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CASE REPORT

Case Report: A Pulmonary Cryptococcosis Presenting as Interstitial Pneumonia in a Patient of IgA Nephropathy

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Purpose: To present a rare case of pulmonary cryptococcosis that exhibited radiological findings consistent with interstitial pneumonia in a patient diagnosed with IgA (Immunoglobulin A) nephropathy.

Patients and Methods: A 66-year-old man was admitted to the hospital with interstitial lung disease. The cryptococcal capsular antigen test was positive in both serum and bronchoalveolar lavage fluid. Histopathological examination of the bronchoscopically obtained lung biopsy and positive culture results revealed the presence of Cryptococcus yeast, while no Cryptococcus species were detected in the cerebrospinal fluid. Collectively, these findings confirmed the diagnosis of pulmonary cryptococcosis.

Results: The fluconazole dosage was tailored according to the patient's renal function, and the lesions in the right lung were significantly improved following one month of antifungal therapy.

Conclusion: This case illustrates that in immunocompromised patients, pulmonary cryptococcosis may manifest with imaging findings resembling interstitial pneumonia. Therefore, clinicians should consider pulmonary cryptococcosis in the differential diagnosis of interstitial pneumonia, particularly in immunocompromised individuals.

Keywords: pulmonary cryptococcosis, interstitial pneumonia, immunosuppression, case report

Introduction

Cryptococcosis represents a significant global burden in terms of morbidity and mortality. Cryptococcus neoformans was ranked as the top priority fungal pathogen in the WHO (World Health Organization) fungal pathogens priority list published in 2022.[1] An updated estimate of the global burden of HIV CM in the year 2020 showed that HIV CM affects 152,000 people and causes 112,000 deaths on an annual basis, with the highest mortality in sub-Saharan Africa.[2] This organism has the capacity to infect virtually any tissue or organ within the human body. The respiratory system is the most frequently affected site, followed by the central nervous system and the skin.[3,4] The main manifestations of the pulmonary infection group were cough, expectoration, and chest pain. In contrast, the extrapulmonary infection group primarily exhibited symptoms such as headache, fever, nervous system symptoms and vomiting.[5] The mortality rate among patients with extrapulmonary cryptococcosis is extremely high, particularly in the case of CM (cryptococcal meningitis), where the mortality rate can reach as high as 60–80% within 6 months after diagnosis.[6]

The imaging characteristics of pulmonary cryptococcosis have been well documented in the literature.[7] On CT (chest computed tomography) scans, the morphological patterns can be classified into several categories, including solitary nodules or masses, multiple nodules or masses, consolidation, and diffuse infiltrates (nodules or masses with consolidation).[8] Among immunocompetent patients, nodular lesions represent the most frequently observed CT pattern, typically presenting as a single lesion. In contrast, consolidation is more commonly observed in immunocompromised individuals. Multiple lesions, air bronchograms, and cavitation are among the predominant CT features associated with

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this condition.[9] Interstitial lung disease (ILD) is a group of diffuse parenchymal lung diseases affecting the pulmonary interstitium. Recently, we encountered an exceptionally rare case of cryptococcal infection manifesting as interstitial pneumonia, a presentation that underscores the importance of considering fungal etiologies in atypical pulmonary presentations. This report aims to heighten clinical awareness and facilitate earlier diagnosis in similar cases.

