



# A Case of Pulmonary Cryptococcosis with Normal Immune Function

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**Abstract:** *Objective* Pulmonary cryptococcosis (PC) is a pulmonary fungal disease caused by *Cryptococcus neoformans* infection, the clinical manifestations are pneumonia or pulmonary nodules, or acute respiratory distress syndrome (ARDS) in severe cases. But its clinical manifestations lack specificity, so it is often misdiagnosed or missed in recent years. Pulmonary cryptococcosis is common in patients with human immunodeficiency virus (HIV) and non-HIV-associated immunosuppression, it has been found that pulmonary cryptococcosis is also common in people with sound immune function. The purpose of this paper is to report the diagnosis and treatment process of a patient with pulmonary cryptococcosis in our hospital, so as to provide reference for the diagnosis and treatment of the disease and reduce the misdiagnosis rate and missed diagnosis rate of the disease. *Methods* The diagnosis and treatment process of a case of pulmonary cryptococcosis in our hospital were reviewed. *Results* Combined with the patient's lung CT Imaging manifestations, and environmental exposure history and immune status, pulmonary cryptococcosis was considered. After empirical anti-cryptococcosis treatment, the patient's symptoms improved, and pulmonary nodules disappeared according to lung CT review. *Conclusion* Clinicians should identify the imaging characteristics of patients with *Cryptococcus pneumonicum* and combine them with their environmental exposure history and immune status to avoid missed diagnosis and delayed disease.

**Keywords:** Pulmonary Cryptococcosis, Immune Function, Case Report, Diagnosis by CT

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## 1. Introduction

Cryptococcosis is a lethal fungal infection and pathogenic cryptococci have mainly *Cryptococcus neoformans* and *Cryptococcus gattii*, the former being more common in HIV positive patients and the latter in immunocompetent individuals [1]. Cryptococcosis often presents as meningitis or pneumonia, pulmonary cryptococcosis (PC) is an important opportunistic invasive fungal disease in immunocompromised patients, such as human immunodeficiency virus (HIV) infection, solid organ transplantation, autoimmune diseases, the use of corticosteroids and other immunosuppressants [2]. According to the 2010 China "Expert Consensus on the Diagnosis and Treatment of Cryptococcal Infections", the diagnosis of pulmonary cryptococcosis is mainly based on

pathological examination of lung tissue or pathogenic smears and culture of pus puncture specimens in the sterile part of the lesion [3]. However, these diagnostic means are invasive examinations, which are difficult for many patients to accept. Chest CT, a noninvasive, reproducible, and comprehensive examination technique to assess the characteristics and scope of lung lesions, is particularly important for the diagnosis of the disease.

## 2. Case Presentation

A 48-year-old male patient came to our hospital for complaints of left shoulder discomfort with hypohidrosis for

1 week. He has a history of hypertension and his blood pressure is controlled well. Physical examination showed good nutritional status, stable vital signs, normal cardiopulmonary and nerve examination.

**2.1. Investigations**

The blood test showed that the white blood cells were  $12.1 \times 10^9/L$ , and the neutrophil ratio was 82.1%. Blood lipids: high-density lipoprotein cholesterol 0.86mmol/L, lipoprotein a 505mg/L. Coagulation function, erythrocyte sedimentation rate, urine routine, infectious disease series, tumor markers,

liver function, thyroid function, ion series, renal function, immune series were normal. G test  $<10\text{pg/ml}$ ; Serum Aspergillus specific antigen (-); Cryptococcus latex qualitative test (-). Mycobacterium tuberculosis specific cellular immune response test ( $\gamma$ -interferon release test): normal, Mycobacterium tuberculosis T cell immune response (-). B-ultrasound examination showed bilateral submandibular multiple enlarged lymph nodes. Chest CT showed multiple pulmonary nodules (Figure 1). After going to superior hospital, further PET / CT examination showed lung nodule (Figures 2 and 3).

