Cryptococcosis in an Immunocompetent Adolescent: A Case Report

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ABSTRACT A 16-year-old male patient was admitted to our hospital with a diagnosis of "community-acquired pneumonia" following a two-week history of recurrent cough and productive expectoration that had failed to respond to prior outpatient anti-infective therapy. Despite initial empirical antibiotic treatment, his symptoms persisted. Chest computed tomography revealed a patchy consolidation in the left upper lobe, accompanied by an "air bronchogram" sign, which raised suspicion of an atypical pulmonary infection. To clarify the etiological diagnosis, bronchoalveolar lavage was performed, and the collected fluid was subjected to pathogen-targeted high-throughput gene sequencing. The results identified a Cryptococcus neoformans infection, confirming the diagnosis of pulmonary cryptococcosis. The patient was subsequently treated with oral fluconazole at a dosage of 300 mg/day for 9 days during hospitalization, leading to significant symptomatic improvement. He was discharged in stable condition and continued oral fluconazole as an outpatient. A 6-month telephone follow-up revealed that the patient remained asymptomatic with no evidence of disease recurrence, indicating a favorable clinical outcome.

INDEX TERMS Immunocompetent host, Diagnosis, Pulmonary cryptococcosis, Cryptococcus neoformans

I. INTRODUCTION

Pulmonary cryptococcosis is a fungal infectious disease affecting both humans and animals, primarily caused by Cryptococcus neoformans and Cryptococcus gattii, with Cryptococcus neoformans accounting for $\geq$ 95% of cases. Previous studies indicate that this disease predominantly occurs in immunocompromised populations, such as patients with acquired immunodeficiency syndrome (AIDS), organ transplant recipients, and individuals receiving immunosuppressive therapy [1]. While previous domestic and international case reports rarely documented pulmonary cryptococcosis in immunologically normal children and adolescents, recent studies in China have shown an increasing incidence among non-AIDS patients [2], with males aged 5–17 years being more susceptible [3]. This article reports a case of cryptococcal infection in an immunocompetent adolescent, summarizes the reasons for misdiagnosis and future diagnostic and therapeutic priorities, and aims to enhance clinicians' awareness of the cryptococcal infection risk in this population.

A. CASE DATA

The patient, a 16-year-old male, was admitted on February 5, 2025, due to "cough with sputum production for two weeks." Two weeks prior, the patient developed cough and sputum production after exposure to cold, accompanied by dyspnea during severe coughing, left-sided chest pain, and increased frequency of bowel movements. No symptoms such as chills, fever, throat discomfort, dyspnea, or hemoptysis were reported. On January 22, 2025, the patient sought medical attention at another hospital and was initially diagnosed with bacterial pneumonia. After two weeks of anti-infective therapy, no significant improvement was observed, prompting transfer to our hospital. The patient has no prior history of specific diseases, immune deficiency disorders, organ transplantation or other surgical procedures, use of immunosuppressive agents, recent travel history, contact with pigeon droppings or soil, or family history of similar conditions or other special medical backgrounds.

Physical examination: Body temperature 36.5°C, pulse 86 beats/min, respiratory rate 20 breaths/min, blood pressure 129/91 mmHg (1 mmHg = 0.133 kPa), height 175 cm, weight 111 kg; BMI: 36.2 kg/m^2; body type obese; no other abnormalities noted on physical examination.

Laboratory tests: C-reactive protein: 5.93 mg/L; procalcitonin: 0.06 ng/ml; complete blood count (CBC), electrolytes, liver and kidney function tests, cardiac enzyme profile, D-dimer, coagulation profile, tumor markers, lipid profile, and glucose levels showed no significant abnormalities. Routine electrocardiogram (ECG) examination revealed no notable abnormalities.

Imaging findings: Chest CT: A patchy consolidation with surrounding patchy hyperdensity is observed in the upper lobe of the left lung, with partially blurred margins and the presence of an "air-containing bronchus sign." No reduction in the volume of the corresponding lung tissue was noted,

suggesting a possible infectious focus (Figure 1).

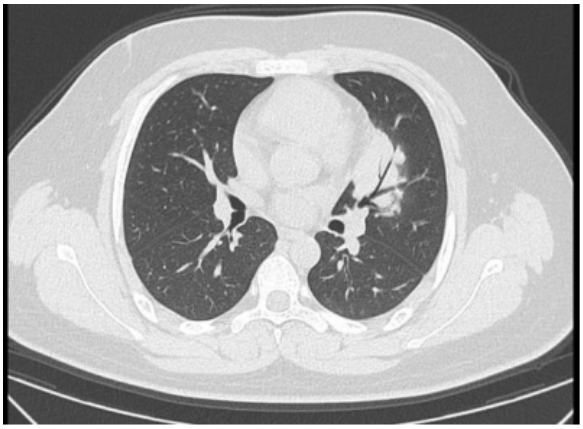

FIGURE 1. Chest CT image of the patient.

