

CASE REPORT

A Case of Disseminated Cryptococcus in an HIV-Positive Patient

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ABSTRACT

A 69-year-old male with a history of untreated Human Immunodeficiency Virus (HIV) was admitted to the emergency department for symptoms such as cough, shortness of breath, lethargy, and weight loss. His physical examination revealed severe wasting, oral thrush, and hypoxia. Chest imaging revealed cavitory lesions and blood work showed an absolute CD4 count of 23 cells/mm³. An IR-guided biopsy revealed abundant necrosis and scattered narrow-based fungal organisms consistent with *Cryptococcus neoformans* infection. The patient was treated with liposomal amphotericin B and flucytosine. Due to the increased risk of Immune Reconstitution Inflammatory Syndrome (IRIS), HIV treatment was deferred. The patient deteriorated, transitioned to comfort care, and unfortunately expired.

INTRODUCTION

Cryptococcus neoformans is a ubiquitous environmental yeast and a leading cause of invasive fungal infection in humans with significant morbidity and mortality that affects both immunocompetent and immunocompromised hosts.^{1,2} Globally, there are approximately 1 million cases of AIDS-related cryptococcosis each year, leading to over 600,000 deaths. This represents a prevalence of 6.0% (95% CI 5.8–6.2) among people with a CD4 cell count of less than 100 cells per uL.² The transmission mode is by inhalation of microscopic fungus (desiccated yeast or spores). Immunosuppression is the strongest risk factor for disease development, including HIV infection, stem cell and solid organ transplantation, prolonged immunosuppressive therapy, invasive medical procedures, hematological malignancies, advanced age, and prematurity.^{1,2,3}

Treatment usually involves a fungicidal regimen of IV liposomal amphotericin B, plus flucytosine followed by

oral fluconazole.^{4,5} Overall, 90-day all-cause mortality in patients with cryptococcal infection is 19.4%. Mortality rates are significantly higher in HIV/transplant patients at 90 days (41.7% versus 8.3%, $p = 0.017$) and one year (41.7% versus 12.5%, $p = 0.047$).^{6,7} This case describes a 69-year-old HIV-positive patient who presented with multisystemic manifestations and cavitary lung lesions with blood and cerebrospinal fluid (CSF) findings of cryptococcal antigen and positive fungal culture and lung biopsy confirmation of *Cryptococcus*.

CASE PRESENTATION

Our patient was a 69-year-old male who presented to the emergency department with symptoms of cough, shortness of breath, lethargy, weight loss, anorexia, dysphagia, and odynophagia for one month. His medical history includes HIV infection, but he was not on treatment due to medication non-adherence. Other comorbidities included untreated hepatitis C and polysubstance use. Physical examination revealed severe wasting, oral thrush, widespread inspiratory crackles, reduced breath sounds, hypoxia with oxygen requirement, and bilateral pitting edema of the feet and ankle. The laboratory showed anemia of 12.7 g/dL, lactic acidosis of 3.8 mm/L, and an absolute CD4 count of 23 cells/mm³. Imaging, chest X-ray, and CT scan of the chest (figures 1A and B, respectively) showed a thick-walled, septated, cavitary mass in the right upper lung lobe, and tuberculosis screening was negative.

The patient was admitted for management of a cavitary lung lesion in an immunocompromised patient. Broad-spectrum antibiotic coverage for infection, prophylaxis for opportunistic infections, and

supportive care were instituted. An IR-guided biopsy of the cavitary lesion showed lung parenchyma with a lot of dead tissue as seen in Figure 2A and scattered, round, narrow-based budding fungal organisms that are consistent with *Cryptococcus neoformans* as depicted by the red arrow as stained by Hematoxylin and Eosin (H&E) staining in Figure 2B; this was confirmed with immunohistochemistry staining for *Cryptococcus* and was positive for mucicarmine stain in Figure 3A and Periodic Acid Schiff (PAS) stain in Figure 3B. On lumbar puncture, opening pressure was 14cm H₂O, and CSF analysis showed elevated protein, a cell count of 94 mg/dL, and a glucose level of 43 mg/dL. CSF and serum analyses for *Cryptococcus* antigen were initially negative. Repeat testing of the same specimen with a higher dilution demonstrated a strongly positive result (1:8000) for cryptococcal antigen exhibiting the prozone phenomenon. Blood cultures also grew *Cryptococcus neoformans*.

