii* infection has been in the Indigenous Australian population of Arnhem Land in the tropical north of the country. More recently *C. gattii* has been responsible for outbreaks of cryptococcosis in the Pacific Northwest of Canada and the United States of America (USA). A previously healthy Indigenous male from Arnhem Land presented with pulmonary cryptococcosis with chest imaging showing > 50 bilateral lung nodules. This unusual occurrence was attributed to probable inhalation of fungal elements from prior use of a high-pressure leaf blower to clear eucalyptus and other debris in a remote bush camp.

1. Introduction

We present the case of an immunocompetent Indigenous Australian male with a clinical presentation and unusual radiological findings suggestive of pulmonary cryptococcosis consequent to massive inhalation of aerosolised fungal elements.

2. Case report

A 31-year-old previously fit Australian Indigenous male ranger from a remote community in Arnhem Land, Northern Territory Australia was admitted to Royal Darwin Hospital with a 2-week history of pleuritic chest pain, fevers and cough.

Several days prior to symptom onset his work had included extensive use of a leaf blower for an environmental clean-up of the ranger camp, with likely exposure to considerable aerosols from debris from tropical savannah eucalypts.

On arrival he was alert but tachypneic and febrile. He was haemodynamically stable and SpO2 was 98% on room air. Chest was resonant on percussion and clear on auscultation apart from a few left mid-lower zone crackles. Blood white cell count was 17.4×10^9/L (4.0–11.0) with 14.0 neutrophils and 1.8 lymphocytes. C-reactive protein was 279.4mg/L (0.0–5.0). His respiratory rate settled to normal over several hours without supplemental oxygen.

Chest x-ray (CXR) and computed tomography (CT) chest revealed numerous bilateral lung nodules (> 50) ranging in size from a few millimetres to several centimetres in diameter and also mediastinal and hilar lymphadenoapthy (Fig. 1a and b). Human immunodeficiency virus (HIV), human T-lymphotropic virus 1 (HTLV-1), serology for melioidosis and vasculitic screen were negative. Provisional diagnosis of metastatic malignancy was made but he was initially given ceftriaxone and gentamicin empirically. Histology of a CT-guided biopsy of a lung nodule showed yeasts in a background of chronic inflammation (Fig. 2a and b). Fungal culture confirmed the yeast to be *C. gattii*. Serum cryptococcal antigen was positive, titre 1:1024. Magnetic resonance imaging brain was normal, as was analysis of the cerebrospinal fluid (CSF), with negative CSF cryptococcal antigen. Once the biopsy result was available he was commenced on intravenous liposomal amphotericin and oral flucytosine. This was continued for 6 weeks, followed by oral fluconazole planned for 6 months. Repeat CT chest at 15 weeks showed significant reduction in the size and number of pulmonary lesions (Fig. 1c and d).

3. Discussion

Cryptococcosis is disease of humans and animals caused by

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Abbreviations list

C. gattii	*Cryptococcus gattii*
C. neoformans	*Cryptococcus neoformans*
CT	Computed tomography
CXR	Chest x-ray
HIV	Human immunodeficiency virus
HTLV-1	Human T-lymphotropic virus 1
USA	United States of America

environmental sampling and genomic analysis of isolates from trees and patients in the Americas and globally has now resulted in substantial revisions to the earlier hypothesis that *C. gattii* originated in Australia and was possibly disseminated globally with export of eucalyptus trees [9]. It is now apparent that many other trees can also harbor *C. gattii* [10]. Recent molecular genomics shows the ancestral origin of *C. gattii*, including the lineages responsible for the Canadian and USA outbreaks, to be from South America [2].