Materials and Methods

Patient Information

A 66-year-old patient was diagnosed with interstitial nephritis in 2024 and initiated treatment with prednisone and mycophenolate mofetil. Since February 2025, he had experienced intermittent chest tightness that progressively worsened, in the absence of symptoms such as headache, nausea, or vomiting. A renal biopsy performed in April 2025 confirmed IgA nephropathy, and prednisone 25 mg once daily was initiated. In May, blood cryptococcal capsular antigen testing at a local hospital returned positive. Chest CT revealed interstitial changes in the right lung, suggestive of inflammatory changes. Bronchoscopy was performed, and targeted next-generation sequencing (tNGS) of bronchoalveolar lavage fluid identified Cryptococcus neoformans (sequence count: 3260), cytomegalovirus (CMV, sequence count: 2,688,560), and Epstein-Barr virus (EBV, sequence count: 815,492). Brain MRI (magnetic resonance imaging) showed no significant abnormalities. Antifungal therapy with fluconazole 0.2 g once daily was initiated, considering the patient's serum creatinine level of 232 μmol/L. The patient was admitted to our hospital on May 20, 2025, for further evaluation of pulmonary lesions.

Physical Examination

Physical examination revealed a normal body temperature of 36.4°C, normal heart rate of 88 beats per minute, and normal respiratory rate of 20 breaths per minute. The patient was alert with clear percussion sounds and normal breath sounds on auscultation of both lungs. Cardiac examination showed a non-enlarged cardiac silhouette and regular rhythm. The abdomen was soft, non-tender, without rebound tenderness; the liver and spleen were not palpable below the costal margin. Bowel sounds were present at a frequency of 4 to 5 per minute. No edema was observed in either lower extremity. Meningeal irritation signs were negative.

Investigations

The complete blood count demonstrated a high white blood cell count of 11.34×10^9/L, with neutrophils comprising 87.5%. Arterial blood gas analysis without supplemental oxygen revealed a partial pressure of oxygen (PaO_2) of 93 mmHg. Laboratory investigations showed a high erythrocyte sedimentation rate (ESR) of 34 mm/h and a normal high-sensitivity C-reactive protein (hsCRP) level of 1.92 mg/L. Serum creatinine was elevated at 232 μmol/L. Tumor markers were mildly elevated, including carcinoembryonic antigen (CEA) at 10.1 ng/mL and carbohydrate antigen 19–9 (CA19-9) at 47.2 U/mL. Autoantibody testing was negative. Cellular immune profiling revealed a CD4+ T-cell count of 123 cells/μL and a CD8+ T-cell count of 246 cells/μL. The serum cryptococcal capsular antigen titer was positive at 1:5120. Both cytomegalovirus (CMV)-DNA and Epstein-Barr virus (EBV)-DNA were undetectable Chest computed tomography (CT) revealed multiple patchy opacities in the right lung, along with fibrous linear densities (Figure 1A-1/A-2). On May 21, 2025, lumbar puncture was performed, which yielded a cerebrospinal fluid (CSF) opening pressure of 165 mmH_2O; CSF routine and biochemical parameters were within normal limits. Cryptococcus smear, capsular antigen testing, and culture of CSF were all negative. Bronchoscopy was performed on May 23, 2025, revealing patent bronchial lumens, smooth mucosa, and the absence of neoplastic growths. The bronchoalveolar lavage fluid (BALF) cryptococcal antigen titer was 1:640. Fungal culture of lung tissue yielded growth of Cryptococcus species. Rapid on-site evaluation (ROSE) identified numerous yeast-like structures within histiocytes and multinucleated giant cells, suggestive of granulomatous inflammation potentially attributable to Cryptococcus or other fungal pathogens. Metagenomic next-generation sequencing (mNGS) of BALF detected Cryptococcus neoformans (SMRN 3701), CMV (SMRN 16446), and EBV (SMRN 513). Histopathological examination, incorporating immunohistochemistry and special staining of lung tissue, supported a diagnosis of fungal infection, most consistent with pulmonary cryptococcosis (Figure 1B and C).