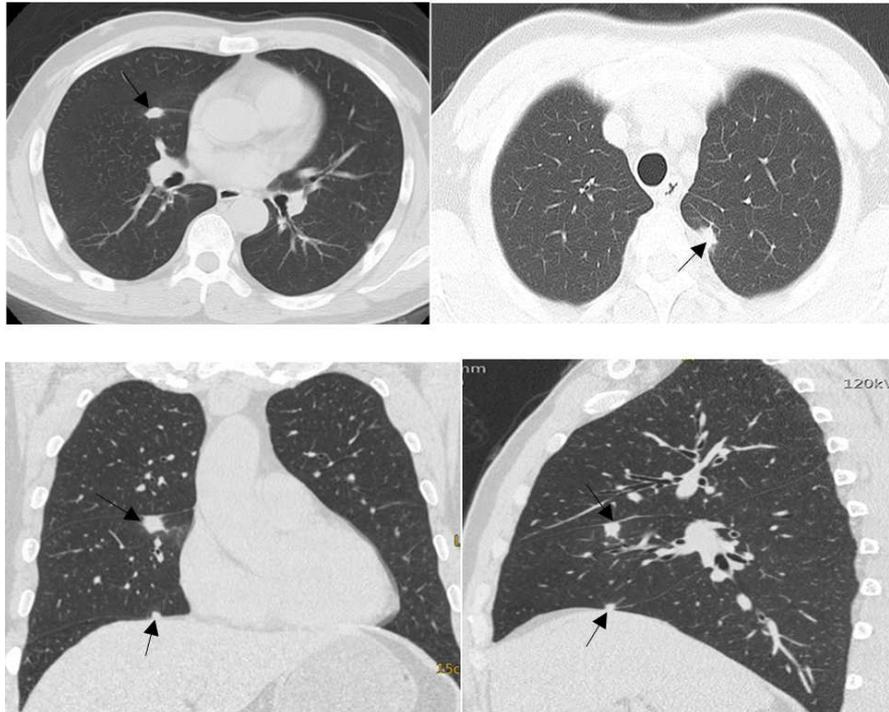


Figure 1. CT of the Lung.

Figure 1 showed multiple round-like nodules in the middle lobe of the right lung, the largest one was about  $1.0 \times 0.8\text{cm}$  (black arrow), the boundary was clear, and the airway was unobstructed. There was a round-like nodule about  $1.0 \times 1.0\text{cm}$  (black arrow) under the pleura of the upper lobe of the left lung with clear borders and airway patency.

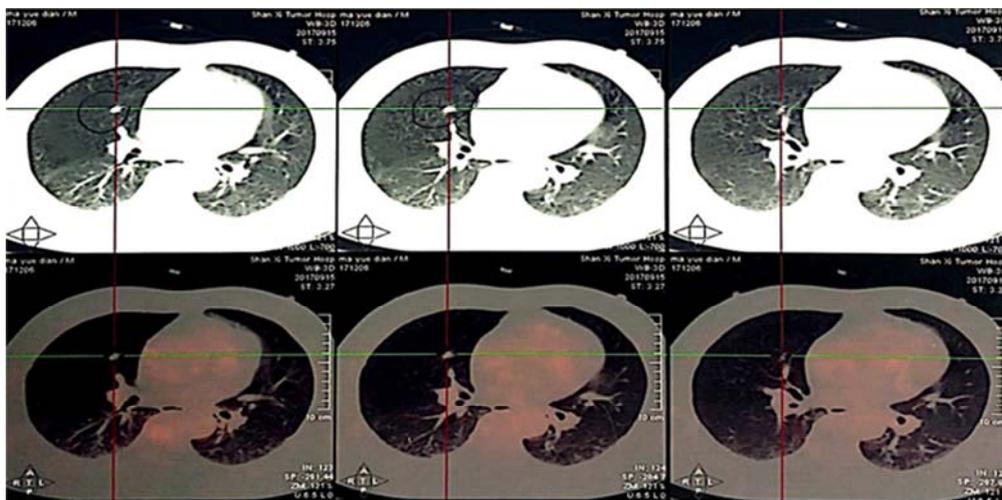


Figure 2. PET-CT of lung.

Figure 2 Right middle lobe showed multiple round nodules, the largest one was about 1.0×0.8cm, the boundary was clear, and the airway was unobstructed.

