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Case Report

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Cryptococcal meningitis in an immunocompetent patient - missed diagnosis – a case report

Abstract

Cryptococcosis is an important opportunistic fungal infection worldwide, but in many countries, including India, many cases are seen among immunocompetent individuals. Cryptococcal meningitis is a severe and fatal infection if not diagnosed and treated specifically in time. Its diagnosis is challenging because its signs and symptoms are indistinguishable from other sub-acute and chronic CNS infections. If it is not suspected and the tests for fungal etiology are not performed for all the cases of meningitis, the diagnosis of Cryptococcal meningitis may be missed. Here we present a case of Cryptococcal meningitis in which the CSF was not tested for fungal etiology and the patient was wrongly treated for Tubercular meningitis. This case highlights the importance of performing the tests for fungal etiology in all cases of meningitis.

Keywords: Cryptococcus, meningitis, immunocompetent, csf analysis, misdiagnosis

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Abbrevations: CNS, central nervous system; HIV, human immunodeficiency virus; AIDS, acquired immuno deficiency syndrome; CM, Cryptococcal Meningitis; CSF, cerebro-spinal fluid; AFB, acid fast bacilli; ATT, anti-tubercular treatment; ESR, erythrocyte sedimentation rate; MRI, magnetic resonance imaging; ADA, adenosine deaminase; SDA, sabouraud dextrose agar

Introduction

Cryptococcosis is an important opportunistic fungal infection worldwide. It causes about 1 million cases and 625,000 deaths per year due to central nervous system (CNS) disease among patients with human immunodeficiency virus (HIV).[1,2] Though extra-pulmonary cryptococcosis is recognized as one of the AIDS defining diseases, studies have reported cases of cryptococcosis in clinically non-immunocompromised patients.[2–4] In many countries of world, including India, about 10-40% of cryptococcal infections are seen among immunocompetent individuals.[2,4–6] Cryptococcal meningitis (CM) is an important fatal infection of the CNS. Its signs and symptoms are indistinguishable from other sub-acute and chronic CNS infections, like tubercular, carcinomatous or lymphomatous meningitis. CSF analysis by India ink preparation and culture for fungal isolation is important for its diagnosis.[5,7,8] Not performing these tests for all cases of meningitis, may lead to misdiagnosis and increased mortality and morbidity. Here, we report a culture proven case of Cryptococcal meningitis in an immunocompetent patient, who was misdiagnosed and treated for Tubercular meningitis.

Case report

A 55 year old male patient was referred to our hospital with complaints of fever and headache for 25 days, altered sensorium for about a week and loss of consciousness for 2 days and presumptive diagnosis of Tubercular meningitis with hydrocephalus. There was no history of trauma or seizure. He had a history of chronic septic Arthritis of left knee, 1-year back, which was diagnosed as Tubercular arthritis, based on histopathologic examination showing occasional AFB. He had taken anti-tubercular treatment (ATT) irregularly. Patient was a chronic alcoholic and smoker. There was no history of any other chronic illness. He worked as a cook in CRPF camp.

Hematological investigations from the referring hospital showed mild anemia with raised ESR (Hemoglobin-9.6 gm%, Total Leukocyte count -6,300/cu mm, ESR-50 mm/hr). Liver function tests, kidney function tests, chest X-ray and urine analysis were reported to be within normal limits. Test for HIV was non-reactive. CSF analysis reported from the referring hospital showed- Protein- 289mg/dL, sugar-27mg/dL, cell count-100, all of which were lymphocytes. Gram's stain of CSF showed occasional Pus cells and no organism, no AFB was seen in Ziehl-Neelsen stain, and CSF culture was sterile. MRI Brain report of a day before referring was suggestive of asymmetric dilation of right lateral ventricle, leading to septal deviation towards left, chronic infarct in left Cerebellar hemisphere and left Occipital lobe. Based on history and investigations, patient was diagnosed as case of Tubercular meningitis with hydrocephalus with partially treated Tubercular arthritis of left knee. He was started on first line ATT. But the clinical condition of the patient continued to deteriorate and he was referred for further management to our hospital.

On admission to our hospital, patient was unconscious with score of E2M3 on Glasgow Coma scale, (i.e. eye opening in response to pain and abnormal flexion in response to pain) and had neck stiffness. Clinical examination showed temperature of 39°C, pulse rate–90 beats/ min, blood pressure -130/90 mm Hg, respiratory rate-22/min and had no abnormality in abdomen, respiratory and cardiovascular system. Hematological investigations showed- raised total Leukocytes count to 10,800/ cu mm, with differential count of 87% neutrophils, 10% lymphocytes, 2% eosinophils, and 1% monocytes. CSF tapping was done for therapeutic purpose. CSF was clear and showed protein level raised to 303 mg/dL, sugar level of 37mg/dL, cell count raised to 200, which were predominantly lymphocytes, Adenosine deaminase (ADA) level was 20.2U/L. Gram's stain of CSF showed Pus cells and Gram-positive budding yeast-like structures, India ink preparation of CSF showed characteristic round budding yeast cells with surrounding clear halo, no AFB was seen by Ziehl-Neelsen stain. Culture of CSF was performed on Blood agar, Chocolate agar and Sabouraud

dextrose agar (SDA) containing antibiotics and pH adjusted to 5.6. No growth was obtained on Blood agar and Chocolate agar after 3 days of incubation. SDA showed growth of mucoid yeast-like colonies at 37°C on the 6th day of incubation. The growth was confirmed to be of Cryptococcus species by Gram's stain, India ink staining and positive urease test (Figure 1–3).

