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Cryptococcal Meningitis in a Young Immunocompetent Male from Northern India: A Rare Case Report

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ABSTRACT

Background: Cryptococcal meningitis is a fungal infection of the brain and meninges, which could be fatal if left untreated, it is most often linked to advanced HIV infection or other states involving weakened cell-mediated immunity. However, a growing number of cases are now being reported among individuals who lack such risk factors, especially in regions with warmer climates. Diagnosing this condition in these patients could be challenging, as symptoms are often mild, and cerebrospinal fluid (CSF) test results may appear nearly normal, which commonly leads to delays in diagnosis and treatment.

Findings: An 18-year-old man from northern India, with no prior medical history, presented to the hospital after two months of progressive generalized headache and occasional low-grade fever, with symptoms such as confusion and marked drowsiness developed over the preceding three days. His family had also noticed changes in his behaviour and a drop in his college performance in the preceding weeks. On neurological assessment, he was disoriented and slow to respond, but no focal deficits or signs of meningeal irritation were observed. Routine blood and biochemistry test results were unremarkable, and his HIV (human immunodeficiency virus) test was negative. Brain imaging by contrast-enhanced computed tomography (CECT) showed no abnormality. Examination of his cerebrospinal fluid revealed a clear fluid with normal opening pressure, near-normal glucose and protein levels, and a low lymphocyte count. All bacterial test results were negative. Given the prolonged course of the illness, fungal causes were subsequently investigated. India ink staining showed encapsulated, budding yeast cells, the cryptococcal antigen test was positive, and fungal cultures yielded *Cryptococcus* species. His condition improved substantially following the administration of intravenous amphotericin B followed by oral fluconazole, resulting in complete clinical recovery and clearance of the organism in subsequent repeat tests.

Conclusion: Even in patients with no immune impairment, cryptococcal meningitis deserves consideration whenever chronic meningitis is on the differential diagnosis, particularly when CSF abnormalities are mild.

Keywords: Cryptococcus, meningitis, immunocompromised

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Introduction

Cryptococcus neoformans and, less often, *Cryptococcus gattii* are the causative agents of cryptococcosis, an invasive fungal disease that could be fatal if left uncontrolled. Both species are abundant in nature and commonly recovered from bird droppings, rotting wood, and other decaying organic matter. People typically become infected by inhaling dried yeast cells or basidiospores originating from these environmental sources. Following inhalation, the fungus may remain confined to the lungs or spread through the bloodstream to almost any organ in the body, though it shows a marked tendency to settle in the brain and its surrounding membranes [1].

Textbooks continue to describe cryptococcal meningitis (CM) as an opportunistic disease that mainly affects individuals whose cellular immunity is compromised: late-stage HIV (human immunodeficiency virus) infection, organ transplantation, prolonged steroid use, and blood cancers are the usual culprits [2]. Cryptococcal meningitis remains a leading cause of fungal meningitis and a major cause of illness and death worldwide, particularly in regions where diagnostic and treatment resources are scarce [3]. Wider access to antiretroviral treatments has reduced case numbers in some regions, but CM remains a serious global public health issue [1].

Within India, most CM cases are diagnosed in people with known HIV infection; however, reports of the disease occurring in apparently healthy, immunocompetent patients have been steadily increasing, particularly in the country's warmer regions [3, 4].

Early diagnosis of such cases is challenging because typical risk factors are absent, the illness progresses gradually, and CSF (cerebrospinal fluid) testing often reveals only mild abnormalities, all of which lead to a delayed diagnosis.

Given that treatment delays worsen the disease outcomes, the prompt identification of these cases is crucial.

The aim of this case report was to describe one such case: a previously healthy young man from northern India, whose cryptococcal meningitis was nearly overlooked because his CSF test results appeared remarkably normal. The aim of reporting this case was to precisely elucidate the diagnostic difficulty and to highlight the fact that the patient achieved complete recovery following the initiation of treatment.

Case description: An 18-year-old man from the Barabanki district of Uttar Pradesh presented to the emergency department after two months of progressive generalized headache and occasional low-grade fever. In the three days prior to admission, his condition had further deteriorated, he had become confused and unusually drowsy and had withdrawn from his family.

His headache was holocranial and constant, gradually intensified over time, rated 8 out of 10 on a pain scale, was relieved partially with analgesics, worsened at night, and was accompanied by sensitivity to light and sound. He had not vomited, did not experience seizures or double vision, had no focal weakness, and had not lost consciousness at any point. In the two weeks prior to hospital admission, his relatives had noticed that he had become irritable, was less able to concentrate, and generally showed less interest in things he usually enjoyed. He was no longer attending university and experienced intermittent blurred vision during his most severe headaches.