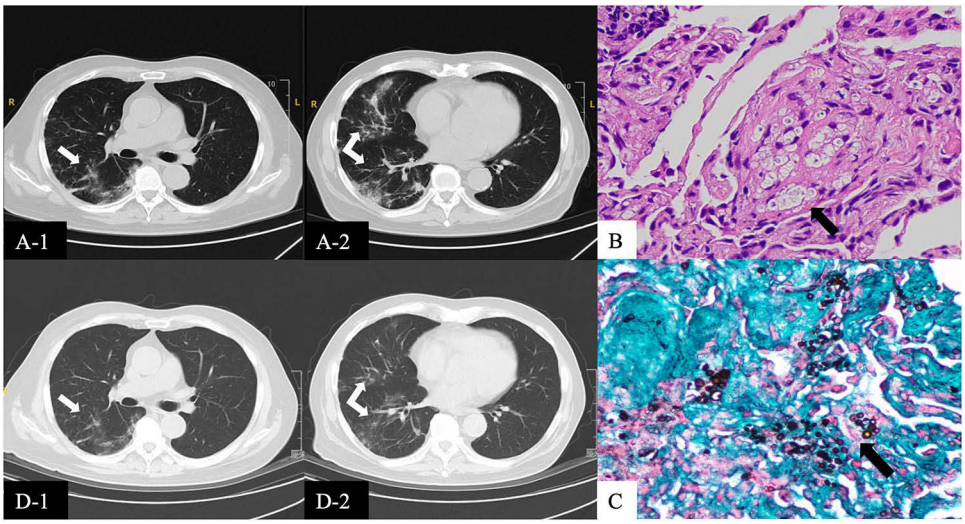

Figure 1 Imaging (**A-1, A-2** and **D-1, D-2**) and pathological findings (**B** and **C**). (**A-1**/**A-2**) Chest CT scan performed on May 20. The white arrow indicates the lesion site exhibiting interstitial pneumonia. (**A-1**) refers to the upper lobe of the right lung, (**A-2**) refers to the lower lobe of the right lung. (**B**) Hematoxylin and eosin (H&E) staining of lung tissue. (**C**) Periodic acid-Schiff (PAS) staining of lung tissue. The black arrow indicates Cryptococcus species. (**D-1**/**D-2**) Chest CT scan performed on June 24. The white arrow indicates the lesion site exhibiting interstitial pneumonia. (**D-1**) refers to the upper lobe of the right lung, (**D-2**) refers to the lower lobe of the right lung. It exhibited significantly better performance compared to that in part (**A-1**/**A-2**).

Management

The patient was administered anti-Cryptococcus therapy with fluconazole at a daily oral dose of 200 mg, achieving a trough fluconazole concentration of 15.6 mg/L (reference range: 6–20 mg/L). For the ongoing management of IgA nephropathy, prednisone 25 mg daily was continued in accordance with nephrology consultation recommendations. Additional supportive treatments, including gastric protection, calcium supplementation, and antioxidant therapy, were also implemented. Although serum CMV-DNA testing remained negative, intravenous ganciclovir 0.125 g every 12 hours (adjusted based on estimated glomerular filtration rate [eGFR]) was initiated due to the detection of a high CMV sequence count in bronchoalveolar lavage fluid (BALF) and the concurrent administration of immunosuppressive corticosteroids.

Results

Following discharge, the patient continued oral ganciclovir therapy, which was subsequently discontinued after two weeks of treatment. A follow-up chest CT scan obtained one month later demonstrated significant improvement in interstitial abnormalities compared to baseline imaging (Figure 1D-1/D-2). The fluconazole plasma concentration was measured at 27.2 mg/L, and the patient was instructed to maintain oral fluconazole at a dosage of 200 mg once daily. At the time of follow-up, the patient's serum creatinine level was 251 μmol/L. In response to this finding, the nephrologist adjusted the prednisolone dosage to 20 mg once daily.