Inoculation of the fungus is usually by inhalation, resulting in either asymptomatic infection or development of pulmonary disease [11]. Either can then lead to haematogenous spread to the central nervous

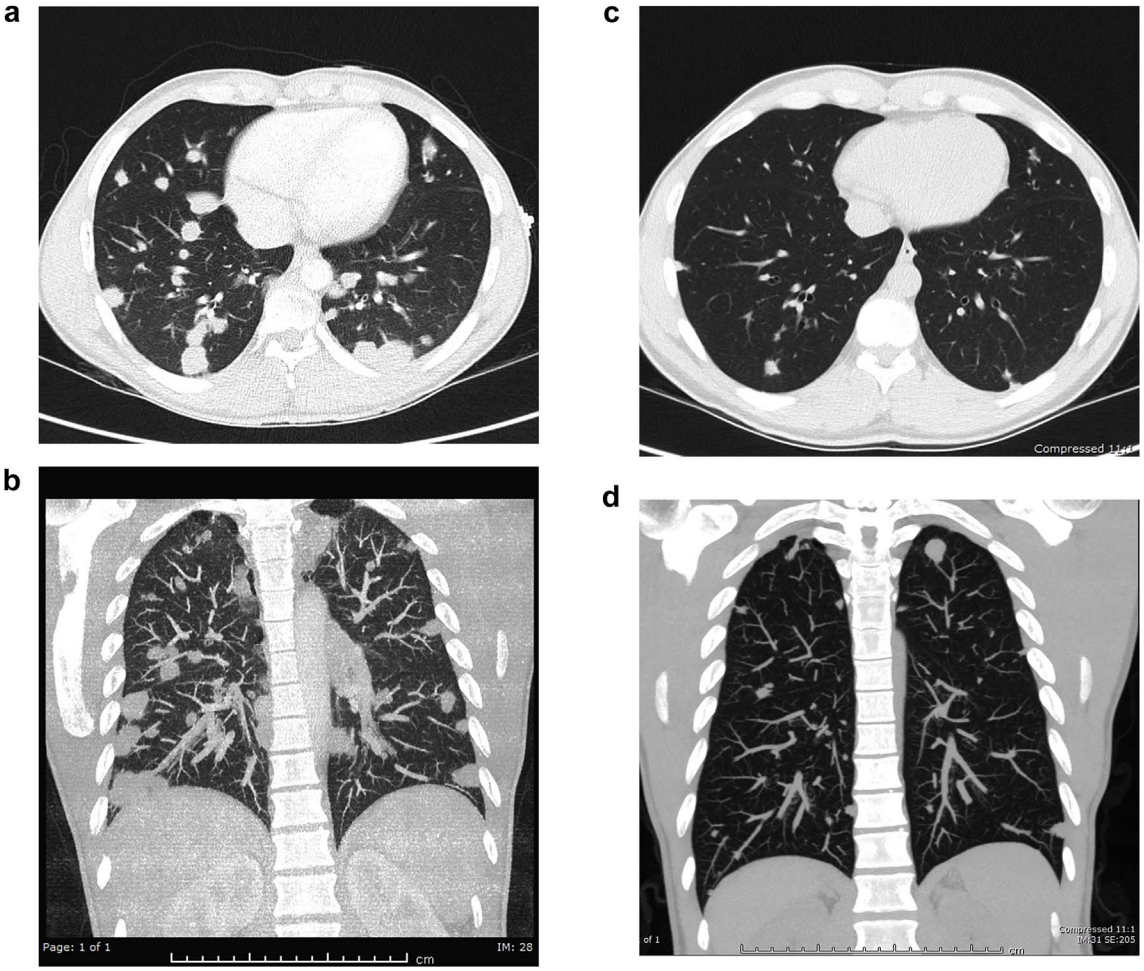

Fig. 1. CT chest at presentation (Fig. 1a and b) showing numerous, bilateral lung nodules of varying size and CT chest after 15 weeks of treatment (Fig. 1c and d) showing significant reduction in the size and number of pulmonary lesions, but not yet complete resolution.

environmental basidiomycetous yeasts in the genus Cryptococcus [1]. The potential numerous pathogenic species are in two species complexes; the *C. neoformans* species complex and the *C. gattii* species complex [2,3]. *C. neoformans* is notable for causing meningitis in immunocompromised patients and being a major cause of death globally in those with untreated HIV infection. *C. gattii* has long been recognized as a cause of pulmonary disease (most notably large pulmonary cryptococcomas) and meningitis in immunocompetent patients in Australia, with the highest published incidence being in the Indigenous Australian population of Arnhem Land in the tropical north [4–6]. More recently *C. gattii* has been responsible for outbreaks of cryptococcosis in the Pacific Northwest of Canada and the United States of America (USA) [7].

