Coexistent pulmonary cryptococcal infection and pulmonary sarcoidosis: a case report and literature review

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Abstract
Cryptococcus is an encapsulated, yeast-like fungus commonly responsible for infections in individuals with impaired T cell-mediated immune responses, including those with acquired immune deficiency syndrome or taking immunosuppressive agents such as steroids or cyclosporine. However, pulmonary fungal infection is rare in patients with untreated sarcoidosis. We report a case of coexistent pulmonary cryptococcal infection in a 43-year-old man with pulmonary sarcoidosis in North-western China. The patient was diagnosed with sarcoidosis via right anterior mediastinal lymph node biopsy and lung biopsy by bronchoscopy. He was treated with oral prednisone 25 mg/day and achieved complete remission of all symptoms. However, repeat chest computed tomography examination revealed enlarged nodules in the left lower lobe, but decreased bilateral diffuse small nodules in the lungs. Computed tomography-guided percutaneous lung puncture biopsy revealed cryptococcal infection. This case highlights the need to consider fungal infection in patients with sarcoidosis at initial presentation, irrespective of their use of immunosuppressive medication.

Keywords
Coexisting disease, cryptococcal infection, pulmonary sarcoidosis, computed tomography, immunocompetent, biopsy

Date received: 31 July 2019; accepted: 8 January 2020

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Introduction
Sarcoidosis is a multisystemic inflammatory disease of unknown etiology that manifests as non-caseating granuloma, predominantly in the lungs and mediastinal lymph nodes. Around 50% of patients present with pulmonary complaints such as dyspnea on exertion, cough, and chest pain. After making a definitive pathological diagnosis, the standard treatment includes corticosteroid treatment, usually prednisone or prednisolone, for several months. However, long-term use of corticosteroids makes patients susceptible to fungal infections such as aspergillosis or cryptococcosis. Cryptococcus neoformans is an encapsulated, yeast-like fungus commonly responsible for infections in individuals with impaired T cell-mediated immune responses, including those with acquired immune deficiency syndrome or those taking immunosuppressive agents, such as steroids or cyclosporine. Cryptococcus is ubiquitous in the environment and is most commonly found in pigeon droppings and contaminated soils. It can be divided into four types: serotypes A and D are distributed worldwide and are responsible for most human immunodeficiency virus (HIV)-associated infections, while serotypes B and C are found in immunocompetent patients who have been exposed to the sources of transmission. However, pulmonary fungal infection is rare in untreated patients with sarcoidosis. We report a case of coexistent pulmonary cryptococcal infection in a 43-year-old

![Image of chest computed tomography scan, right anterior mediastinal lymph node biopsy, and lung biopsy](image_url)
immunocompetent man with pulmonary sarcoidosis in North-western China.

**Case presentation**

A 43-year-old man was admitted to hospital with a 5-month history of cough and mucoid sputum, but no fever, night sweat, or weight loss. He had previously been fit and well with no medical history, and had never received oral corticosteroids or any other immunosuppressive agents. A chest computed tomography (CT) scan on admission showed mediastinal and hilar lymphadenopathy and bilateral diffuse small nodules throughout the lungs (Figure 1a). Right anterior mediastinal lymph node biopsy and lung biopsy by fiberoptic bronchoscopy both demonstrated non-caseating granulomas (Figure 1b and 1c). Fite stain was negative, and broncholaveolar lavage fluid culture and serum HIV test were also negative. The patient was diagnosed with sarcoidosis. He was treated with oral prednisone 25 mg/day and achieved complete remission of all symptoms. However, a repeat chest CT scan at 3 months follow-up revealed enlarged nodules in the left lower lobe, but decreased diffuse small nodules in the bilateral lungs (Figure 2a).

The patient was readmitted to the hospital and given antibiotic therapy for 10 days before the pathogens were identified, based on past experience. A third CT scan showed that the nodules in the left lower lobe had enlarged further forming a pulmonary mass, but the bilateral diffuse small nodules had reduced compared with the previous CT scan (Figure 2b). CT-guided percutaneous lung puncture biopsy of the left lower lobe revealed cryptococcal infection with broad and refractive colloidal capsule (Figure 2c).