Nothing in his medical history pointed toward tuberculosis, sinus disease, ear infection, head injury, or recent travel, and he recalled no contact with birds or their droppings.

He was drowsy upon arrival but arousable, responded slowly to commands, and had a Glasgow Coma Scale (GCS) score of 13 out of 15 (E3V4M6). His vital signs were stable

(HR: heart rate 94 bpm, BP: blood pressure 120/84 mmHg, RR: respiratory rate 18/min, and body temperature 37.2 °C). General examination showed no pallor, jaundice, enlarged lymph nodes, skin lesions, or other features suggesting a chronic underlying illness.

Neurologically, he was disoriented regarding time and place, and suffered from attention deficits and marked slowness of thought, though there was no neck stiffness or other sign of meningeal irritation. All 12 cranial nerves tested normally, and the patient's motor and sensory examinations were unremarkable, with symmetric tendon reflexes and downgoing plantar responses on each side. The patient's gait was mildly ataxic. Fundoscopy showed no papilloedema.

Baseline blood tests showed a haemoglobin level of 13.5 g/dL, a white blood cell count of 9,900/mm^3 (with a normal breakdown of cell types), and a platelet count of 281,000/mm^3. His liver and kidney function, electrolyte levels, and blood glucose level were all within the normal limits, though his erythrocyte sedimentation rate (ESR) was mildly raised at 26 mm/hr. His HIV test result was negative, and there were no signs of diabetes or any other conditions that compromise the immune system.

Given the deterioration of his mental state over a subacute course, a contrast-enhanced computed tomography (CECT) scan of the brain was performed on the first day of admission before attempting a lumbar puncture, mainly to rule out a mass lesion or raised intracranial pressure that would make the procedure unsafe. The scan was unremarkable: no focal lesion, abnormal meningeal enhancement, hydrocephalus, cerebral swelling, haemorrhage, or mass effects were observed. These findings ruled out the possibility of tuberculous meningitis or other space-occupying processes.

The lumbar puncture was done on the same day, which yielded clear, colourless fluid with a normal opening pressure of 16 cmH_2O. Analysis showed a glucose level of 72.5 mg/dL, consistent with normal blood glucose, a protein level of 26 mg/dL, a lactate dehydrogenase level of 10.85 U/L, and a total cell count of just 1 cell/mm^3. Both Gram staining and bacterial culture results were negative, and cytological examination showed no malignant cells.

Given the prolonged course of the illness, his altered mental state, and the CSF results that looked almost normal, the investigation was extended to consider fungal aetiologies. India ink preparation revealed round-to-oval yeast cells budding on a narrow base, each surrounded by a wide, clear capsule consistent with *Cryptococcus* species. The cryptococcal antigen test on his CSF was positive, and culture on Sabouraud dextrose agar subsequently produced the organism's characteristic creamy, mucoid colonies, confirming the diagnosis on the fifth day of admission (Figure 1).

Intravenous amphotericin B induction therapy was started following confirmation of the fungal aetiology and continued for a total of 6 weeks with regular monitoring of kidney function and electrolyte levels throughout the treatment course. His headache briefly worsened during the first few days (possibly due to an amphotericin B-related febrile/inflammatory reaction) but resolved without evidence of clinical deterioration, repeated neurological and ophthalmological examinations remained normal throughout this period.

Within five days, his fever subsided, his headache diminished considerably, his mental status fully returned to baseline (GCS15/15), and his unsteady gait and visual symptoms resolved. A CSF sample taken following the completion of induction therapy showed no organisms on India ink examination and sterile fungal culture. The treatment was

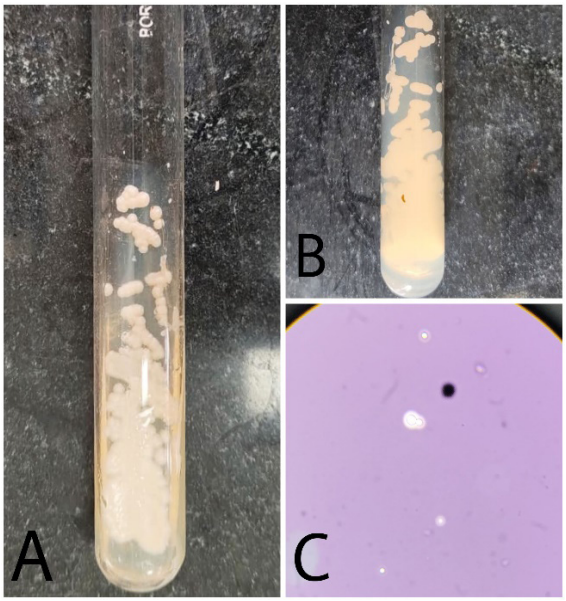


Figure 1) (A) Obverse view of the culture on Sabouraud dextrose agar, showing smooth, creamy, mucoid *Cryptococcus* colonies with a glistening surface. (B) Reverse view of the same culture, showing an unpigmented colony. (C) India ink preparation of cerebrospinal fluid, showing round-to-oval yeast cells budding on a narrow base, each ringed by a wide, clear zone corresponding to the polysaccharide capsule of *Cryptococcus* species.

then switched to oral fluconazole at a dose of 400 mg/day for 8 weeks to complete consolidation therapy, and the patient was discharged following clinical stabilization [13].

