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The Journal of Clinical Microbiology

ISSN 2995-8539

Case Report

Non-HIV Pulmonary Cryptococcosis Complicated with Bloodstream Infection.

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Abstract

An elderly male patient presented with subacute onset. His immune function was normal and he had a history of diabetes. He was admitted to the hospital due to "coughing and expectoration, fatigue and shortness of breath for 1 month, and aggravation with fever for 1 week." The diagnosis was pulmonary cryptococcosis, which rapidly progressed to bloodstream infection.This report aims to provide experience and assistance for future clinical diagnosis and treatment of cryptococcosis, enhance clinical understanding, facilitate early diagnosis and treatment, improve patient prognosis and survival rate.

Keywords : pulmonary cryptococosis, bloodstream infection, severe pneumonia.

INTRODUCTIONS

Cryptococcus is widely distributed in nature and can be found in bird droppings, soil and rotten wood. It is a free-living activated encapsulated yeast, and usually causes infection in patients with compromised immune function (such as HIV infection, hematological malignancies or organ transplantation).Pulmonary cryptococcosis is a subacute or chronic pulmonary fungal disease caused by infection with Cryptococcus neoformans. It is a rare pulmonary fungal infection in clinical practice.Cryptococcus neoformans is a opportunistic pathogen that often occurs in immunocompromised individuals. In recent years, it has been found that the prevalence of pulmonary cryptococcosis in immunocompetent individuals has been increasing year by year.Pulmonary cryptococcosis has an insidious onset, often presenting as non-specific pulmonary or systemic symptoms. It is mild and prone to misdiagnosis. The imaging manifestations are mostly single or multiple nodules, which can also be presented as masses, cavities, consolidation, etc. It is easily misdiagnosed as pulmonary tuberculosis, tumors, pneumonia and other diseases.This report focuses on pulmonary cryptococcal invasion into the bloodstream, which leads to bloodstream infection. The aim is to provide experience and assistance for future clinical diagnosis and treatment of cryptococcal disease.

CLINICAL DATA

General Data

Patient, male, 62 years old, has a history of smoking for over 40 years, averaging 20 cigarettes per day, and has not quit smoking.In January, the patient developed cough and expectoration after catching a cold. The expectoration was white and viscous. Accompanied by fatigue and shortness of breath after activities, especially when climbing slopes or going upstairs. The symptoms were more obvious when the patient was engaged in such activities.One week ago, after the patient was exposed to cold again, his cough worsened. Nighttime cough was particularly severe. He coughed up white sticky phlegm which was difficult to expel. He also had intermittent fever with the highest temperature of 38°C. His activity decreased, he felt tired and short of breath, and had dizziness and headache. He also felt discomfort in the xiphoid process area. On February 6, 2025, he was admitted to the hospital with "pulmonary infection and bronchitis".

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Email: 1505103256@qq.com.
Received: 09-September-2025, Manuscript No. TJOCMB-5103 **; Editor Assigned:** 09-October-2025 **; Reviewed:** 14-October-2025, QC No. TJOCMB-5103 **;**
Published: 16-October-2025, **DOI:** 10.52338/tjocmb.2025.5103.
Citation: Xiaoli Jiang. Non-HIV pulmonary cryptococcosis complicated with bloodstream infection. The Journal of Clinical Microbiology. 2025 October; 13(1). doi: 10.52338/tjocmb.2025.5103.

Physical examination upon admission to hospital

Body temperature is 36.1°C, pulse rate is 78 beats per minute, respiratory rate is 20 breaths per minute, blood pressure is 141/81 mmHg, and the saturation of finger pulse oxygen is 89%.The development is normal, the nutrition is good, consciousness is clear, speech is clear, the physical examination is cooperative, there is no jaundice on the skin and mucous membranes of the whole body, no enlargement of superficial lymph nodes, no deformity of the facial features of the head and face, no cyanosis of the lips, the neck is soft, the trachea is centered, the chest is symmetrical without deformity, the breathing sounds of both lungs are coarse, wet rales can be heard in both lungs, the heart boundary is not palpable, the heart rhythm is regular, no pathological murmurs are heard in all valve areas, the abdomen is flat and soft, no tenderness, and there is no edema in both lower extremities.

Laboratory Inspection

Blood cell analysis: White blood cell (WBC) 13.33×10^9/L, mean corpuscular hemoglobin concentration (MCHC) 315g/L, neutrophil percentage (NEUT%) 95.1%, lymphocyte percentage (LYMPH%) 3.3%, monocyte percentage (MONO%) 1.4%, eosinophil percentage (EOS%) 0.0%, neutrophil count (#NEUT) 12.66×10^9/L, lymphocyte count (LYMPH#) 0.44×10^9/L, eosinophil count (EOS#) 0.01×10^9/L, high-sensitivity C-reactive protein (hs-CRP) 94.18mg/L, fasting blood glucose (GLU) 12.55mmol/L, interleukin-6 (IL6) 806.10pg/ml, procalcitonin (PCT) 0.116ng/ml.

