

Case Report

Pulmonary cryptococcosis suspected due to inhalation of swallow excreta presenting with multiple infiltrative shadows

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ABSTRACT

A 70-year-old woman had been treated with methotrexate for rheumatoid arthritis by a rheumatologist who opened a clinic near our hospital. In January of a certain year, she had respiratory symptoms of cough, sputum, and fever. Laboratory test results showed a white blood cell count of 8600/ μ L (neutrophil count of 5330/ μ L, lymphocyte count of 2490 μ /L), C-reactive protein (CRP) of 3.30 mg/dL. Chest radiography showed multiple infiltrative shadows in the right middle and lower lobes. Bronchoalveolar lavage fluid (BAL) lymphocyte count was increased (65.1%), and histopathological findings were consistent with numerous bowl-shaped cryptococcus cells stained black by Grocott staining. Added measurement of serum cryptococcal antigen titers was 4096-fold. Treatment with fluconazole 400 mg/day was initiated, and her symptoms resolved; the shadows of the lung fields improved. When asked in detail, the cryptococcus infection route was suspected from swallow excreta. There have been no reported cases of pulmonary cryptococcosis suspected due to inhalation of swallow excreta presenting with multiple infiltrative shadows.

1. Introduction

Pulmonary cryptococcosis is an opportunistic infection that commonly occurs in immunocompromised patients. Pigeon excreta are the main route of pulmonary cryptococcosis, and swallow excreta are rare. On CT images, pulmonary cryptococcosis shows a single nodule, multiple nodules, infiltrative shadow, and ground-glass opacities, and multiple infiltrative shadows type is very scarce. We experienced a rare case of pulmonary cryptococcosis with multiple infiltrative shadows whose infection route was suspected from swallow excreta.

2. Case presentation

A 70-year-old woman had been affected by rheumatoid arthritis two years ago and started treatment with methotrexate one year ago by a rheumatologist who opened a clinic near our hospital. There were no complications of rheumatoid-related interstitial pneumonia or chronic lower respiratory tract infection. In January of a certain year, she underwent transurethral lithotripsy in the urology department due to right ureteral calculi and calculous pyelonephritis. She had respiratory symptoms of cough, sputum, and fever before surgery. The COVID-19 and Flu antigen tests were negative. A postoperative chest radiograph showed infiltrative shadows in her right middle and lower lung field. She was suspected of developing bacterial pneumonia, and tazobactam/piperacillin 13.5 g/day and

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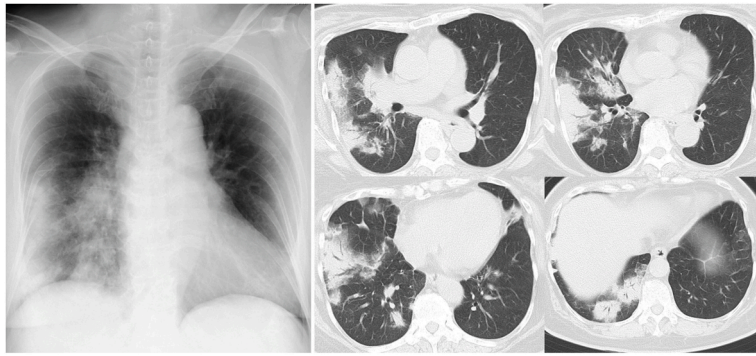


Fig. 1. Chest radiography showed multiple infiltrative shadows with surrounding consolidation of the right middle and lower lobes.

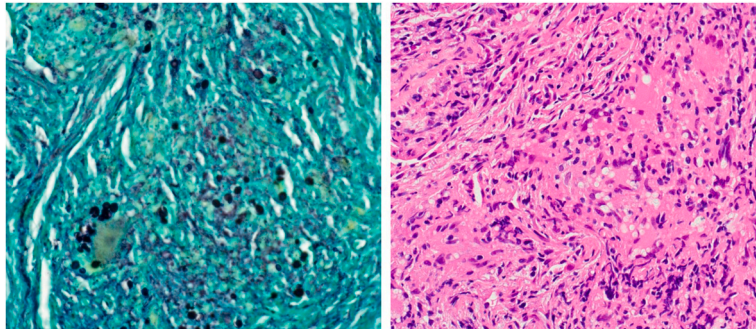


Fig. 2. Histopathological findings were consistent with numerous bowl-shaped cryptococcus cells stained black by Grocott staining. (Grocott staining $\times 400$). Cryptococcus cells produced granulomatous lesions, and the bacterial cells themselves are not stained and only appear missing with HE staining. (HE staining $\times 200$).

levofloxacin 500 mg/day were administered. However, symptoms and infiltrative shadows did not improve. She visited the respiratory medicine department for an investigation.

A physical examination revealed a body temperature of 37.7 °C, and coarse crackles were heard in the right lower lungs. Laboratory test results showed a white blood cell count of 8600/ μ L (neutrophil count of 5330/ μ L, lymphocyte count of 2490/ μ L), C-reactive protein (CRP) of 3.30 mg/dL, serum rheumatoid factor (RF) of 25 IU/mL, and anti-cyclic citrullinated peptide (CCP) antibody of 856 U/mL. β -D-glucan, anti-mycobacterium avium complex (MAC) antibody, QuantiFERON (QFT), and HIV antibodies were negative.

