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CASE STUDY

CRYPTOCOCCAL MENINGITIS IN AN IMMUNOCOMPETENT YOUNG MALE

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ABSTRACT

The incidence of cryptococcal infection is high in developing countries like as in India. Cryptococcal meningitis is considered rare in immunocompetent patients and is mainly a disease of immunocompromised patients. Cryptococcal meningitis in immunocompetent patients are less likely to be fatal, because of the powerful immune response. Here we present a case of cryptococcal meningitis occurring in an immunocompetent host with no definite underlying diseases and no history of taking immunosuppressive agents. We emphasis on the importance of timely diagnosis and optimal treatment of the cryptococcal infection in immunocompetent patients.

INTRODUCTION

Cryptococcal meningitis, caused by the cryptococcus a ubiquitous environmental fungus, is a fatal HIV-related opportunistic infection. With the enhancement of the relevance ratio and recognition of its life-threatening effect, cryptococcal meningitis draws more and more clinicians' attention. According to the official statistics, there are approximately one million new cases each year worldwide and the lethality is more than 50 percent. (Lin *et al*., 2015; Panackal *et al*., 2015) As an encapsulate yeast, cryptococcus can be constantly found in soil, pigeon feces, milk and human beings'oral cavity as well. (O'Meara and Alspaugh, 2012) It usually invades the immunocompromised hosts through respiratory tract and damaged skins exposure to pigeon feces, leading to the varied infection pulmonary cryptococcosis, skin nodules, cryptococcal meningitis, cryptococcus bacteremia etc. (O'Meara and Alspaugh, 2012) Cryptococcus frequently causes opportunistic infections in immunocompromised patients with underlying diseases, such as HIV, solid organ transplantation, liver cirrhosis, tuberculosis, SLE and other diseases which need the long-term therapy of immunosuppressive agent. (Galanis and MacDougall, 2010) However, immunocompetent hosts are rarely reported to get cryptococcal infection. It is easy to make a misdiagnosis as viral or bacterial meningitis, when immunocompetent patient manifests with headache, fever and altered mental status. (Louro *et al*., 2016) Therefore, the early confirmation needs accumulated clinical experience and sensitive laboratory tests. We report here a rare case of cryptococcus as the cause of meningitis in an immunocompetent young male.

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CASE REPORT

A 15- year-old male resident of suburban area in Punjab, India was admitted to Internal Medicine department with chief complaints of high grade fever, moderately severe headache associated with multiple episodes of vomiting from the past 25 days. He had altered sensorium for last 2 days. He had no history of seizures, ear discharge or earache, nor any focal neurological deficit, head trauma, chronic cough, weight loss, drug abuse or high –risk behavior. No history of tuberculosis, diabetes, malignancy or any other chronic illness was present. There was no history of exposure to avian excreta. On examination, the patient was febrile (39.3°C) and unconscious with a Glasgow coma scale of E4M5V6 with blood pressure 134/74 with a regular pulse of 78 beats/min. Neck rigidity and Kernig's sign were positive. Pupillary response were normal, plantars were bilaterally flexor and all deep tendon reflexes were sluggish. Fundus examination showed no evidence of papilloedema. Examination of other systems revealed no abnormality. Laboratory investigations revealed ESR 45mm at the end of one hour. Serum electrolytes, liver function tests, renal function tests were within normal limits. A cerebrospinal fluid (CSF) examination revealed 30 cells mainly lymphocytes with protein of 28gm/dl and glucose29mg/dl (corresponding blood glucose was 136mg/dl). A computerized tomography

(CT) scan of the head and chest X ray were normal. PCR for mycobacterium by CB-NAAT was found to be negative. The CSF specimen was sent to microbiology department and processed. Upon examination, the CSF was clear and without coagulum. With microscopy, mononuclear cells were seen. There were no microorganisms on gram and Ziehl-Neelsen (Z-N) stains. India ink preparation showed characteristic no round budding yeast cells. A bacterial culture was sterile. A culture was performed on Sabouraud's dextrose agar (SDA) which yielded smooth colonies of yeast after 3 days of incubation at 37°C. (Fig.1) India ink preparation from culture showed the presence of round budding yeast cells with distinct halo of around 5-20um in size. (Fig.2) The patient was tested for HIV1 &2 antibodies and found to be non –reactive. His CD4 count was within normal limits. Intially ATT was started till the report of CSF culture arrived. Then patient was started on Amphotericin B at 1mg/kg per day as intravenous infusion with intravenous fluids. Serum electrolytes and renal functions were monitored on a daily basis. After three days of treatment, the patient developed aspiration pneumonia & was put on ventilator support. The condition of the patient deteriorated and was referred to higher centre for further management and patient did not return back.