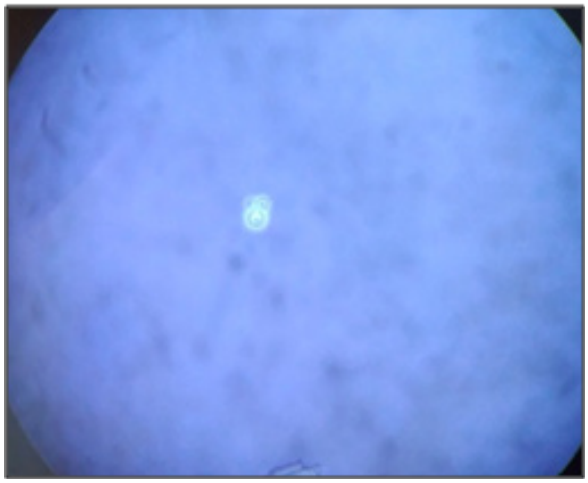

Figure 1 Round budding yeast cell with surrounding halo seen in India ink preparation of CSF.

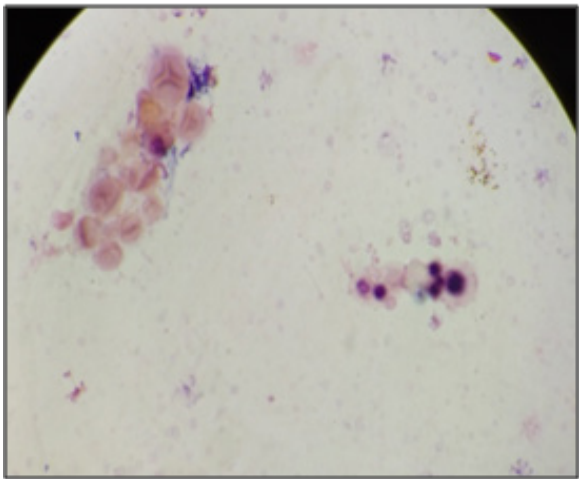

Figure 2 Gram's positive budding yeast-like structures seen in Gram's stain of CSF.

Figure 3 Mucoid yeast-like colonies grown on SDA at 37°C.

The patient was started on induction therapy with Liposomal Amphotericin B (3 mg/kg/day) and Fluconazole (400mg/day), as Flucytosine was not available.5,9 The treatment with ATT was continued with same dosage. The clinical condition of patient improved, and by 3rd day of starting of anti-fungal treatment, he regained consciousness. Repeat CSF analysis after 7 days of treatment showed reduction of protein level to 175 mg/dL, sugar level raised to 77 mg/dL, very few lymphocytes were seen, ADA levels came down to 2.3U/L, India ink preparation showed occasional round budding yeast cells, but CSF culture on SDA was sterile. The patient was discharged-on-request and was unavailable for follow-up.

Discussion

Though Cryptococcal infection is considered to be an opportunistic infection, increasing reports are there of the infection in apparently immunocompetent patients, in 10-40% cases.[2,4–6] The organism is ubiquitous in environment mainly associated with animal and bird droppings, decaying organic matter, tree bark and soil. It is also frequently associated with use of broad-spectrum antibiotics, corticosteroids, immunosuppressive drugs and in organ-transplant and malignancy patients.[2,5,10,11] CM is more prevalent in male patients as compared to females.[5,6,10] The disease presents at an older age (45±11.5 years) in immunocompetent patients as compared to immunocompromised patients.[6,10] Fever, headache, altered sensorium, neck stiffness and raised intracranial pressure are common features of CM. CSF analysis shows high protein with lymphocytic predominant pleocytosis. Meningoencephalitis, infarct and hydrocephalus are common findings of brain imaging techniques.[5,8,10,11] All these features of CM are vague and overlap with features of other causes of meningitis, especially Tubercular meningitis.[5,7] In the present case, the patient presented with all these nonspecific findings, along with a strong history of irregularly treated Tubercular arthritis. The CSF work up done in the referring hospital was short of tests for diagnosis of any fungal etiology. This incomplete protocol led to misdiagnosis of the patient as a case of dissemination of Tuberculosis. Medical history as well as the cytological and biochemical findings of CSF analysis in this case, led to misdiagnosis of the cause of meningitis, as the complete microbiological analysis was not performed. Hence, it is important that India ink preparation and culture for fungal isolation should be made part of CSF analysis in all cases of meningitis. Early diagnosis and treatment are of paramount importance in CM cases as majority of patients respond well to therapy if treated early.[10]

Conclusion

Diagnosis of CNS cryptococcosis can be challenging because of the nonspecific presentation. The disease should be suspected in any patient presenting with fever, headache and symptoms or signs referable to CNS. India ink preparation and culture for fungal isolation should be made part of CSF analysis in all cases of meningitis.

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Conflict of interest

The author declares no conflict of interest.

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