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Pulmonary Cryptococcosis in a Nurse Initially Suspected of Having Pulmonary Tuberculosis

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Conflict of interest: None declared

Patient: Female, 34-year-old
Final Diagnosis: Pulmonary cryptococcosis
Symptoms: None
Medication: —
Clinical Procedure: Bronchoscopy
Specialty: Infectious Diseases

Objective: Unusual clinical course

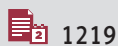
Background: Pulmonary cryptococcosis can be associated with various imaging findings and can occur in immunocompetent hosts. It is sometimes difficult to distinguish pulmonary cryptococcosis from pulmonary tuberculosis based on imaging findings.

Case Report: A 34-year-old female nurse who worked in an endoscopy examination room visited our hospital because of an abnormal lung shadow. At her workplace, a gastrointestinal endoscopy had been performed on a patient with infectious tuberculosis. The nurse was asymptomatic, and acid-fast staining and culture of her sputum were negative. Chest computed tomography depicted multiple nodules distributed along the bronchi. An acid-fast smear test of bronchial lavage was negative and cytological investigations revealed many yeast-like fungi. Fluconazole was administered and the computed tomography findings improved.

Conclusions: It is important to consider cryptococcosis, even in patients suspected of having tuberculosis.

MeSH Keywords: Bronchoscopy • Cryptococcosis • Tuberculosis, Pulmonary • Fungi, Unclassified

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/919267>



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Background

Cryptococcosis can cause pulmonary lesions, fungemia, and meningitis in both immunocompromised and immunocompetent hosts. Pulmonary cryptococcosis can be associated with various imaging findings such as boundary-clear nodules and tumor shadows [1,2]. It is sometimes difficult to distinguish pulmonary cryptococcosis from pulmonary tuberculosis based on imaging findings [3]. Tuberculosis is moderately prevalent in Japan and the relative risk of pulmonary tuberculosis in nurses in Japan is 2.7 [4]. In symptomatic medical professionals who have been exposed to tuberculosis, tuberculosis is usually suspected first. Here, we present a case of pulmonary cryptococcosis in a nurse who was initially suspected of having pulmonary tuberculosis.

Case Report

A 34-year-old female nurse visited our hospital because of an abnormal lung shadow detected during a health check-up. She worked in an endoscopy examination room in a hospital. Eight months before the current visit, gastrointestinal endoscopy was performed at her workplace in a patient with tuberculosis whose sputum smear was positive, but she was not mentioned as a contact person for tuberculosis. She did not present with the typical tuberculosis symptoms such as fever, coughing, or night sweats. She had no remarkable medical history and was not taking any long-term medication. In addition, she had no family members who had been diagnosed with tuberculosis. Furthermore, she had not traveled abroad in recent years, including North America, where *Cryptococcus gattii* infection is endemic. Lastly, she did not have any pets

and had had no contact with birds, including pigeons. Her vital signs were normal, and a physical examination did not reveal any abnormal findings. Laboratory investigations also did not reveal any abnormalities. Both HIV p24 antigen and antibody tests were negative. Chest radiography depicted multiple nodules in the right middle and lower lung fields (Figure 1A). Chest computed tomography (CT) depicted multiple nodules distributed along the bronchi (Figure 1B), which was consistent with pulmonary tuberculosis. Acid-fast staining and culture of her sputum were negative. Although an interferon- γ release assay (QuantiFERON TB-2G[®], Cellestis Ltd., Victoria, Australia) conducted at the time she had commenced her current job 12 years prior was negative, a re-examination was conducted on the present occasion (QuantiFERON TB-3G[®], Cellestis Ltd.), which also yielded a negative result. Based on the above-described findings, she was putatively diagnosed with pulmonary tuberculosis. Bronchoscopy was performed for bronchial lavage to confirm the presence of *Mycobacterium tuberculosis* before the initiation of treatment. An acid-fast smear test and culture of bronchial lavage fluid (BALF) from the right lower lobe was negative. After bronchoscopy, antituberculosis chemotherapy was initiated, consisting of isoniazid 300 mg/day, rifampicin 450 mg/day, ethambutol 750 mg/day, and pyrazinamide 1250 mg/day. However, cytological investigation of BALF revealed many yeast-like fungi via Papanicolaou staining, and the presence of *Cryptococcus* fungi was suspected (Figure 2). Her serum cryptococcal antigen titer was positive. However, because *Cryptococcus* was only detected by cytology of BALF samples and the culture of BALF was negative, the species of *Cryptococcus* could not be identified. Lumbar puncture was performed, and cerebrospinal fluid analysis did not yield any abnormal findings. The spread of *Cryptococcus* to the central nervous system was excluded, and she was diagnosed