On February 5, 2025, chest CT examination revealed patchy consolidation in the upper left lung lobe with surrounding patchy areas of increased density, partially blurred margins, and an "air-containing bronchial sign" observed within the lesion.

Initial diagnosis upon admission: community-acquired pneumonia. Empirical treatment with cefoperazone-sulbactam sodium (Supernase) was initiated on February 5, but the therapeutic response was poor. On February 7, ultrasonic bronchoscopy revealed a hypoechoic area in the left upper lobe; a brush biopsy was performed for cytological examination, and lung segmental lavage samples were collected for analysis (Figure 2). Pathological examination on February 10 identified numerous bronchial epithelial cells and a small number of lymphocytes. Bacterial and fungal cultures, acid-fast staining, and galactomannan tests of the alveolar lavage fluid were all negative. All tumor markers, two antinuclear antibodies, three vasculitis markers, hepatitis markers, anti-Syphilis antibody, and human immunodeficiency virus antibodies were negative. Targeted next-generation sequencing (tNGS) of the alveolar lavage fluid indicated Cryptococcus neoformans infection (sequence count: 39; relative abundance: 2.61%). Subsequent serum testing for Cryptococcus capsular polysaccharide antigens confirmed positive results. Given the patient's prolonged ineffective antimicrobial therapy, persistent symptoms, and absence of bacterial evidence in pathology findings, bacterial infection was temporarily ruled out, and a definitive diagnosis of Cryptococcus neoformans infection was established. Lumbar puncture was recommended to assess central nervous system involvement, but the patient's family declined. Unenhanced cranial MRI showed no significant abnormalities, leading to a decision for observation. On February 12, oral fluconazole capsules (Dafukang) 300 mg/day were initiated as antifungal therapy, resulting in gradual symptom improvement. After 9 days of antifungal therapy, the patient's symptoms improved, and no significant abnormalities were detected in laboratory tests. The patient was discharged on February 13, 2025, and continued oral fluconazole capsules outside the hospital. During a telephone follow-up six months post-discharge, the patient's condition remained stable with no adverse symptoms reported.

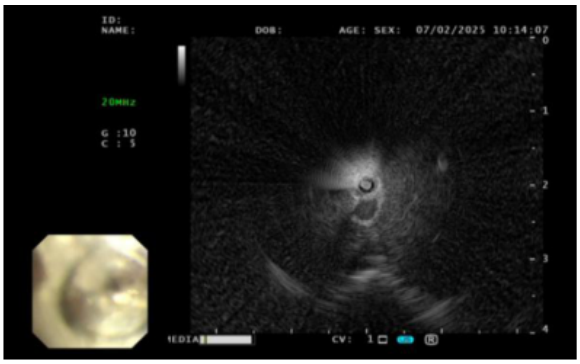

FIGURE 2. Ultrasound bronchoscopy 1image of the left upper lobe of the patient.

On February 7, 2025, ultrasonic bronchoscopy with a small probe revealed hypoechoic areas within the left upper lobe (B1+2).

B. DISCUSSION

Cryptococcal infection is an invasive fungal infection where Cryptococcus species colonize the lungs upon human inhalation. When immune system function is compromised, the fungus activates its escape mechanism and downregulates immune responses, disseminating the pathogen to other organs (e.g., the brain) and causing damage [4]. In patients with pulmonary infection, some cases present only with incidentally detected pulmonary nodules on imaging studies without any symptoms; most patients exhibit clinical manifestations such as cough, sputum production, fever, dyspnea, and chest pain [5]. Chest CT scans in these patients typically reveal pulmonary nodules or masses upon hospital admission. However, research by Cai Renhui et al. demonstrated that immunocompetent patients often exhibit air bronchogram findings on chest CT–characterized by alveolar consolidation due to pathogen invasion of alveolar spaces while maintaining intact pulmonary structural integrity, resulting in proximal bronchial hyperinflation [6]. Additionally, novel drug development has emerged as a recent focus: Cheng's team identified the extracellular heme carrier protein secreted by Cryptococcus neoformans as a shared target and heme as a high-affinity ligand, enabling the development of active targeted liposomes capable of overcoming multiple barriers and targeting both intracellular and extracellular infections [7]. Li et al. proposed the use of the plasma membrane protein Lip3-related membrane protein 1Δ strain for producing anti-cryptococcal vaccines [8].

The patient in this case was an adolescent male without immunodeficiency, no history of exposure to pigeon droppings or soil, and was obese. Based on the clinical presentation, the potential causes and limitations of the misdiagnosis are summarized as follows:

① The patient was relatively young, had no history of immunosuppression, and generally maintained good health, which may have led to underdiagnosis of cryptococcal infection during initial evaluation.
② The symptoms were atypical, manifesting solely as cough with sputum production, left-sided chest pain during coughing, and loose stools, making them easily confused with common upper respiratory tract infections.
③ The medical facilities at the lower-level hospital were relatively limited, preventing accurate identification of the pathogen.
④ The patient had a prior opportunistic cryptococcal infection secondary to bacterial pneumonia, suggesting a possibility of concurrent infection.