Liposomal amphotericin B and flucytosine were initiated, along with treatment for other AIDS-defining illnesses and prophylaxis for opportunistic infections. The patient developed a worsening clinical condition and multiorgan failure, which were managed at the intensive care unit. Septic shock complicated his clinical course, which required IV vasopressor support. While antifungals were continued, the patient was empirically treated for sepsis with broad-spectrum antibiotics, but repeat blood cultures only demonstrated fungemia. The patient was transitioned to comfort care after discussing the goals of care with his family. Unfortunately, he went into cardiac arrest on the 26th day of admission and expired.

Figure 1. Chest x-ray (A) and chest CT scan (B) of patient

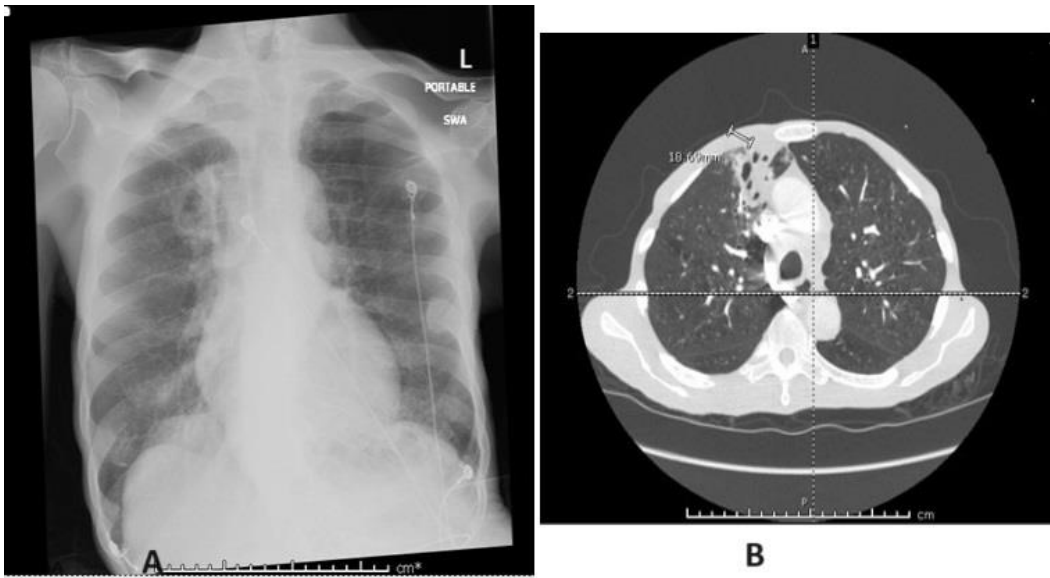


Figure 2. Biopsy of cavitary lesion showing *Cryptococcus neoformans* (red arrows)

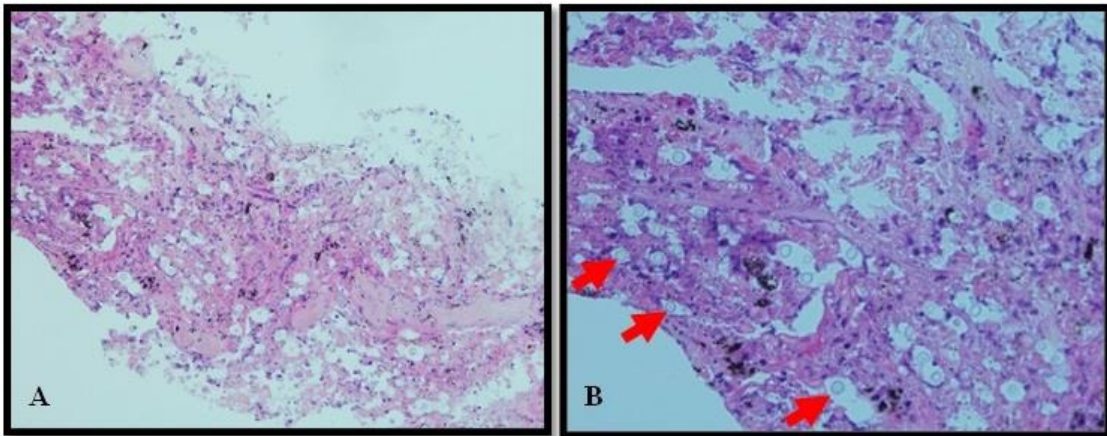
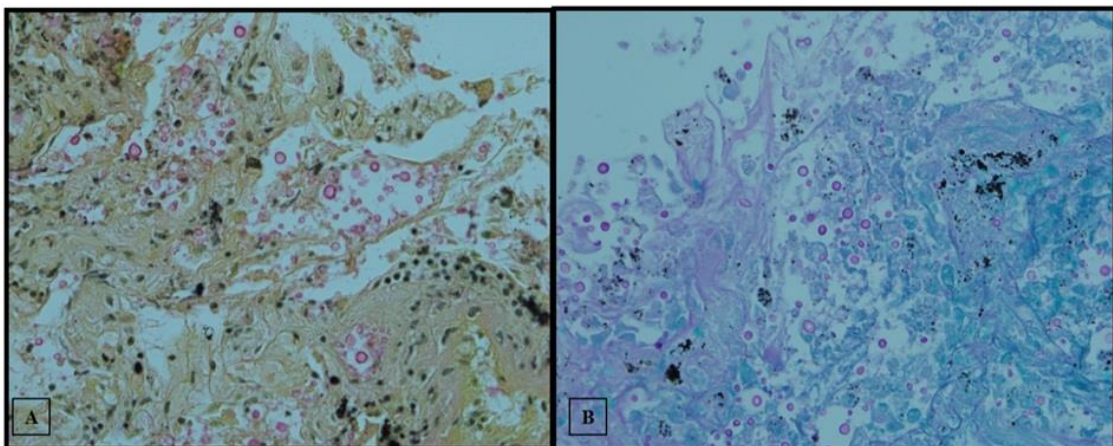


