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Cryptococcal Lymphadenitis Without Meningitis in an HIV-Positive Patient: A Rare Case Report

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ABSTRACT

Cryptococcal infection is a chronic opportunistic infection in patients with the Human Immunodeficiency Virus (HIV). A rare case of cryptococcal lymphadenitis is presented here in a 27-year-old woman with an enlarged cervical lymph node. Fine needle aspiration from the involved lymph nodes showed variable-sized, rounded yeast cells surrounded by halos with a prominent capsule. Early diagnosis by fine-needle aspiration is essential and reduces morbidity and mortality.

Introduction

Cryptococcal species (*Cryptococcus neoformans* and *Cryptococcus gattii*) is an opportunistic infection in patients with immune suppression diseases, such as AIDS, diabetes, chronic liver disease, and chronic renal disease, and in cases with prolonged use of steroids [1].

Cryptococcal infection is the second most life-threatening infection and a chronic opportunistic infection in patients with the Human Immunodeficiency Virus (HIV) after *Mycobacterium tuberculosis* [2]. Primary infection is usually in the respiratory system and secondary involvements are in the Central Nervous System (CNS), skin, lungs, bone marrow, and gastrointestinal tract [3]. Lymph node involvement is rarely the primary manifestation in cryptococcal infection in both HIV-positive or HIV-negative patients [4].

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In the present case, a case of cryptococcal lymphadenitis is described in an HIV-infected woman.

Case Presentation

A 27-year-old woman was admitted to the infectious diseases ward of a referral hospital in Bandar Abbas, Iran, with the chief complaints of fever, generalized weakness, and weight loss for the past two months. On physical examination, she was febrile, weighed 39 kg, her blood pressure was 110/70 mmHg, and her heart rate (pulse) was 92/min. One non-tender, posterior cervical lymph node enlargement with the dimensions of 2.5 cm×2.5 cm was observed in the patient.

Blood investigations revealed a hemoglobin level of 11.1 g%, a total leukocyte count of 4,000 cells/cu.mm, platelet count of 51000 cell/mm^3, and a total lymphocyte count of 1600 cells/cu.mm.

Erythrocyte Sedimentation Rate (ESR) was 70 mm measured by Westergren's method. All examinations, including electrolytes, kidney function test, fasting blood sugar, routine urine, liver function test, and lipid profile were within normal limits.

An infectious diseases specialist was consulted to work up tuberculosis, and analysis of sputum smear was negative for acid-fast bacilli. PPD test was 10 mm and the chest radiograph showed no radiological abnormality. Then, blood was tested for HIV I and II and was found to be positive for HIV I. CD4 count and HIV viral load were respectively 57/mm^3 and 109520 (copies/mL), which signified stage 4 of the disease. Then, treatment was started with Cat-I of Antitubercular Therapy (ATT), consisting of Isoniazid, Rifampicin, Pyrazinamide and Ethambutol, and HAART consisting of Zidovudine, Lamivudine, and Efavirenz.

After 3 weeks, no clinical improvement was seen in the patient. Thus, Fine Needle Aspiration Cytology (FNAC) was advised from the cervical lymph node. FNAC was done followed by aspiration of grey-white material. The slides were stained with Papanicolaou.

Cytological reports on cellular smear showed variable-sized, rounded yeast cells surrounded by halos with a prominent capsule admixed with a polymorphous population of lymphoid cells, plasma cells, foamy macrophages, and epithelioid cells in the background of necrotic debris. These observations suggested a Cryptococcus involving the lymph nodes (Figures 1, 2 & 3) and were confirmed by mucicarmine staining.

Ziehl–Neelsen staining did not reveal any acid-fast bacilli, ruling out any coexisting tuberculous infection. Following this report, ATT was stopped and antifungal treatment with liposomal amphotericin B was started for 7 days, followed by oral fluconazole. Symptoms of the patient, especially cervical lymphadenopathies, were resolved after 3 weeks of treatment, and she was discharged after induction treatment with oral fluconazole maintenance therapy. The patient signed a written informed consent for participating in the study. The ethical approval code for this study was IR.HUMS.REC.1399.184.

