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Disseminated Cryptococcal Infection in a Newly Diagnosed HIV Patient: A Case Report

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Abstract

Cryptococcus acts as an opportunistic fungal pathogen, causing Cryptococcosis specifically in individuals with HIV AIDS. The most common form of cryptococcal infection is meningoencephalitis, which usually presents as subacute or chronic meningitis. However, the lesions are characteristically active and reveal a broad peripheral penetration of the brain tissue and meninges. The mortality rate for this condition is exceptionally high, even when treated with antifungal combinations.

Keywords

Disseminated cryptococcosis, HIV/AIDS, Opportunistic infection.

Introduction/Background

Cryptococcosis is an invasive infectious mycosis and an opportunistic disease caused by Cryptococcus neoformans or Cryptococcus gattii, often found in patients with immunosuppression, notably those infected with HIV. However, it also exists in patients with standard immune systems **[1]**. Available evidence suggests that C. gattii initiates infections in immunocompetent individuals, while C. Neosporosis is responsible for more advanced invasive disease processes in the immunocompromised **[2]**. Its virulence factor has been described to include a polysaccharide capsule made of glucuronoxylomannan (its central component), galactoxylomannan, and some galactomannan proteins, which can elicit macrophage phagocytosis after inhalation into the alveolar macrophages **[3]**. These fungal cells spread in the body after phagocytosis through cell lysis or vomocytosis, a nonlytic form that avoids immune response **[3]**. These fungal cells may bring about asymptomatic conditions or cause pneumonia-like symptoms in some cases **[4]**. Neurological conditions may include cryptococcal meningitis, meningoencephalitis, and cryptococcomas **[4]**. There is increasing understanding of this pathogen, and treatment is improving, leading to better patient prognoses; however, mortality from cryptococcal meningoencephalitis remains high, with a 24%-47% mortality rate across different studies **[5]**. Cryptococcal meningitis is reported to be the second leading cause of death in HIV-infected patients, contributing 19% of AIDS related deaths globally **[6]**. We describe a case of newly diagnosed HIV infection and disseminated cryptococcosis presenting with altered mental status and cough.

Case Description

A 29-year-old female was admitted to the ER with complaints of fever, cough, and body aches. She was diagnosed with a common cold and discharged. Two weeks later, she returned with more severe symptoms such as headache, dizziness, persistent cough, and decreased appetite, for which she was subsequently hospitalized. She is a migrant worker from sub-Saharan Africa and moved to Saudi Arabia approximately fourteen months ago. During the standard medical examination conducted upon arrival, she was deemed fit medically, and her screening for infectious diseases was negative. Because of a language barrier, her past medical history, social history, familial history, and drug history could not be ascertained. Furthermore, there was no companion with her.

On physical examination, she presented as an agitated, lethargic patient with 11/15 on the GCS and afebrile vitals (T: 37.7), BP: 123/89, HR: 149. Oximetry showed 90% SpO2 on room air, but it improved to 97% on a 5L mask. Severe thrush was noted in the oropharynx.

Laboratory testing revealed leucopenia with absolute lymphopenia (WBCs: 2*10^3/ul, lymphocytes: 0.6*10^3/ul, mild microcytic hypochromic anemia (HB: 10.6 g/dl, MCV: 73 fl, MCH: 22.7 pg), CRP: 54.4 mg/L, LDH: 632 U/L, ESR: 46 mm/h, procalcitonin 32.2 ng/ml. Other lab tests were within normal limits.

Virology Screening: reactive HIV on two samples with a supra optical density of 215, confirmatory NAAT testing showed reactivity to HIV. A CT scan of the brain was within normal limits.

Treatment started with injecting dexamethasone 16mg, cefuroxime 750mg tid, and paracetamol 1 gm q8 h. Blood cultures were taken before administering the antibiotic and were aerobic and anaerobic.

Headache and dizziness, unresponsive to treatment, prompted the collection of a CSF sample two days after admission. Examination revealed hyper opening pressure: 25cmH20, clear cerebrospinal fluid **(Figure 1)**, pleocytosis of 580 cells/µL (lymphocytic predominance, nonhematopoietic cells), protein 86 mg/dL, glucose 33 mg/dL (with a blood glucose of 119 mg/dL). CSF culture was negative. Gram stain showed oval budding cells. India Ink staining positive for Cryptococcus spp **(Figure 2),** confirmed by biofire testing.