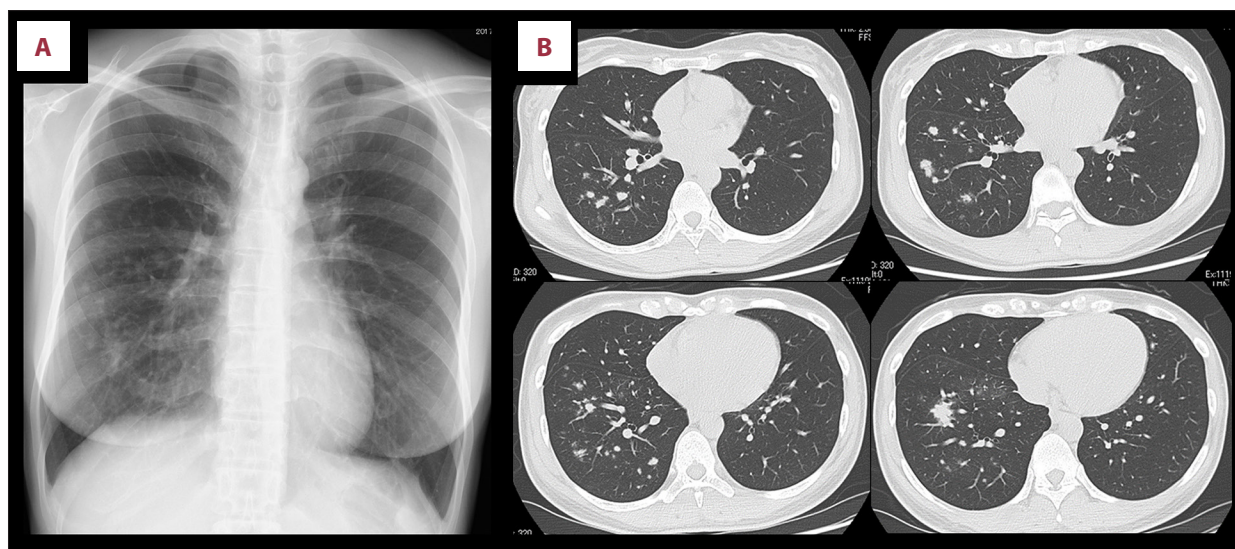


Figure 1. (A) Chest radiograph depicting multiple nodules in the right middle and lower lung fields. (B) Chest computed tomography depicting multiple nodules distributed along the bronchi, consistent with pulmonary tuberculosis.

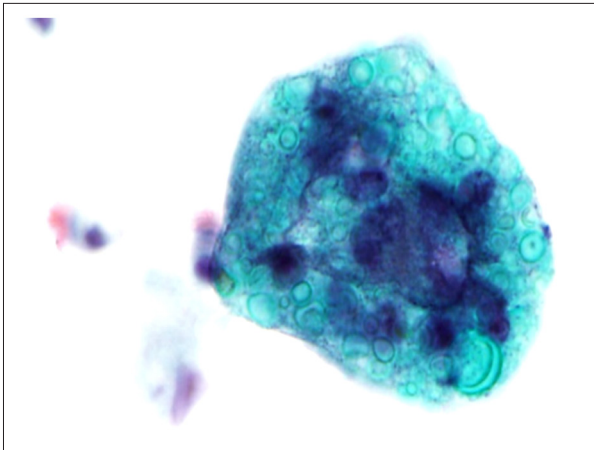


Figure 2. Cytological analysis of bronchial lavage fluid revealed many yeast-like fungi via Papanicolaou staining, and infection with cryptococcus fungi was suspected.

with pulmonary cryptococcosis. Antituberculosis chemotherapy was discontinued, and fluconazole (400 mg/day) was administered for 6 months. The CT findings improved, and at 18 months after the discontinuation of fluconazole, there had been no recurrence.