Chest radiography showed multiple infiltrative shadows with surrounding consolidation of the right middle and lower lobes (Fig. 1). The administration of antibiotics was ineffective. On the 10th day, after consulting with our department, a bronchoscopy was performed, followed by bronchoalveolar lavage (BAL) and endobronchial ultrasonography with a guide sheath (EBUS-GS). The BAL lymphocyte count was increased (65.1%). Histopathological findings were consistent with numerous bowl-shaped cryptococcus cells stained black by Grocott staining. Cryptococcus cells produced granulomatous lesions, and the bacterial cells themselves are not stained and only appear missing with HE staining (Fig. 2). Added measurement of serum cryptococcal antigen titers was 4096-fold. When asked in detail, swallows had built nests at the patient's house entrance, and there had been a large amount of swallow excreta. She cleaned without putting on a mask and inhaled much excreta for one year before developing symptoms. Considering that the incubation period from being infected with Cryptococcus fungi to developing symptoms can range from 6 weeks to 2 years, there was a possibility of the infection route of Cryptococcus from swallow excreta. We consulted with a neurologist regarding the necessity of cerebrospinal fluid testing. However, since no symptoms or findings suggest meningitis, the neurologist decided that a cerebrospinal fluid test was unnecessary. Therefore, we considered that we did not need to perform a head MRI. Treatment with fluconazole 400 mg/day was initiated, and her symptoms resolved; the shadows of the lung fields improved, her blood CRP count decreased to normal, and serum cryptococcal antigen titers decreased to 4-fold. We finished the treatment in about a year (Fig. 3). No recurrence was observed after that.

3. Discussion

Cryptococcosis is an infectious disease with worldwide distribution and a wide array of clinical presentations caused by pathogenic encapsulated yeasts in the Cryptococcus genus. Currently, two species of Cryptococcus commonly cause disease in humans: *Cryptococcus neoformans* and *Cryptococcus gattii* [1]. *C. neoformans* are found worldwide and associated with excreta from certain birds, such as pigeons, and cause disease in immunocompromised hosts [1,2].

Mohammad et al. evaluated the isolation of *C. neoformans* from swallow excreta in two northern cities of Iran. Ninety-seven swallow excreta were assessed, and 498 yeast-like colonies were isolated and identified as *C. neoformans* (8.7%). *Cryptococcus neoformans* was isolated from 5/97 (5.2%) of collected samples. The results of this study demonstrate that swallow excreta may harbor *C. neoformans*.

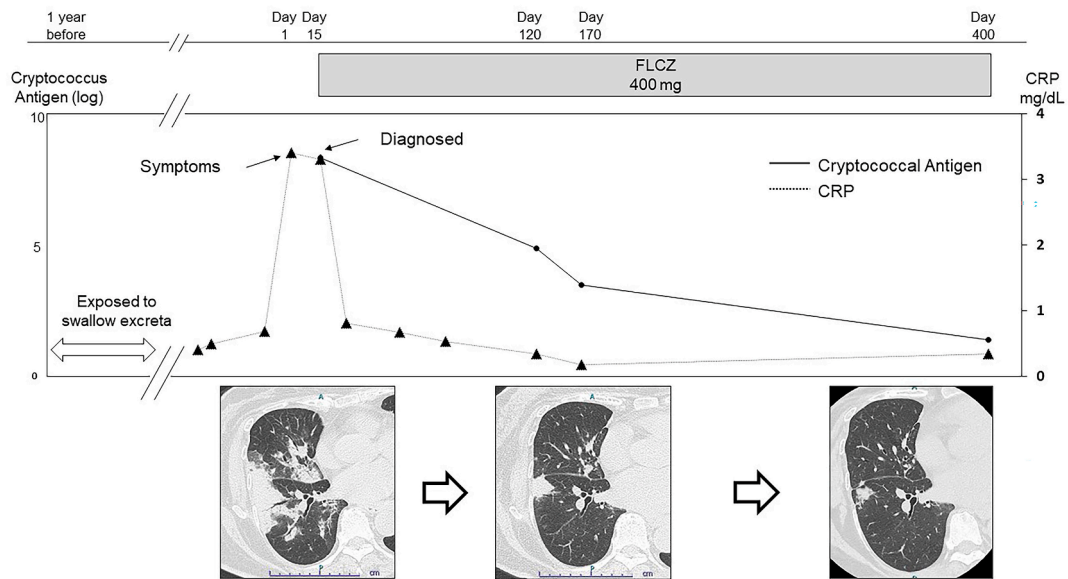


Fig. 3. The timeline from the exposure to the swallow excreta to finishing the fluconazole treatment.

mans [3]. Incubation periods of the *Cryptococcus* spp. can vary between 6 weeks and 2 years [4]. In our case, swallow excreta was suspected as the route of cryptococcal infection in this patient based on the medical history, and there were no other suspected causes of cryptococcosis infection.

On CT images, pulmonary cryptococcosis shows a single nodule, multiple nodules, infiltrative shadow, and ground-glass opacities. Multiple infiltrative shadows type is very scarce, and there have been no reported cases of pulmonary cryptococcosis with multiple infiltrative shadows whose infection route was suspected from swallow excreta. Kohno et al. reported that serum cryptococcal antigen titers are likely higher in infiltrative shadows type than other types [5]. Therefore, pulmonary cryptococcosis should be considered in the differential diagnosis of infiltrative pneumonia in immunocompromised patients, and serum antigen titer measurement should be considered.

4. Conclusion

We experienced a case of pulmonary cryptococcosis suspected due to inhalation of swallow excreta presenting with multiple infiltrative shadows. Pulmonary cryptococcosis should be considered in the differential diagnosis of infiltrative pneumonia in immunocompromised patients, and serum antigen titer measurement should be considered.

CRedit authorship contribution statement

Kei Kanata: Writing – original draft. **Toshihiro Shirai:** Writing – review & editing. **Yutaro Ito:** Investigation. **Koshiro Ichijo:** Investigation. **Masahiro Uehara:** Investigation.

Declaration of competing interest

No conflict

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