On the same day, an alarm for aerobic blood culture flagged, and subculture was performed on routine media, and later on an SDA plate after India Ink tests came positive. After 37 °C incubation for two days, growth was detected on blood, chocolate, and SDA agar plates as white, smooth colonies. Cryptococcus neoformans/gattii was found using Gram staining and was identified on the Phoenix system **(Figure 3)**

Due to a lack of flucytosine, alternative induction therapy was started using amphotericin B in combination with fluconazole. Antiretroviral therapy (ART) was not initiated due to a fear of Immune Reconstitution Inflammatory Syndrome (IRIS).

The patient's condition became more critical two days later, and she developed tachypnea alongside respiratory distress. CT chest showed bilateral ground glass opacities, consolidations, and zonal \T\T-basal segment pneumonia. Due to worsening hypoxia, she was then intubated the next day. Respiratory distress exacerbated rapidly, and she passed away (5 days after antifungal therapy).

To enhance results, diagnosing cryptococcal infection early is essential, especially in newly diagnosed HIV patients presenting with subacute or chronic headache and exceedingly low lymphocytic count. Such individuals should be assessed for cryptococcal meningitis.

Figure 1: CSF Sample

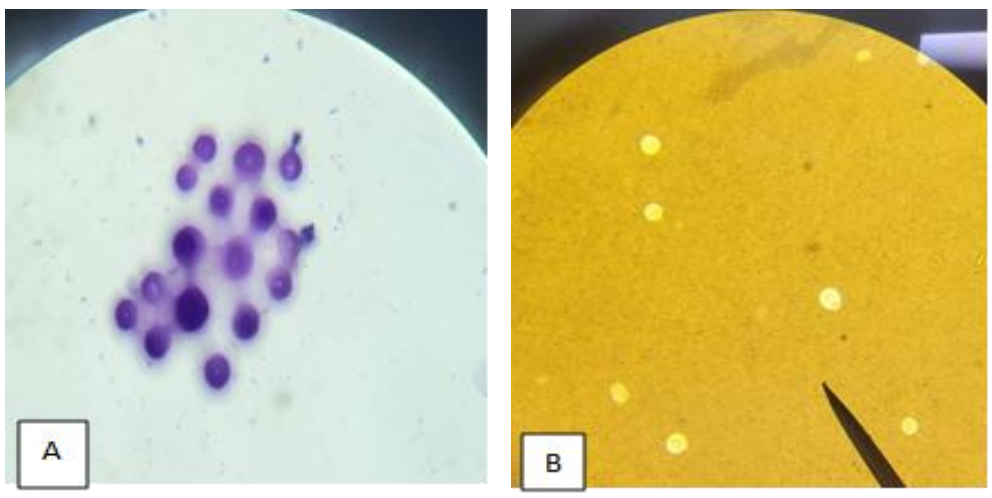

Figure 2: Direct microscopic examination of CSF with Gram stain (A), Direct microscopic examination of CSF with India Ink (B).