Discussion

The common causes of interstitial pneumonia include occupational and environmental exposures, drug or radiation induced lung injuries, connective tissue diseases, idiopathic interstitial pneumonia and infectious etiologies.[10–12] Among infectious causes, viral infections such as COVID-19 and influenza virus, as well as Pneumocystis jirovecii pneumonia, are the most commonly observed. Interstitial lung involvement due to cryptococcal infection is exceedingly rare.[13,14] The patient had undergone bronchoscopic lavage at a local hospital, where tNGS detected fungal and viral sequences. Given that the imaging manifestations of pulmonary cryptococcosis were atypical and the tNGS sequence count was elevated, we recommended that the patient undergo transbronchial lung biopsy to further clarify the etiology of the pulmonary infection.[15]

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In immunocompromised individuals, cytomegalovirus (CMV) infection is associated with an increased risk of developing CMV pneumonia.[16] The diagnosis of CMV pneumonia (CMP) typically requires clinical signs of pulmonary infection such as fever, cough, dyspnea, radiological findings consistent with interstitial pneumonia, and confirmatory evidence of CMV infection in lung tissue through methods such as viral isolation, rapid culture, histopathological examination, immunohistochemistry, or DNA hybridization, along with the exclusion of other potential causes of pneumonia. In this case, the patient exhibited mild clinical symptoms, and CMV-DNA was undetectable in blood. Although CMV was identified via targeted next-generation sequencing (tNGS) and metagenomic next-generation sequencing (mNGS) of bronchoalveolar lavage fluid (BALF), histopathological analysis did not reveal characteristic changes or inclusion bodies indicative of CMV infection. Therefore, the diagnosis of CMP remained uncertain. However, given the patient's immunosuppressed status, empirical antiviral therapy with ganciclovir was initiated.

This patient was diagnosed with IgA nephropathy and requires long-term hormonal therapy; the recent addition of immunosuppressive agents was warranted due to an inadequate therapeutic response. However, given the ongoing pulmonary cryptococcal infection that remained uncontrolled, the decision—made in consultation with a nephrologist—was to prioritize the management of the infectious complication and delay the intensification of corticosteroid and immunosuppressive therapy. Given the patient's concurrent renal insufficiency, fluconazole was administered at a dose of 200 mg once daily, achieving the targeted therapeutic drug concentration. Although the fluconazole concentration at the second follow-up was slightly above the reference range, the dose was not modified, as the patient demonstrated clinical improvement and maintained stable renal function.

This article presents a rare case of pulmonary cryptococcosis associated with pulmonary interstitial changes, representing a distinctive feature of this report. The single-case nature of the study constitutes a limitation. With the advancement of organ transplantation techniques and the increasing use of monoclonal antibody therapies, the population of transplant recipients and immunocompromised individuals is steadily growing. Consequently, pulmonary cryptococcosis may manifest with atypical imaging findings, warranting heightened clinical awareness.

Conclusion

This case illustrates that in immunocompromised patients, pulmonary cryptococcosis may manifest with imaging findings resembling interstitial pneumonia. Therefore, clinicians should consider pulmonary cryptococcosis in the differential diagnosis of interstitial pneumonia, particularly in immunocompromised individuals.

Abbreviations

IgA, Immunoglobulin A; WHO, World Health Organization; CM, cryptococcal meningitis; CT, chest computed tomography; tNGS, targeted next-generation sequencing; CMV, cytomegalovirus; EBV, Epstein-Barr virus; MRI, magnetic resonance imaging; ESR, erythrocyte sedimentation rate; hsCRP, high-sensitivity C-reactive protein; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; CSF, cerebrospinal fluid; BALF, bronchoalveolar lavage fluid; ROSE, rapid on-site evaluation; mNGS, metagenomic next-generation sequencing; SMRN, strict mapping read number; eGFR, estimated glomerular filtration rate.

Ethics Approval and Consent to Participate

This project was approved by the Ethics Committee of Zhongshan Hospital (Ethics approval number B2024-276), and informed consent was obtained from the subject. Written informed consent was obtained from the patient for the publication of this case report and any accompanying data and images. Institutional approval was not required to publish the case details.

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Disclosure

The authors report no conflicts of interest in this work.

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