The first isolation of *C. gattii* from the environment was from an Australian river red gum (*Eucalyptus camaldulensis*) [8]. Recent

system (meningitis and cryptococcomas), or less commonly other organs, such as bone or skin [11].

The commonest pulmonary finding with *C. gattii* is a single, two or several circumscribed cryptococcomas, both in those with combined pulmonary/central nervous system disease and in those with pulmonary infection alone [4,6]. Cryptococcomas may vary in size (range from approximately 1 to 7cm in diameter), with smooth or ill-defined edges, and have no specific lobar preference. [12,13] With even large cryptococcomas the patient may be asymptomatic. It is not uncommon for those with *C. gattii* meningitis to have few or no pulmonary symptoms, irrespective of the presence of pulmonary lesions.

Treatment involves antifungal therapy and consideration of surgical resection in patients with large cryptococcomas [14].

Whilst there are many case reports of pulmonary cryptococcosis, to the best of our knowledge radiological presentation with as numerous a

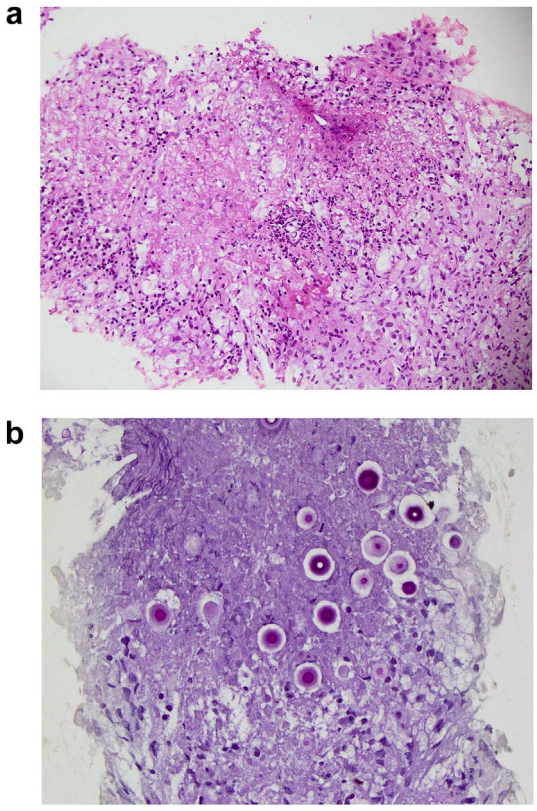

Fig. 2. Histopathology of CT-guided biopsy of lung nodule from left lower lobe. a: H&E section demonstrating tissue necrosis with cryptococci (eosinophilic, thin-walled, round yeast forms surrounded by a polysaccharide capsule). b: Yeast cells are positive for D-PAS stain.

number of lung nodules of varying size such as in our patient (> 50) has not been published previously. The Arnhem Land region in tropical Australia where the patient worked has the highest incidence of *C. gattii* infection documented globally, but no prior patient has presented with such extensive multiple cryptococcomas. The landscape he works in is dominated by tropical woodland and savannah and rocky escarpments. Of interest there are no *E. camaldulensis* in that region [15] but *C. gattii* has been recovered from the two dominant eucalypt species, *E. tetrodonta* (the Darwin stringybark) and *E. miniata* (the woollybutt) (unpublished data). The specific activity considered likely to have generated aerosols of fungal elements in quantity enough to cause such extensive inhalational disease was high-pressure leaf blowing whilst clearing a camp area.

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