Imageological Examination

Chest CT

1. Multiple scattered infectious lesions in both lungs, with partial bronchiectasis. 2. Local calcification of the walls of the thoracic aorta and coronary arteries.

Diagnose

Pulmonary cryptococcosis complicated with bloodstream infection, severe pneumonia, diabetes

Therapeutic Process

After being admitted to the Respiratory Department on February 6th, intravenous infusion of piperacillin sodium and tazobactam sodium 4.5g every 8 hours and moxifloxacin 4.0g every day was given for severe bilateral lung infection. On February 7th, the examination results showed positive cryptococcal capsular antigen; the sputum smear indicated that the specimen was qualified and 2+ fungi were found; no acid-fast bacilli were detected; the sputum culture result was Cryptococcus neoformans; the respiratory tract pathogen antibody was negative. The G test and Gm test were negative. The cerebrospinal fluid routine was normal, and the cerebrospinal fluid biochemistry was: glucose (GLU) 6.82 mmol/L, chloride (CL) 123.3 mmol/L, protein (PRO) 317.90 mg/L; no Cryptococcus neoformans, bacteria, or acid-fast bacilli were found in the cerebrospinal fluid smear; the cerebrospinal fluid bacterial culture was negative; HIV: negative. The antibacterial drugs were adjusted to: piperacillin-tazobactam + fluconazole for anti-infection treatment. On February 10th, the patient still had intermittent fever, with obvious cough, expectorating yellow sticky sputum, and complained of dizziness and headache; the white blood cells, neutrophil percentage, PCT, all showed an upward trend, and the blood culture result was Cryptococcus neoformans; the tNGS result of bronchoalveolar lavage fluid was Cryptococcus neoformans; chest CT suggested that bilateral lung infection worsened. The patient progressed to cryptococcal bloodstream infection. Currently, the treatment effect is not good, and the antibacterial drugs were adjusted to: meropenem 1g ivgtt every 8 hours + amphotericin B lipid complex 200mg ivgtt every day. The patient's condition has slightly stabilized.On February 16th, the patient's condition worsened compared to before. Moreover, the patient's cough and shortness of breath did not show significant improvement compared to before. Cryptococcus bloodstream infection combined with respiratory failure was diagnosed. The oxygenation index was 172 mmHg. Chest CT indicated that the infection had worsened and the treatment effect was poor. The antibacterial drugs were adjusted to: flucytosine 1.5g every 8 hours + amphotericin B lipid complex 200mg ivgtt every day + compound sulfamethoxazole tablets 4 tablets every 6 hours for 4 days to treat PCP. After the above treatment, the patient's body temperature returned to normal, but the patient was old, had poor basic lung function, and the lung infection was severe, making the treatment very difficult. On March 8th, the patient again presented with fever symptoms, and the cough symptoms worsened compared to before. The patient's spirit was extremely poor, and the condition was extremely critical with rapid breathing. The family refused further treatment and the patient was discharged voluntarily on March 12th.

Treatment outcome, follow-up and prognosis

Therefore, the diagnosis of disseminated cryptococcal meningitis was confirmed for this patient. Subsequently, the patient's condition worsened and the family refused further treatment, resulting in the patient's voluntary discharge. The follow-up outcome was that the patient died after discharge.

Figure 1. Cryptococcus under microscopic observation after Gram staining of sputum smear(×1000).

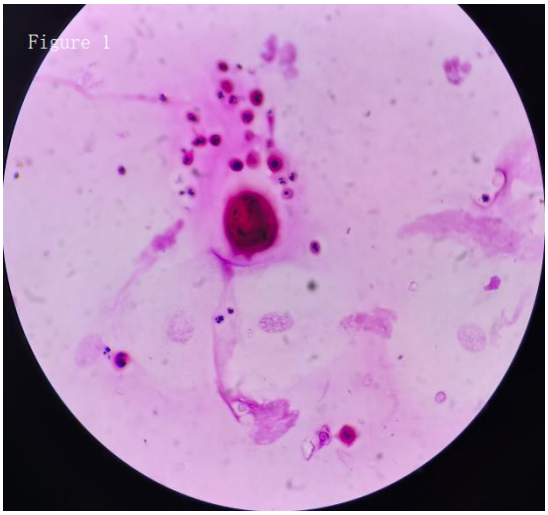
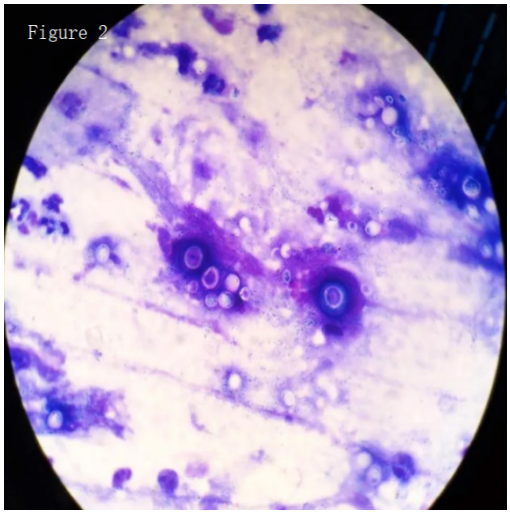


