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# Disseminated Cryptococcosis in an Immunocompromised Patient with Altered Mental Status and a Lung Nodule

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## Abstract

**Introduction:** Disseminated cryptococcosis is an opportunistic infection that commonly affects the central nervous and respiratory systems and is often fatal in immunocompromised host patients. Diagnosing disseminated cryptococcosis is challenging at times due to the nonspecific presentation, resulting in delayed treatment and increased mortality.

**Case presentation:** A 48-year-old man presented with altered mental status and shortness of breath requiring intubation. Medical history was significant for rheumatoid arthritis, diabetes mellitus, chronic kidney disease, sarcoidosis, and polymyalgia rheumatica. Home medications included prednisone, methotrexate, and tocilizumab. Computed tomography chest revealed multifocal pneumonia with a cavitary nodule with halo sign. One week after extubation, the patient remained confused. Lumbar puncture (LP) was positive for *Cryptococcus neoformans* within 5 days. Bronchoalveolar lavage (BAL) yielded similar results on fungal culture one month later.

**Conclusion:** An immunocompromised host patient who presents with altered mental status with concomitant lung nodules should have disseminated cryptococcosis as a differential diagnosis. CT chest commonly demonstrate peripheral lung nodules with cavitation, air bronchograms, halo sign, and/or enlarged mediastinal lymphadenopathy, as found in our patient. If the clinical suspicion for disseminated cryptococcosis is high, an LP should be performed, as BAL results may often be delayed since *Cryptococcus* grows slowly from the lungs. Empiric antifungals should be started immediately, given increased mortality if treatment is delayed.

**Keywords:** Cryptococcosis, *Cryptococcus*, Pulmonary nodule, Immunocompromised, Intensive care unit, Mechanical ventilation, Pneumonia

## 1. Introduction

Cryptococcosis is an opportunistic infection caused by an encapsulated yeast, *Cryptococcus neoformans*. Cryptococcosis commonly affects multiple organ systems throughout the body especially in immunocompromised host patients. The central nervous system is most commonly affected, with the respiratory system the second most common site of infection.<sup>1</sup> Patients with acquired immunodeficiency syndrome (AIDS) account for approximately 70% of cryptococcal infections in the Western world.<sup>2,3</sup> However, other risk factors contributing to immunocompromised host states may also be responsible

for cryptococcosis including diabetes mellitus, sarcoidosis, autoimmune diseases, malignancy, and organ transplant.<sup>4</sup> Diagnosing disseminated cryptococcosis is challenging at times due to the nonspecific presentation, resulting in delayed treatment and increased mortality. We present a case of a patient who presented with altered mental status and a lung nodule and was found to have disseminated cryptococcosis.

## 2. Case presentation

A 48-year-old man presented with altered mental status and shortness of breath. Medical history was significant for rheumatoid arthritis,

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hypertension, diabetes mellitus, cerebellar hematoma, chronic kidney disease, sarcoidosis, and polymyalgia rheumatica. Home medications included 5 mg prednisone twice daily, 10 mg methotrexate weekly, and tocilizumab injection weekly. The patient was not on *Pneumocystis jirovecii* pneumonia (PJP) prophylaxis. Vital signs on admission: temperature 102.6 °F, heart rate 150 beats/minute, blood pressure 101/54 mmHg, respiratory rate 22 breaths/min, and an oxygen saturation in the low 80s on room air. The patient was agitated, diaphoretic, and in respiratory distress with accessory muscle use. He was alert, but disoriented, and moved all extremities. On physical exam, his neck was supple and rhonchi were auscultated in the right middle and lower lung fields. Laboratory tests were significant for glucose 304, lactate 7.4 mmol/L (reference: 0.7–2.0 mmol/L), hemoglobin 8.1 g/dL (reference 11.9–15.7 g/dL), potassium 5.4 mmol/L (reference: 3.5–5.1 mmol/L), and creatinine 3.8 mg/dL (reference: 0.70–1.50 mg/dL). CD4 count was 984, human immunodeficiency virus (HIV) was negative, and hemoglobin A1c was 9.5%. The patient was intubated for acute hypoxic respiratory failure. Chest x-ray showed right lung opacities and was started on broad-spectrum antibiotics. Computed tomography (CT) of the chest revealed multifocal pneumonia with a right upper lobe cavitory nodule with halo sign and mediastinal lymphadenopathy (Fig. 1). A bronchoscopy was performed and bronchoalveolar lavage (BAL) samples were obtained for further testing.

