Endobronchial cryptococcosis induced by Cryptococcus gattii mimicking metastatic lung cancer

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Keywords
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Abstract
A 41-year-old previously healthy Japanese man complained of cough for 2 months. A chest computed tomography scan revealed a mass in his left lung with multiple mediastinal lymphadenopathy. Brain magnetic resonance imaging showed many small, enhancing lesions. He was admitted to our hospital for further evaluation of an abnormal shadow suspicious for metastatic lung cancer. Bronchoscopy showed aggregated white nodes in the compressively stenosed left main bronchus. A specimen from transbronchial biopsy showed many foamy and yeast-like cells. Cultures and additional gene analysis identified these cells as Cryptococcus gattii. Antifungal treatment was commenced and his symptoms clearly improved. To our knowledge, this is the first case of an aggressive form of endobronchial cryptococcosis caused by C. gattii.

Introduction
Deep-seated mycosis is a fungal infection that mainly occurs in immunocompromised patients. It often leads to poor outcomes and has a high mortality rate. Cryptococcosis is usually caused by the yeast-like fungus Cryptococcus neoformans, which is distributed throughout the world. In contrast, Cryptococcus gattii is a rare species endemic to tropical countries, where it is isolated from eucalyptus trees. However, reports of C. gattii infection in non-endemic areas have been increasing in recent years. Global warming and the exportation of woods and trees may be risk factors. Pulmonary cryptococcosis is typically identified as a single well-defined mass or as multiple nodules, while endobronchial lesions are quite rare [1, 2]. Here, we report a case of endobronchial cryptococcosis caused by C. gattii in a Japanese man.

Case Report
The patient, a 41-year-old Japanese man who was an office worker, was previously healthy and had not visited tropical areas within the past 10 years. He complained of cough, wheezing, febricula, and headache for 2 months. His chest radiograph and computed tomography scan showed a mass lesion in his left lower lung, and he was referred to our hospital.

On examination, his oxygen saturation was 98% in room air. His temperature was 37.2°C. He had an expiratory wheeze over the left lung field. Laboratory studies showed no abnormal findings, including no human immunodeficiency virus antibody or human T-cell lymphotropic virus type I antibody. Radiological examinations revealed a mass in his left lower lung and multiple mediastinal lymphadenopathy. The left main bronchus was stenosed (Fig. 1A, B).
Brain magnetic resonance imaging with gadolinium enhancement showed many small, enhancing lesions (Fig. 1C). Bronchoscopic findings showed aggregated white nodes in the compressively stenosed left main bronchus (Fig. 1D). Although tumor markers were negative, these findings were highly suggestive of advanced lung cancer with multiple brain metastases. However, a specimen from a transbronchial biopsy showed many foamy and yeast-like cells and the absence of malignant cells. These cells were deeply stained with both Grocott’s methenamine silver and Alcian blue (Fig. 2). As a result, he was diagnosed with cryptococcosis. The yeast was identified as \textit{C. gattii} by culture and gene analysis. Although his cerebrospinal fluid culture was negative, we suspected comorbid cryptococcal meningitis from his cerebrospinal fluid examination and radiological findings.

Antifungal treatment (liposomal amphotericin B and flucytosine) was commenced according to the Infectious Disease Society of America guidelines. After induction therapy, he received consolidation and maintenance therapy with oral fluconazole. Finally, he recovered from his subjective symptoms and the radiological abnormalities disappeared.

**Discussion**

To the best of our knowledge, this is the first case of endobronchial cryptococcosis induced by \textit{C. gattii}.

Cryptococcosis is a systemic mycosis caused by the haploid, encapsulated, basidiomycetous yeast, \textit{Cryptococcus}. It is commonly associated with pigeon excreta and plant materials. Inhalation of the organism is considered to be the usual route of infection. The respiratory and central nervous systems are frequently affected sites. The infection causes symptoms such as fever, weight loss, cough, sputum, headache, vomiting, and impaired consciousness.

Cryptococcosis is induced by \textit{C. neoformans} and \textit{C. gattii}. \textit{C. neoformans} is present throughout the world, whereas the distribution of \textit{C. gattii} is restricted to tropical and subtropical areas. Compared with \textit{C. neoformans}, \textit{C. gattii} infection commonly occurs in immunocompetent hosts, and requires a longer treatment period because there is a slower response, higher rates of complications, and persistent abnormalities [3]. Recently, \textit{C. gattii} caused a cryptococcosis outbreak on Vancouver Island (British Columbia, Canada) [4]. In Japan, Okamoto et al. reported the first case of a Japanese \textit{C. gattii} infection with no recent history of traveling to disease-endemic areas [5]. Resulting from global warming and the exportation of woods and trees, reports of mycosis induced by \textit{C. gattii} may be increasing. It is of concern that \textit{C. gattii} is currently distributed worldwide.

Single or multiple nodules are common radiographic features in pulmonary cryptococcosis, and there are only a few descriptions of cryptococcosis presenting as endobronchial lesions (all of which were caused by...
C. neoformans) [1, 2]. In the present case, the radiological findings revealed a mass in the left lower lung accompanied by mediastinal lymphadenopathy. Bronchoscopy showed a compressively stenosed left main bronchus. These findings would have been unusual in pulmonary cryptococcosis, suggesting an aggressive form of a Cryptococcus infection. From the radiological and bronchoscopic findings, the pathogenesis of the endobronchial lesion may have been caused by invasion from the mediastinal lymph nodes. Our case shows that cryptococcosis has the capacity to cause serious endobronchial lesions resulting in stenosis of the bronchi. Cryptococcosis should be considered in the differential diagnosis when endobronchial lesions are detected without an elevation of tumor markers.

In conclusion, we report the first case of C. gattii infection presenting as endobronchial lesions mimicking metastatic lung cancer.

**Disclosure Statements**

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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**Figure 2.** Pathological findings. A specimen stained with hematoxylin and eosin (A: ×400) showed many foamy and yeast-like cells. This lesion was deeply stained with both Grocott’s methenamine silver (B: ×400) and Alcian blue (C: ×400).