Discussion

Cryptococcal meningitis is usually regarded as a disease affecting immunocompromised individuals; however, this picture is incomplete, as Indian studies have shown that approximately 10 to 30% of CM cases occur in HIV-negative individuals [5-7]. These patients are typically younger, follow a more prolonged subacute course, and show milder CSF abnormalities than those with HIV-associated CM. Proposed explanations include greater exposure to environmental factors in tropical climates, a higher infectious fungal load, and subtle, not yet clearly defined defects in host immunity [8].

This case of CM studied illustrated why that issue is significant in practice. Despite genuinely significant neurological symptoms, the patient's CSF findings were nearly normal, exactly the kind of scenario that could lead to misdiagnosis. Immunocompetent patients with CM may present with normal or only mildly elevated opening pressure, minimal pleocytosis, and near-normal protein and glucose levels [9,10]. This CSF profile is far milder than the pronounced inflammatory response typically observed in bacterial or tuberculous meningitis, both of which are considerably more common in endemic regions such as India.

India ink staining is less sensitive than the cryptococcal antigen testing; however, it remains a fast and inexpensive option in resource-limited regions, considering that early diagnosis followed by prompt antifungal therapy is what actually determines the outcome [11].

Amphotericin B remains first-line induction therapy. Combination treatment with flucytosine is recommended where available, but in Indian settings amphotericin B monotherapy is more commonly used, largely because flucytosine access is limited, and flucytosine was not administered in this case for the same reason. Amphotericin B can still produce good outcomes if started early [12]. Specifically, for non-HIV and non-transplant hosts, the Infectious Diseases Society of America recommends using a combination of amphotericin B deoxycholate and flucytosine for an induction period of at least four weeks where flucytosine is available, or continuing amphotericin B monotherapy for four to six weeks where flucytosine is unavailable- an approach consistent with the treatment regimen used for this case [13].

Elevated intracranial pressure plays a major role in the morbidity and mortality associated with CM. Although the initial opening pressure in this patient was normal, pressure may rise during the course of the illness, making ongoing monitoring crucial; in re-

source-limited regions, serial lumbar puncture remains the standard method for managing elevated pressure. The fact that the patient did not develop intracranial pressure, despite a genuinely prolonged symptomatic course of the disease, could be attributed to a comparatively lower CSF fungal load, individual variability in CSF outflow dynamics, or simply the specific stage of the disease at which he presented; therefore, this observation should be regarded as a characteristic unique to this particular case rather than a generalisable finding.

Overall, immunocompetent patients with CM tend to fare better than immunocompromised ones, provided that the diagnosis is made early. The primary challenge, especially in endemic regions like northern India, lies in reaching the diagnosis stage: delayed presentation and misdiagnosis remain factors that often stand between the patient and a more favourable outcome.

Given the recognized risk of relapse in cryptococcal meningitis, even after apparent clinical and microbiological cure, systematic follow-up is recommended, clinical assessments should be scheduled at 2, 4, 8, and 12 weeks after discharge, with subsequent evaluations determined by clinical necessity. A low threshold for repeating CSF analysis is the recurrence of headache, fever, or neurological symptoms.

Conclusion

In short, whenever a patient, whether immunocompetent or immunocompromised, presents with subacute or chronic meningitis in a region where the organism is endemic, cryptococcal meningitis should be considered in the differential diagnosis. Reassuring CSF results do not rule out the diagnosis of CM. Early diagnosis, the prompt performance of specific tests for fungal infection (including India ink staining and cryptococcal antigen testing), and the immediate initiation of antifungal treatment are the factors that ultimately determine whether a favourable outcome is achieved or the opportunity for successful treatment is lost.

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Authors' contributions: T.S. conceived the report, carried out the microbiological workup (including fungal identification and result interpretation), reviewed relevant scientific literature, wrote the first draft, and critically revised the manuscript prior to the approval of the final version. R.V. was responsible for the patient's clinical care, took part in diagnostic and treatment decisions, supplied clinical and neurosurgical details, critically reviewed the manuscript for its intellectual content, and likewise approved the final version. Both authors take responsibility for the work as a whole, including its accuracy, and both signed off the manuscript before submission.

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