Approximately one week after extubation, the patient's mentation did not improve and he reported a headache. CT head was negative for any acute intracranial process. A lumbar puncture (LP) was performed. LP revealed an elevated white blood cell count 1130, glucose 81, and an elevated opening pressure. The patient received serial LPs which provided symptomatic relief and improved his headache; LP had elevated opening pressures initially ranging from 25 to 30 and decreased to 14. His LP was positive for *Cryptococcus neoformans* within 5 days. Serum Cryptococcus antigen was also positive. He was started on 3 mg/kg liposomal amphotericin B for cryptococcal meningitis and was treated for two weeks. Flucytosine was also started, but was discontinued due to the association with the patient's anemia and risk of bone marrow suppression. The patient was started on 600 mg fluconazole daily and was discharged home. BAL results yielded *Cryptococcus neoformans* one month later. Two months after his initial presentation, the patient presented back to the ED for syncope followed by cardiac arrest and unfortunately expired.

### 3. Discussion

Disseminated cryptococcosis commonly affects multiple organ systems and patients should be started on empiric therapy if the clinical suspicion is high due to increased mortality rates, approximately 63% with a median survival of 21 days.<sup>5</sup> We present a case of an immunocompromised host patient who presented with altered mental status and a lung

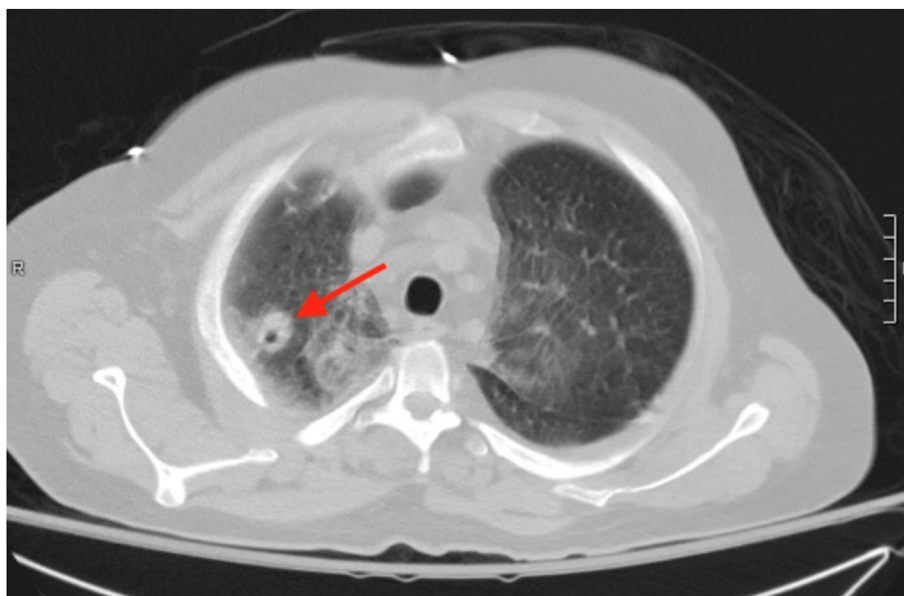


Fig. 1. Computed Tomography (CT) chest demonstrating a cavitory nodule with halo sign as depicted by the red arrow.

nodule and was found to have disseminated cryptococcosis. Chest CT findings of cryptococcosis commonly demonstrate peripheral lung nodules with cavitation, air bronchograms, halo sign and/or enlarged mediastinal lymphadenopathy,<sup>6</sup> as demonstrated by our patient's CT chest imaging.

Cryptococcosis commonly affects immunocompromised hosts, however, emerging literature has shown that immunocompetent hosts can be infected as well. Adzic-Vukicevic et al. presented a case of a 66-year-old immunocompetent patient who presented with cough and vertigo whose chest imaging showed bilateral patchy opacities with nodules, initially concerning for metastasis, and subsequently became confused, had a lumbar puncture that was positive for Cryptococcosis.<sup>7</sup> Mada et al. reported a case of a 56-year-old immunocompetent patient who presented with knee pain, magnetic resonance imaging (MRI) of the knee showed findings concerning for malignancy and pan-imaging showed a lung nodule, and fungal staining was positive for *Cryptococcus neoformans*.<sup>8</sup>

Bernard et al. performed a study in France that showed out of 2749 cases of cryptococcosis, approximately 0.6% cases of patients had sarcoidosis and 2.9% of cases were HIV-seronegative patients.<sup>4</sup> Furthermore, 11 out of 30 cases of patients were using corticosteroids had cryptococcal infections.<sup>4</sup> Hassoun et al. reported a case of an 18-year-old HIV-negative patient who presented with photophobia, ocular symptoms, fever and was found to have cryptococcal chorioretinitis. Our patient's history of sarcoidosis, use of immunosuppressants such as prednisone, tocilizumab, and methotrexate, and his history of uncontrolled diabetes increased his risk for disseminated pulmonary cryptococcosis and meningitis.

#### 4. Conclusion

Patients who present with altered mental status with concomitant lung nodules should have disseminated cryptococcosis included in the differential diagnosis. Providers should have a low threshold to perform an LP, especially if the clinical suspicion for disseminated cryptococcosis is high, as BAL results may often be delayed since *Cryptococcus* grows slowly from the lungs. Empiric antifungals should be started immediately, given increased mortality if treatment is delayed.

#### Conflict of interest

The authors declare no conflicts of interest.

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