After pulmonary infection with Cryptococcus, the pathogen can rapidly disseminate directly from the nasal cavity to the bloodstream or brain [9]. In this case, the patient's failure to respond to two weeks of conventional antibiotic therapy delayed diagnosis and treatment, potentially leading to cryptococcal encephalitis or even hematogenous cryptococcosis. Additionally, the chest CT findings in this patient align with the conclusions reported by Cai Renhui et al. In summary, four key considerations should guide future diagnostic and therapeutic approaches:
① For patients with unexplained pneumonia showing no significant improvement after one week of antibiotic therapy and negative sputum culture results, targeted next-generation sequencing (tNGS) should be performed to identify the causative pathogen; if local hospital resources are limited, prompt referral is recommended.
② In immunocompetent, healthy individuals aged 5–17 years presenting with unexplained cough and sputum production, atypical nodules, or air bronchus signs on chest CT–regardless of history of bird droppings or soil exposure–Cryptococcus infection should be strongly suspected when broad-spectrum antibiotics prove ineffective.
③ Obesity may serve as a risk factor for cryptococcosis.
④ Ant cryptococcal vaccines represent an emerging research direction, with early prevention in susceptible populations constituting the optimal treatment strategy.

In summary, this article presents a case of pulmonary cryptococcosis in an adolescent patient with normal immune function and no specific exposure history. The patient's atypical symptoms highlight the importance of including cryptococcal infection in the differential diagnosis of respiratory diseases that are unresponsive to conventional anti-infective therapy, aiming to alert clinicians to the possibility of cryptococcal infection in immunocompetent hosts without a specific exposure history and the necessity of timely referral and early treatment.

REFERENCES

[1] J. Qu, X. Zhang, Y. Lu, X. Liu, and X. Lv, "Clinical analysis in immunocompetent and immunocompromised patients with pulmonary cryptococcosis in western China," Sci. Rep., vol. 10, no. 1, Art. no. 9387, Jun. 2020, doi: 10.1038/s41598-020-66094-7.
[2] Z. Mo, C. Li, Z. Liang, J. Cui, L. Yu, and L. Chen, "Clinical analysis of non-AIDS patients with pulmonary cryptococcosis and the change in their clinical features over 30 years in a tertiary hospital in Beijing, China," Jpn. J. Infect. Dis., vol. 75, no. 5, pp. 476–483, Sep./Oct. 2022, doi: 10.7883/yoken.JJID.2022.141.
[3] Q. Dai, Y. Wang, Q. Ying, and Q. Ye, "Cryptococcosis with pulmonary cavitation in an immunocompetent child: a case report and literature review," BMC Infect. Dis., vol. 24, no. 1, Art. no. 162, Feb. 2024, doi: 10.1186/s12879-024-09061-1.
[4] J. Julian, R. A. Robiatul, and S. W. Sri, "Biomolecular activity of Cryptococcus during cryptococcosis: A review of molecular interactions of Cryptococcus with human immune system and blood–brain barrier," Afr. J. Infect. Dis., vol. 18, no. 1, pp. 11–22, 2023, doi: 10.21010/Ajidv18i1.3.
[5] Z.-G. Cai, "Primary pulmonary cryptococcosis: One case report and literature review," J. Med. Theory Pract. (Chin.), vol. 34, no. 8, pp. 1380–1381, 1414, 2021, doi: 10.19381/j.issn.1001-7585.2021.08.058.
[6] R.-H. Cai and Y. Wang, "Clinical features and CT analysis of 45 non-HIV pulmonary cryptococcosis cases," Chin. J. Mycol., vol. 19, no. 6, pp. 613–618, 644, 2024, doi: CNKI:SUN:ZJXZ.0.2024-06-013.
[7] L. Cheng, Z. Ma, X. Yang, X. Wang, Y. Wang, X. Liu, et al., "All-stage targeted therapy for invasive cryptococcosis through interaction between the secretory protein Cig1 and hemin," Asian J. Pharm. Sci., vol. 20, no. 4, Art. no. 101053, 2025, doi: 10.1016/j.ajps.2025.101053.
[8] C. Li, Y. Meng, H. Li, W. Du, X. Gao, C. Suo, et al., "Immunization with a heat-killed prm1deletion strain protects the host from Cryptococcus neoformansinfection," Emerg. Microbes Infect., vol. 12, no. 2, Art. no. 2244087, 2023, doi: 10.1080/22221751.2023.2244087.
[9] J. M. Davis, "A deep cut into early cryptococcal pathogenesis," mBio, vol. 15, no. 8, Art. no. e0065724, 2024, doi: 10.1128/mbio.00657-24.