Figure 3. *Cryptococcus neoformans* on mucicarmine stain (A) and PAS stain (B)



DISCUSSION

In recent decades, there has been a concerning increase in invasive fungal diseases, resulting in 1.5 million deaths annually. These diseases particularly affect individuals with weakened or dysfunctional immune systems, putting them at high risk for developing severe fungal infections.¹⁻³ *Cryptococcus* enters the body by inhaling spores or desiccated yeast cells from the environment, leading to an asymptomatic infection that is either cleared or controlled by a strong cell-mediated immune response.¹⁻³ In immunocompromised patients, the fungus can spread from the lungs to the central nervous system and cause fatal meningoencephalitis, if left untreated.^{1,3,7} The mode of dissemination of infection is by leaking granulomas, macrophage transportation, or direct invasion of adjacent tissues or vessels next to enlarging granulomas.^{6,7}

Clinical presentation in most cases is likely due to the reactivation of latent infection, but primary infection in a naïve host or reinfection with a new strain is also possible.^{3,7} Immunocompromised hosts generally have more symptoms than immunocompetent hosts and are more likely to present with extrapulmonary disease.³ The disease may range from asymptomatic pneumonia to acute respiratory failure to disseminated disease.^{3,7} The presentation of pulmonary cryptococcosis in patients with HIV is more acute and severe than in other hosts; the severity of symptoms and extent of dissemination is inversely proportional to the CD4 lymphocyte count; most symptomatic cases occur in patients with CD4 counts less than 100 cells/mm.^{3,8}

Treatment is guided by the American Thoracic Society (ATS) and Infectious

Disease Society of America (IDSA) recommendations: For immunocompetent patients with mild-moderate pulmonary infections, fluconazole 400–800 mg daily for 6–12 months is recommended.^{8,9} Alternative therapy includes itraconazole, voriconazole, posaconazole, or isavuconazole.^{8,9} For immunocompromised HIV patients with severe pulmonary disease, disseminated disease, or cryptococcal meningitis, recommended management includes a fungicidal regimen of IV liposomal amphotericin B (0.7 to 1 mg/kg/day) plus flucytosine (100 mg/kg/day) for 4 to 6 weeks, followed by oral fluconazole 400 mg once a day for 6 to 12 months, and serial lumbar punctures for increased intracranial pressure.^{8,9} Surgery may be indicated when vital structure compression or failure to reduce the size of cryptococcal granuloma occurs.^{8,9} For newly diagnosed HIV patients, antiretroviral therapy is started 2–10 weeks following the initiation of antifungal therapy to mitigate the risk of IRIS.^{8,9}

The prognosis varies overall with 90-day mortality rate estimated at 19.4%.¹⁰ Integrated therapy of HIV and cryptococcosis that includes fungicidal therapy, intracranial pressure management for cryptococcal meningitis, and the delayed introduction of antiretroviral drugs (ARVs) to restore immune function is required for successful treatment. Despite treatment modality, mortality is still high, especially in disseminated disease, as found in the case presented.

CONCLUSION

This case of a 69-year-old man with advanced AIDS and multiple comorbidities, including an opportunistic *Cryptococcus neoformans* infection, underscores the high

mortality rate among HIV-infected patients with advanced cryptococcosis. The successful treatment requires integrated therapy with antifungal agents and the delayed introduction of ARVs to restore immune function. Despite the treatment, mortality rates remain high, especially in cases of disseminated disease, as was observed in the presented case.

Notes

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