Figure 2. Cryptococcus under microscopic observation after acid-fast staining of sputum smear(×1000).



DISCUSSION

Cryptococcus neoformans is an opportunistic pathogen. The infection rate of Cryptococcus neoformans among people with normal immune function is relatively low, approximately 1 in 100,000. However, in patients with HIV infection, the infection rate of Cryptococcus neoformans is as high as 30%[5]. Apart from HIV infection, the use of immunosuppressants, solid organ transplantation, chronic organ failure (kidney and liver), hematological malignancies, diabetes, and chronic pulmonary diseases may all lead to opportunistic infections in the body.The lungs are the necessary entry point for Cryptococcus spores to be inhaled. After Cryptococcus spores are inhaled through the respiratory tract, they can survive in lung tissues and remain latent in alveolar macrophages for a long time. When the immune function of the body is compromised, Cryptococcus can spread from the lungs to any organ throughout the body via the bloodstream.Under the condition of normal immune function of the body, the lung lesions of patients with pulmonary cryptococcosis are mostly localized and rarely show disseminated conditions [6]. The disseminated infection that occurs in normal individuals without underlying diseases [7] may have its pathogenesis related to the interaction between Cryptococcus and the immune system [8], and it is mostly caused by the dissemination of pulmonary cryptococcosis.This case presented with disseminated cryptococcal infection through bloodstream. It was considered that the new type of cryptococcus entered the lungs via the respiratory tract and left the lungs through various extracellular pathways in the form of free fungi. It utilized the endocytosis pathway of host cells to facilitate the passage of fungi across the epithelial barrier and enabled the new type of cryptococcus to enter the interstitial lung tissue, vascular system, lymphatic system or enter the bloodstream for bloodstream infection. Although this was not a case of HIV infection, the patient had diabetes mellitus, which increased the risk of cryptococcus bloodstream infection.

The clinical manifestations of patients with pulmonary cryptococcosis can be either asymptomatic or fatal. Currently, the diagnosis of pulmonary cryptococcosis mainly relies on pathogenic and histopathological examinations. Serum cryptococcal capsular polysaccharide antigen is a commonly used initial screening method, which is characterized by its rapidity, specificity and sensitivity [9-11].

The therapeutic goal of pulmonary cryptococcosis is to alleviate the clinical symptoms and signs of patients and prevent the dissemination of Cryptococcus neoformans to the central nervous system. In clinical practice, the selection of drugs for the treatment of new-type cryptococcal infections is limited because Cryptococcus neoformans not only has resistance to echinocandin drugs but also can develop resistance to azole drugs through a series of defense mechanisms [12-13]. Amphotericin B has always been the main treatment method for cryptococcal infections. Fluconazole is usually used as the initial monotherapy for patients with mild or asymptomatic localized cryptococcal infections; clinical trials have shown that the combination of amphotericin B and 5-fluorocytosine can improve survival rates and reduce drug toxicity compared with using amphotericin B alone [14].

In conclusion, cryptococcosis is a subacute infection with an insidious onset. During the diagnosis and treatment process, it is necessary to conduct evidence-based research from multiple aspects and angles. In particular, it is important to utilize simple and rapid laboratory examination methods to actively seek diagnostic clues, make early diagnosis, and carry out targeted treatment as early as possible to improve the prognosis of patients and increase the survival rate.

Conflict of interest statement

All the authors declare that there is no conflict of interest in this research.

Author Contributor Statement

Y W and Y L were involved in the treatment of the patients, while Y F, G Z, W C and W L were responsible for the follow-up of the patients. XJ participated in the primary culture of the pathogen and provided pictures. Y F and XJ were involved in the final diagnosis based on the fungal knowledge and the writing of the paper. All authors read and approved the final version of the clinical photos. “Informed; Notified”. The publication can only be carried out after obtaining the patient’s consent.

Moral Approval Statement

This is an observational study. The ethics committee of our hospital has confirmed that no ethical approval is required.

Informed Consent Statement

The patient information in this study was anonymized, and there were no identifiable images of individuals in the submitted content.

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