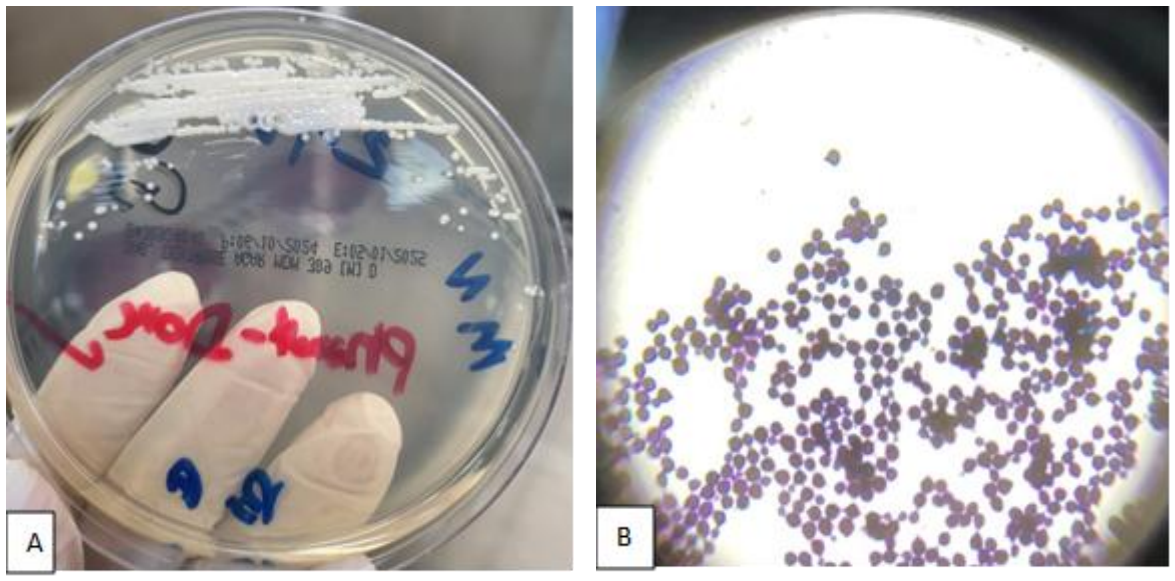

Figure 3: Blood culture showing white smooth colonies of Cryptococcus neoformans in Sabouraud dextrose agar (A), Oval budding colonies from blood culture Gram stain (B).

Discussion

Disseminated cryptococcal infection is epidemiologically significant among HIV-infected individuals across the globe and is one of the primary causes of mortality in individuals with AIDS, following tuberculosis **[7]**. In immunocompromised patients, Cryptococcus's most common portal of entry is inhalation of spores or dehydrated yeasts **[8]**. Cryptococcus can initially induce mild respiratory symptoms in such patients, but can quickly escalate to acute respiratory distress syndrome.

After pulmonary infection, these fungi can spread hematogenously to the central nervous system (CNS) **[9]**. Prior investigations have proposed that Cryptococcus may access the CNS in two ways: through transcytosis, migration through the endothelium, and transport by macrophages **[10]**.

Involvement of the CNS amongst individuals infected with HIV is common and can serve as the first presenting manifestation of HIV illness in about two percent of cases **[11]**. In this case report, the authors document a case of cryptococcal meningitis in a 29-year-old female patient. The patient was a sub-Saharan African migrant domestic worker who came to Saudi Arabia one year and two months ago. Her HIV-serology screening at that time was negative, indicating her HIV infection is likely recent, with cryptococcal meningitis being the first symptom.

Multiple clinical features may be involved in cryptococcal-CNS involvement, but the proportion of patients developing these features is quite low.

Subacute meningitis may present with headaches, nausea, and fever, as well as memory loss, changes in level of consciousness, confusion, seizures, and auditory dysfunction **[10]**. Equally important, the patient's primary concerns were enduring headaches, along with lightheadedness, persistent cough, and diminished appetite.

Disseminated cryptococcosis may be diagnosed if cultures from two disparate sites or blood cultures are positive **[12]**. In this instance, positive cryptococcal blood cultures and positive cryptococcal meningitis with India ink cytology diagnosed disseminated cryptococcosis.

First-line therapy should always include antifungal agents. Initial treatment consists of a two-week administration of amphotericin B 3mg/ kg/ day and flucytosine 100 mg/kg/day. Then, fluconazole should be administered for 8 to 12 months during the consolidation phase **[11]**. Some studies showed that the combination of amphotericin B and flucytosine was more effective at eliminating fungi with lower treatment failure than the combination of amphotericin B and fluconazole **[12]**. Because of the unavailability of flucytosine in our institution, we treated our patient with fluconazole plus amphotericin B.

Initiation of Antiretroviral Therapy (ART) should be postponed for a minimum of two weeks after commencing antifungal treatment, owing to the phenomenon of immune reconstitution inflammatory syndrome (IRIS) that may cause exacerbation of symptoms, and in some cases, death **[10]**. Consequently, ART was not started in our patient.

Patients suffering from cryptococcosis often have a severe prognosis with high mortality rates, especially among HIV positive individuals. Approximately 10% to 25% of patients with HIV and cryptococcosis remain untreated even after undergoing antifungal treatment, as was the case with our patient **[9]**.

Conclusion

This case highlights the critical importance of early recognition and prompt management of disseminated cryptococcal infection in individuals with newly diagnosed HIV, particularly those with advanced immunosuppression. Cryptococcosis remains a significant opportunistic infection with high morbidity and mortality in this population. Clinicians must maintain a high index of suspicion for cryptococcal disease in patients presenting with nonspecific systemic symptoms, especially in the context of low CD4 counts. Early initiation of antifungal therapy and antiretroviral treatment, along with close monitoring for complications such as immune reconstitution inflammatory syndrome (IRIS), are essential for improving clinical outcomes. This case underscores the need for timely HIV diagnosis and routine screening for opportunistic infections in patients at risk.

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