Fig. 1. Sabouraud's dextrose agar (SDA) showing smooth colonies of yeast

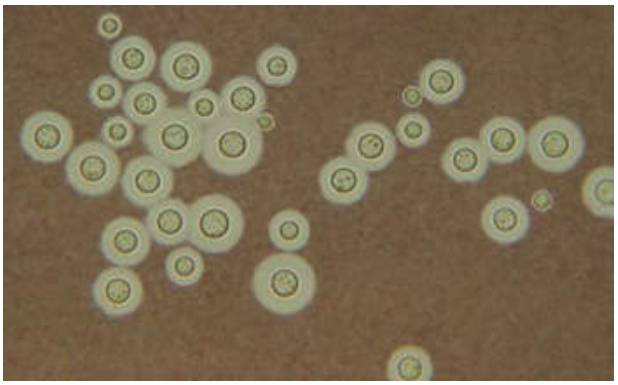

Fig. 2. India Ink Preparation from SDA culture showing capsulated and budding morphology of Cryptococcus neoformans (400X)

DISCUSSION

Most cases of cryptococcal meningitis occur in patients with conditions that weaken their immune system, such as acquired immunodeficiency syndrome (AIDS). Cryptococcal meningitis has also been reported in HIV-negative patients caused by organ transplant and chemotherapy related immunosuppression, reticuloendothelial malignancies, corticosteroid therapy and sarcoidosis. (Galanis and MacDougall, 2010) Occasionally, no obvious underlying cause can be detected. (Madan *et al*., 1999; Prasad *et al*., 2003) Immunocompetent hosts are reported to be infected with *C.neoformans* accounting for 70-80% of cryptococcal infections in such hosts. (Viviani *et al*., 2003) The patient in this case report was also immunocompetent and developed meningitis due to cryptococcus. Our patient had subacute presentation with a history of fever and headaches over a duration of 25 days, our baseline test and other investigations were within normal limits other than CSF biochemistry, so patient was started on ATT assuming as TB meningitis till the report of fungal culture was obtained. Once the cryptococcal meninigitis was confirmed, patient was started on Amphotericin B. Despite all the measures taken, condition of the patient worsened and was referred to higher centre. Despite the availability of newer antifungal agents such as fluconazole, cryptococcal disease in HIV-negative hosts continues to be associated with substantial morbidity and mortality. (Pappas *et al*., 2001) Mortality rates can vary from 0 to 47% in non-HIV-infected patients. Morever, in tropical countries it can vary from 0 to 38% where a low percentage of patients have underlying diseases. (Shih *et al*., 2000) Several factors are associated with mortality in the overall population and among specific groups of patients with central nervous system (CNS), pulmonary or other sites of cryptococcosis. These include age over 60 years, presence of underlying disease especially organ failure syndromes and hematologic malignancy. (Pappas *et al*., 2001) In our patient, no underlying disease was found. Recent management of cryptococcal meningitis in immunocompetent patients include amphotericin B alone or with flucytosine and fluconazole. (Datta *et al*., 2003) In immunocompetent patients, initial therapy should be amphotericin B alone or in combination with flucytosine. Amphotericin B can be administered alone for six to ten weeks or in combination with flucytosine for two weeks, followed by fluconazole for a minimum of ten weeks. (King and DeWitt, 2010) Our patient was treated with amphotericin B, but patient developed complications like aspiration pneumonia and put on ventilator. With early diagnosis of cryptococcal infections in patients with no underlying immunosuppression, amphotericin B therapy, with or without flucytosine would be effective in controlling or terminating infection in 70-75% of patients. (King and DeWitt, 2010) The patient in this case report could be prevented from complications if he had been diagnosed early in the course of the disease.

Conclusion

Cryptococcosis could not only present in immunocompromised patients but also in immunocompetent patient as a cause of meningitis. So, Cryptococcal meningitis should always be a differential diagnosis of TBM on the basis of clinical and laboratory findings as both have similar presentation in immunocompetent patients.

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