**Figure 2.** Diagnosis of cryptococcosis. Chest computed tomography scan on second admission (a) and 10 days after second admission (b). (c) Lung biopsy in the left lower lobe (hematoxylin and eosin staining ×100).
He was then diagnosed with pulmonary cryptococcosis and treated with oral fluconazole 400 mg/day for cryptococcal infection. Further chest CT images showed improvements 1 and 2 months later (Figure 3a and 3b).

This study was approved by the local ethics review committees and the patient gave written informed consent for publication of this case report.

Discussion

Sarcoidosis is a common disease involving abnormal collections of inflammatory cells, primarily occurring as granulomas in the lungs, skin, or lymph nodes. In the current case, the patient’s symptoms were relieved by prednisone therapy but the nodules in the left lower lobe remained. CT-guided percutaneous lung puncture biopsy subsequently revealed cryptococcal infection, indicating coexisting pulmonary cryptococcal infection in this patient with pulmonary sarcoidosis, despite no previous steroid treatment. Pulmonary cryptococcal infection is a rare complication in patients in North-western China with sarcoidosis but without steroid treatment. The present patient was immunocompetent and had not been exposed to pigeon droppings or contaminated soils, but developed pulmonary cryptococcal infection even in the absence of these predisposing factors. This case demonstrates the need to consider the possibility of fungal infection in these circumstances, especially in the event of a unilateral abnormal chest shadow and ineffective antibiotic therapy.

When fungal particles enter the host, the development of a fungal infection depends on the host immune status and the virulence of the fungus. Host factors may involve either insufficient immunity or excessive immunity from T-helper 1 or 2 cytokine responses. A previous case report presented a 48-year-old man with sarcoidosis who was treated with steroids for 13 months with slow tapering to a dosage of 20 mg/day. After readmission to hospital, skin, blood, and cerebrospinal fluid cultures confirmed the presence of *Cryptococcus neoformans*. Although coexistent pulmonary cryptococcal infection is usually associated with abnormal excessive immunity, especially after long-term steroid use, the present case reveals that a possible fungal infection should be borne in mind even in immunocompetent patients.

The current patient had cough and mucoid sputum, and chest CT scan displayed mediastinal and hilar lymphadenopathy and bilateral diffuse small nodules.
throughout the lungs. Meanwhile, lymph node biopsy and lung biopsy by fiberoptic bronchoscopy both showed non-caseating granulomas. The patient’s symptoms improved dramatically after prednisone treatment. A diagnosis of pulmonary sarcoidosis was determined based on the clinical manifestations, pathology, and clinical therapy. Most patients with cryptococcal infection are asymptomatic and lung lesions are detected incidentally on chest imaging. Some patterns indicating possible pulmonary cryptococcal infection include peripheral pulmonary granulomas, granulomatous pneumonitis, diffuse pneumonia, and pleural diseases. However, the illusive pulmonary lesion presentation in this patient meant that we did not consider cryptococcal infection at his initial presentation. The patient’s disease progression, diagnosis of cryptococcal infection, and recovery after antifungal treatment highlight the need to consider possible fungal infection in patients with sarcoidosis at initial presentation, irrespective of the use of immunosuppressive agents.

In conclusion, this case report presents a patient with coexistent pulmonary cryptococcal infection and pulmonary sarcoidosis, in whom cryptococcal infection developed prior to steroid treatment for his pulmonary sarcoidosis. This case indicates the need to consider the possibility of a fungal infection, even in immunocompetent patients.

Acknowledgments
We appreciate the technical support and materials from the Department of Pathology, the First Affiliated Hospital of Xi’an Jiaotong University. This work was supported by programs from the National Natural Science Foundation of China (81800390), the National Science Foundation of Shaanxi province (2018KW067, 2014JM2-8185), and the Fundamental Research Funds for the Central Universities in China (1191329724, 191329849).

Declaration of conflicting interest
The authors declare that there is no conflict of interest.

Funding
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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