Discussion

Cryptococcos includes two important species, *C. neoformans* and *C. gattii* [5]. This organism is commonly found in soil, pigeon excreta, chickens, and decayed wood [6]. The primary site of infection in humans is

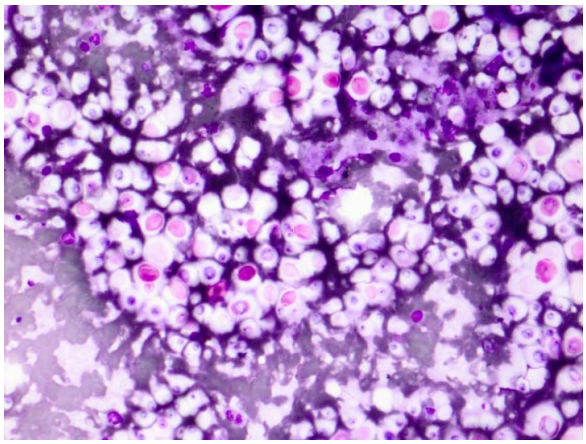

Figure 1. Cryptococci in lymph node aspirate (H&E-10 x)

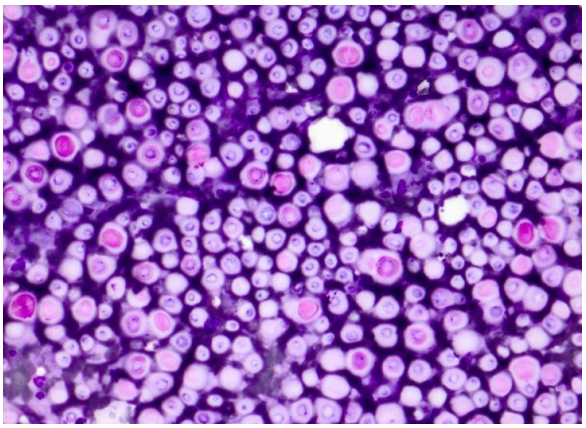

Figure 2. Cryptococci in lymph node aspirate (H&E-20 x)

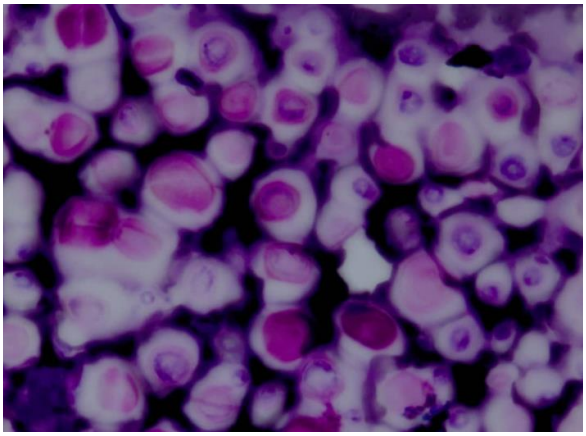

Figure 3. Cryptococci in lymph node aspirate (H&E-40 x)

mainly the respiratory tract, and the CNS is the most common site of secondary involvement resulting in meningoencephalitis. Organs, such as the skin, respiratory tract, gastrointestinal tract, and bone marrow seem to be involved. Lymph node involvement is rarely a primary manifestation in cryptococcal infection in both HIV-positive and HIV-negative patients [4, 7, 8].

In developing countries, tuberculosis is the differential diagnosis of cryptococcal lymphadenitis and more common than cryptococcal lymphadenitis; hence, the acid-fast stain was done to rule out tuberculosis [2].

Early diagnosis and initiation of cryptococcosis treatment are important because cryptococcosis is disseminated in immunocompetent HIV-positive people, and becomes life-threatening with an 80% mortality rate in untreated cases [9].

The diagnosis of cryptococcosis is confirmed by the isolation of the fungus through microbiological methods (detection of cryptococcal capsular polysaccharide antigen in serum and Cerebrospinal Fluid (CSF), sputum, and bronchial washings), and histopathological methods (FNA smears of the lymph nodes, thyroid, spleen, adrenal gland, bones, and the lung) [5, 10].

The organism is a single, narrow-based, budding yeast with 5-15 µm in diameter and is surrounded by a mucopolysaccharide capsule. Special stains for facilitating the identification of this organism are Gomori's Methenamine Silver (GMS), Periodic Acid-Schiff (PAS), and mucicarmine [10].

The Infectious Diseases Society of America has published a clinical practice guideline for the management of the cryptococcal disease. It recommends amphotericin B plus flucytosine followed by fluconazole for cryptococcal meningoencephalitis and severe pulmonary cryptococcosis in immunocompromised patients [11] Besides, fluconazole is a choice drug for localized cryptococcal infection without CNS involvement [8, 9, 12].

A case of cervical cryptococcal lymphadenitis is reported here in an immunocompetent HIV-positive woman without meningitis, lung involvement, or mediastinal lymphadenitis. During the follow-up, all symptoms of the patient recovered completely after a period of induction treatment with amphotericin, without recurrence of the symptoms.

Conclusion

Fine needle aspiration is a simple, economical, reliable, and useful technique in the diagnosis of fungal infections. This method enables rapid diagnosis and quick start of treatment. Negative staining was confirmed by the India ink.

Ethical Considerations

Compliance with ethical guidelines

The patient signed a written informed consent for participating in the study. The ethical approval code for this study was IR.HUMS.REC.1399.184.

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Conflict of interest

The authors have no conflict of interest.

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