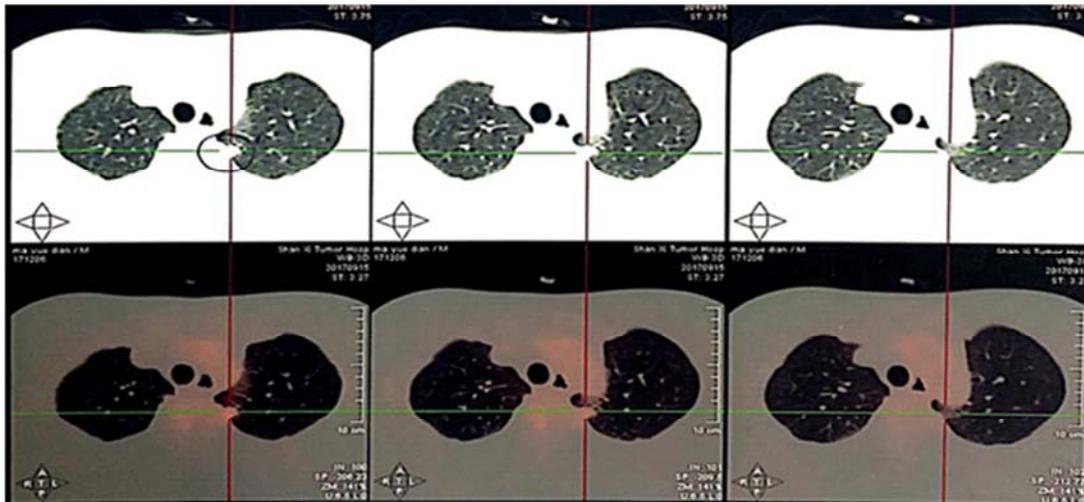


Figure 3. PET-CT of lung.

Figure 3 A circular nodular shadow was seen near the pleura in the posterior segment of the upper lobe tip of the left lung, the size was about 1.0 \* 1.1cm, the boundary was clear, and the airway was unobstructed.

Asked the patient's medical history again and learned that the patient had raised pigeons. Combined with the CT findings of the patient's lungs, he was highly suspected of pulmonary cryptococcosis. It was suggested that the patient further underwent histopathological examination to clarify the diagnosis, and the patient refused invasive examination.

## 2.2. Treatment

Experimental antifungal therapy with fluconazole at 400mg/d for 6 months.

## 2.3. Outcome and Follow-up

After 6 months of treatment, the patient's condition improved, and there was no complaint of discomfort. Repeated chest CT showed that the lung nodules were significantly reduced to disappear (Figure 4).

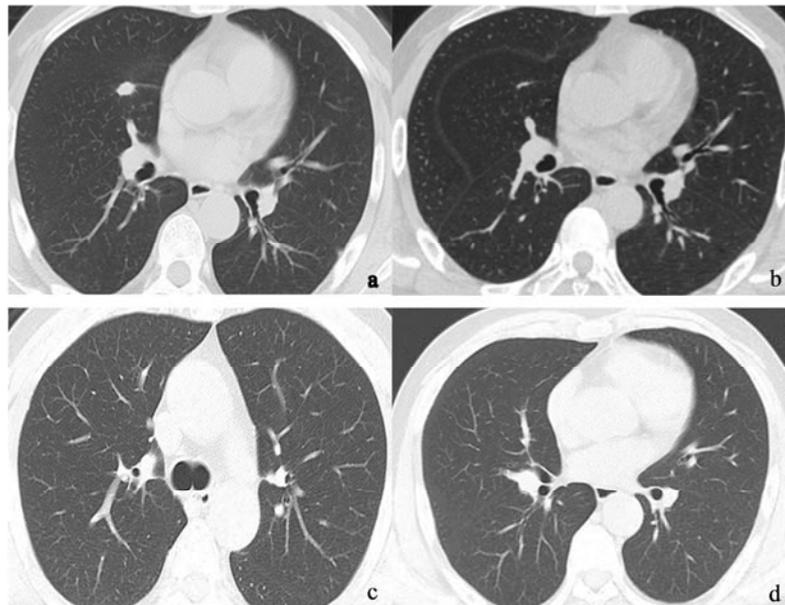


Figure 4. CT of the Lung.

Figure 4 a is 2019-09-09 lung CT, b is 2019-10-9 lung CT, c is 2019-12-13 lung CT, d is 2020-8-13 lung CT, it can be seen that the lung nodules are significantly reduced to disappear.

## 3. Discussion

Cryptococcus is a kind of saprophytic fungus with capsule

that exists widely in nature [4]. Cryptococcosis in China is mainly caused by *Cryptococcus neoformans* serovar A, and pigeon manure is the most important infectious source [5]. Aerosol infection with *Cryptococcus neoformans* via respiratory inhalation, with invasion of the central nervous system being the most common (80%), and with invasion of the lung as the sole manifestation accounting for only 20% [6]. Cough and fever are the most common symptoms of immunocompromised patients, and cough is the most common symptoms of immunocompromised patients [7].

