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Case Report

A rare case of fungal meningitis with atypical presentation in immunocompetent patient

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ABSTRACT

Fungal meningis is uncommon in general population especially in immunocompetent indivisuals. Meningitis, when caused by the fungal mycoses *Cryptococcus neoformans*, is normally seen in immunocompromised hosts. However, it is also seen in immunocompetent patients. In patients with an intact immune system, CM usually presents with the typical signs and symptoms of meningitis: fever, stiff neck, dizziness and headache. We report a rare case of fungal meningitis in a immunocompetent patient on antiseizure drugs for last 12 years misdiagnosed as phynetoin toxicity.

Keywords: Atypical presentation, Antifungal therapy, Altered mental status, HIV/AIDS, Lumbar puncture

INTRODUCTION

Cryptococcal meningitis (CM) is caused by an infection from the encapsulated yeast, *Cryptococcus neoformans (C. neoformans)*. In immunocompromised patients e.g. HIV/AIDS, it is generally found as opportunistic infection, with incidences ranging from 10% in the United States to as high as 30% in Africa.[1]

As an encapsulate yeast, *C. neoformans* can be constantly found in soil, pigeon feces, milk and human beings' oral cavity as well.[2] 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.[2]

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 other altered mental status.[3]

CASE REPORT

The 41-year-old female resident of rural part of Haryana, Northern India, presented to the emergency department (ED) with an 8-week history of dizziness, headache, nausea, and fatigue. She was a known case of seizure disorder for last 12 years and was on phenytoin 300mg od for same period she was on regular follow-up for same with a qualified neurologist every six monthly. Seven weeks prior to admission, had visited her primary care physician for these symptoms, she was worked up for routein investigation and common endemic infections, reports were found to be normal, hence she was managed symptomatically.

Later she improved clinically but didn't recovered completely. Patient changed more than three physicians over last 7 weeks but none of them reached to a conclusion for her present illness, meanwhile patient continued on symptomatic medication. Two days ago she developed seizure followed by aggrevation of previous symptoms.

Upon admission to the ED, a CT scan of her head and general blood investigations including serum electrolytes was found to be normal. Hence, she was admitted and planned for further evaluation. While lab investigation her serum level of phenytoin was found to be more than normal therapeutic levels. Hence a primary diagnosis of phenytoin toxicity was made and her phenytoin was stopped and she was shifted on valproate (400mg b.d) and levetiracetam(500mg b.d) I/V therapy. Over next two days patient slightly improved but her headache persisted and there was no significant improved clinically. Later her MRI brain and brain stem done, which also came normal. Clinically there was no evidence of meningitis. Finally her lumbar pucture was planned in view of persistent headache for CSF analysis. Again her primary CSF analysis found to be normal.

Table 1: CSF fluids examination findings before and after treatment.

CSF parameters	Before starting antifungal therapy	After two weeks of antifungal therapy
Glucose	65mg/dl	61mg/dl
Protein	0.08gm/dl	0.05gm/dl
TLC	4 cells	4 cells
DLC	N0%, L100 %	N0%, L100%
Gram stain	No micro organism seen.	No micro organism seen.
Acid fast stain	AFB not seen	AFB NOT SEEN
India ink	Encapsulated budding yeast cells seen	No budding /encapsulated yeast cells
Cryptococcal antigen titer	CSF-1:3200	CSF-1:720
CSF VS serum	SERUM - 1:4800	Serum- 1:1200
Fungal culture	Sabourds agar culture positive for *Cryptococcus neoformans*	Negative

Meanwhile she started developing high grade fever with chills with nausea and vomitting. Her blood samples were repeated again for routein investigation, malaria, typoid and other endemic infections in northern india.No significant result obtained, hence lumbarpucture was replanned for reanalysis of cerebrospinal fluid to rule out atypical infections. This time we got india-ink test positive for cryptococcus infection, which was missed last time.Later csf antigen titer and fungal culture was also found positive for cryptococcus, hence a conclusive diagnosis fof cryptococcal meningitis was made. She was immediately put on inj Amphotericine b injection after test dose she was started on 0.5mg/kg on day 1, increased upto 1mg/kg on day three there after continued same dose for next 2 weeks. Second drug planned to be started flucytocin (5-fc) but because of financial constraint, patient was put on high dose oral fluconazol 400mg b.d. Patient responded significantly to medical therapy. Almost all symptoms improved completely with in 72 hours of amphotericin and fluconazol therapy.

Patients kft monitoring was done every third day while amphotericin therapy, patient accepted I/v amphotericin and oral fluconazole therapy well. On 14th day of treatment patient's repete lumbar puncture was done and csf analysis shows no evidence of cryptococcal infection. After completion of 2 weeks of above treatment patient was discharged on oral fluconazole 400mg o.d for next three month. Newer anti seizure drugs were continued as such.

DISCUSSION

A patient with CM usually is immunocompromised. Until the increase of HIV/AIDS cases, more than 85% of patients diagnosed with CM had some associated deficiency of cell-mediated immunity, and this number is likely higher today.[4] Other immunocompromised conditions associated with a typical presentation include a history of alcoholism, cancer, or transplantation; sarcoidosis; Hodgkin's lymphoma; collagen vascular disease; splenectomy; chronic organ failure; or systemic corticosteroid treatment. M's history did not include any of these risk factors. However, M and her partner had been in a monogamous relationship for 23 years and both had previously tested negative for HIV. While it was appropriate to repeat M's HIV test, the search for the cause needed to focus elsewhere.

To date, three serotype varieties of *C. neoformans* have been identified: *C. neoformans* (n), *C. neoformans grubii* (gr), and *C. neoformans gattii* (g). Serotyping is important because of the fungal contact mechanism and virulence of individual strains. The neoformans (n) variety is found predominantly in contaminated soil and in bird droppings, and is responsible for the majority of CM cases in immunosuppressed patients.[5,6] Because M lived in rural part of northern india, there is a high possibility that she had caught this infection via her respiratory tract from either moist soil, avium (bird feces) or decayed wood.

CM patients with intact immune systems usually present with the typical signs and symptoms of meningitis: fever, stiff neck, and headache.[7] In patients with AIDS, CM symptoms may be subtle and include fever and lethargy. Signs of a lesion rarely are seen even when cryptococcal elements are present in cerebral spinal fluid.[7,8] However. her immune system was intact, and her first symptom, headache, was subtle and nonspecific. But 7 weeks later, her symptoms progressed to include nausea, fatigue, lethargy, and altered mentation. These signs and symptoms are nonspecific for meningitis. At initial presentation, M's symptoms seemed more related to the space-occupying lesions than to meningitis.[6] Found that patients with *C. neoformans* (g) infection had more nonspecific symptoms at onset and a longer duration of symptoms before presentation.[9]

CONCLUSION

CM is a debilitating and potentially deadly disease that affects patients with both intact and impaired immune systems. M's case illustrates how subtle the initial signs and symptoms of this infection may be, a proper work up is mandatory till final diagnosis is made. C.M can present in immunocompitent patient with atypical presentation. Cost of antifungal drugs like flucytocin is a major concern for its frequent use in developing world. According to us, high dose fluconazol is a good alternative for flucytocin therapy for non affording patients of developing world.[9] But further trials are needed before declaring it as guidelines. Also patients with CM need contineous monitoring for vital organ functions, including kidney function test.

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