Discussion

The present case yielded 2 notable clinical indications. One is that because pulmonary cryptococcosis and pulmonary tuberculosis can be associated with similar imaging findings, pulmonary cryptococcosis should also be considered even in patients who have potentially been exposed to tuberculosis. The other is that it is important to perform serum antigen and antibody tests for various mycoses in addition to bronchoscopy to differentiate between pulmonary cryptococcosis and pulmonary tuberculosis.

Pulmonary cryptococcosis can be associated with lung shadowing similar to that associated with tuberculosis, and cryptococcosis should be considered a possibility even in cases of suspected tuberculosis. As well as 1 or more boundary-clear nodules/shadows, pulmonary cryptococcosis can be associated with a wide range of reticular shadows and ground-glass opacities [1]. In addition, chest CT images of pulmonary cryptococcosis can show a single nodule/mass (39.7%), multiple nodules/masses (30.9%), ground-glass opacity with or without nodules (23.5%), miliary nodules (2.9%), and enlarged mediastinal lymph nodes (2.9%). Furthermore, lesions with irregular margins (77.9%), spiculated lesions (48.5%), air bronchograms (47.1%), cavities (13.2%), and calcifications (5.9%) may also be observed [2]. Active pulmonary tuberculosis can also be associated with various findings on chest CT, such as centrilobular granular shadow/branched shadow with a diameter of

2–4 mm (97%), bronchial wall thickening (79%), cavity (76%), tree-in-bud appearance (72%), and nodule with an unclear edge (69%) [5]. In particular, the most common CT findings of active pulmonary tuberculosis are nodular lesions (centrilobular nodules) (96.8%), followed by consolidation (75.1%) and cavity (54.0%) lesions. A recent study reported that the majority of patients with pulmonary tuberculosis had lesions in the upper lobe (92.6%) and multiple lobes (81.5%) [6]. Notably, while cryptococcosis often occurs in immunocompromised patients [6–8], half of the patients with pulmonary cryptococcosis are immunocompetent [9,10]. Due to the possibility that the present patient had been in contact with a patient with tuberculosis and the presence of multiple nodules in the right middle and lower lung on chest CT, she was initially diagnosed with pulmonary tuberculosis. Therefore, the diagnosis of pulmonary cryptococcosis was delayed. Bronchoscopy ultimately led to the correct diagnosis of cryptococcosis. Because cryptococcosis can involve meningitis as a complication, and meningitis is an extremely serious condition, it is important to rule out pulmonary cryptococcosis rather than delay its diagnosis, even in patients suspected of having tuberculosis.

Bronchoscopy is an important modality for differentiating between pulmonary cryptococcosis and pulmonary tuberculosis in patients whose sputum examinations are not indicative of tuberculosis. The rate of serum cryptococcus antigen positivity is higher in patients with wider lung lesions [11]. Pulmonary cryptococcosis can be definitively diagnosed by isolating and culturing *Cryptococcus neoformans* from respiratory specimens such as sputum, alveolar lavage fluid, or lung tissue, or confirming the presence of fungus via pathological examination or cytology [9]. Pulmonary cryptococcosis was initially not considered and corresponding antigen-based examinations were not conducted because the patient in the present case was immunocompetent. Bronchoscopy was performed in the current patient because some medical professions were suspected of having been exposed to tuberculosis. Bronchoscopy resulted in the exclusion of pulmonary tuberculosis, leading to a diagnosis of pulmonary cryptococcosis. The species of *Cryptococcus* could not be identified in this patient. However, because infection of *Cryptococcus gattii* is very rare in Japan [13] and she had never traveled to any areas endemic for *Cryptococcus gattii*, it was highly likely she was infected with *Cryptococcus neoformans*. If cryptococcosis had been considered as a possibility from the beginning and corresponding serum antigen testing had been conducted, cryptococcosis might have been diagnosed earlier. When the diagnosis is not confirmed by sputum examination in cases of suspected pulmonary tuberculosis, bronchoscopy and serum cryptococcal antigen testing are recommended.

Conclusions

Because pulmonary cryptococcosis and pulmonary tuberculosis can be associated with similar imaging findings, pulmonary cryptococcosis should also be considered in patients who have potentially been exposed to tuberculosis. Bronchoscopy and serum cryptococcal antigen testing should be performed in such patients to distinguish between pulmonary cryptococcosis and pulmonary tuberculosis.

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Acknowledgments

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Conflicts of interest

None.