This disease needs to be differentiated from lung cancer, tuberculosis, pneumonia, and pulmonary aspergillosis. Pulmonary cryptococcosis is easily confused with peripheral lung cancer when it presents as nodular shadow [8], and it has been suggested that the halo sign could be used to differentiate PC from lung cancer [9]. In patients with cryptococcosis of any type and regardless of size, the tree bud sign is not visible on CT images, whereas it is frequently observed in tuberculosis [10]. In addition, the increased density of pulmonary cryptococcosis is often seen subpleurally in the lower lobes of both lungs, while tuberculosis tends to occur in the upper lobe tips, posterior segments, and dorsal segments of the lower lobes of both lungs. PC also needs to be differentiated from pneumonia in the clinic, which is often seen with air bronchograms within solid lung tissue [11]. Pulmonary aspergillosis cavities are mostly thick walled cavities (mostly larger than 2 cm), which is different from the thin-walled cavities of cryptococcal lung disease (often less than 2cm). Usually, immunocompromised individuals can be easily misdiagnosed as TB, while immunocompetent individuals can be misdiagnosed as tumor, which needs to be distinguished. Patients with PC often present with pulmonary nodules or masses and patchy shadows on chest CT [12]. PC should be considered in the case of subpleural nodules or mass or patchy infiltrative type lesions in the lower lung field with halo sign, retrohalo sign, proximal bronchial sign or cavitation [13].

It can be diagnosed as a PC if it meets one of the following conditions [3, 12]: (1) mation of diagnosis mainly relies on histopathological examination of the lungs or on the presence of pathognomonic smears and culture of intralesional, pus aspirated specimens in sterile sites; (2) the clinical suspected diagnosis mainly depends on the positive of serum cryptococcal capsular polysaccharide antigen (CrAg) latex agglutination test. Serum cryptococcal antigen (CrAg) is the most commonly used noninvasive test for the diagnosis of pulmonary cryptococcosis, however, in the clinic, many PC patients are negative for CrAg, so a negative serum crag does not exclude pulmonary cryptococcosis [14]. But high CrAg titer can indicate disease progression [15]. Histopathology is invasive and not easily accepted by patients, so chest CT is particularly important in the diagnosis of PC.

For this patient, a middle-aged male, there is no immunodeficiency, only lung nodules and lymph nodes are enlarged, which is easy to be misdiagnosed as a malignant tumor and ignore cryptococcal infection. By repeatedly asking the medical history, it was learned that the patient had

raised pigeons, combined with the existing auxiliary examination results, so highly suspicious of PC was diagnosed, and the patient's condition improved significantly after receiving the experimental treatment. PC as a curable disease, especially in HIV negative patients with a good prognosis [16]. Most PC patients without CNS infection, especially those with normal immune function, respond well to fluconazole monotherapy, and the abnormal lung imaging manifestations of the patients can be significantly improved after treatment [17]. Antifungal therapy is preferred, including amphotericin B, 5-fluorocytosine (5-FC), clotrimazole and fluconazole. Among them, fluconazole treatment is recommended as the first choice [18, 19]. The treatment regimen of fluconazole is 200-400 mg/d, 3-6 months for asymptomatic patients, 6-12 months for patients with mild to moderate symptoms, and more than 12 months for patients with severe lung infection [19]. For patients with normal immune function with a single lung disease, the initial invasive surgery should be carefully selected to reduce unnecessary lobectomy. As the incidence of pulmonary cryptococcosis is increasing among people with normal immunity, medical workers also need to pay more and more attention to the occurrence of this disease, strengthen the interpretation of preoperative CT focus image features, so as to reduce the occurrence of misdiagnosis and mistreatment, and achieve early diagnosis and treatment.

## 4. Conclusion

With the increasing number of patients with pulmonary *Cryptococcus* with normal immunity, early diagnosis and early treatment have become particularly important. Clinicians should try their best to find its characteristics, such as: when CT shows that consolidation lesions are located under the lower lobe pleura, they are distributed unilaterally, accompanied by angiographic signs, proximal bronchial signs, and dizziness signs, and the enhanced scan shows uniform mild to moderate enhancement, combined with the patient's environmental exposure history and Immune status, should think of pulmonary cryptococcosis, so as not to miss the diagnosis and delay the condition.

## Contributors

All authors contributed to this case report. And the authors agree to be accountable for all aspects of the work. All authors read and approved the final manuscript.

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