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CRYPTOCOCCAL MENINGITIS PRESENTING AS CHRONIC HEADACHE IN A PERSON LIVING WITH HIV/AIDS: A CASE REPORT

Prof. Dr. Rathnakumar MD[1], Prof. Dr. Shavana MD[1], Dr. Lakshmi Rani MD[2], Dr. Sri. Thyagesan[2*]

[1]Chief Department of Medicine Tirunelveli Medical College.
[2]Assistant Professor Department of Medicine Tirunelveli Medical College.
[3]First Year Postgraduate, Department of Medicine Tirunelveli Medical College.

***Corresponding Author: Dr. Sri. Thyagesan**

Assistant Professor Department of Medicine Tirunelveli Medical College.

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ABSTRACT

We report the case of a 36-year-old woman, a person living with HIV/AIDS (PLHA), who presented with chronic headache, fever, and significant weight loss over three months. Examination revealed pallor and neck stiffness, with no focal neurological deficits. Laboratory investigations showed advanced immunosuppression (CD4 count of 9 cells/μL) and positive autoimmune markers (ANA 2+, anti-Mi2 antibody, anti-Sp100 antibody). CSF studies and clinical evaluation confirmed cryptococcal meningitis. The patient was treated with liposomal amphotericin B and fluconazole following detection of flucytosine resistance with symptomatic improvement in a few weeks. This case highlights the complexity of diagnosing headache in PLHA, the importance of considering cryptococcal meningitis even when classical features are absent, and the challenges of treatment in case of antifungal resistance and resource-limited and immunosuppressed settings.

KEYWORDS: Examination revealed pallor and neck stiffness, with no focal neurological deficits.

INTRODUCTION

Cryptococcal meningitis is a serious opportunistic fungal infection primarily affecting immunocompromised individuals, notably those with advanced HIV/AIDS. It is caused by the encapsulated yeast Cryptococcus neoformans, which typically enters the body through the respiratory tract and disseminates hematogenously to the central nervous system. The infection often presents subacutely with symptoms such as headache, fever, neck stiffness, and neurological deficits. Due to overlapping neuropsychiatric symptoms, CM can be misdiagnosed as an autoimmune disease, especially in cases with high CSF protein or pleocytosis.[6] Despite effective antifungal therapies, cryptococcal meningitis remains a leading cause of morbidity and mortality in people living with HIV. This case presents a 36-year-old HIV-positive woman with severe headache, fever, significant weight loss, and immunological markers, highlighting the diagnostic and therapeutic challenges associated with cryptococcal meningitis, especially in the context of complex immune responses and antifungal flucytocine resistance. Cryptococcus develops resistance to 5-FC through genetic mutations, particularly in DNA mismatch repair, leading to rapid, high-level resistance.[9] The case underscores the importance of multidisciplinary evaluation and tailored management to improve patient outcomes in such severe fungal CNS infections.

CASE PRESENTATION

A 36-year-old homemaker from Thoothukudi presented with intermittent holocranial headache of three months duration, insidious in onset, moderate in intensity, and affecting daily activities. There was associated low-grade fever and significant weight loss. No history of photophobia, vomiting, seizures, visual disturbances, focal neurological deficits, or constitutional symptoms suggestive of tuberculosis was reported. She had multiple prior admissions with symptomatic treatment only.

Past medical history: Recurrent oral ulcers and multiple blood transfusions. There was no history of diabetes, hypertension, thyroid disorders or addictions. Family history was unremarkable.

Initial clinical examination: On admission, she was conscious, oriented, and thin-built with pallor. No icterus, lymphadenopathy, clubbing, or pedal edema were noted. Vitals were stable (pulse 90/min, BP 100/80 mmHg, afebrile).

Neurological examination showed Higher mental functions and cranial nerves were intact. Motor, sensory, reflex, and coordination examinations were normal except for neck stiffness. Other systemic examinations were unremarkable.

Routine Investigations including CSF analysis were sent and patient was started on Emperical Treatment regimen for meningitis but patient did not show improvement. HIV serology came out to be Reactive but HBsAg, Anti-HCV and VDRL were Negative. MRI brain showed leptomeningeal enhancement. CD4 count was sent and in view of the immunocompromised state and MRI reports, CNS tuberculosis was suspected and CSF ADA and CBNAAT were sent and ATT was started empirically. ANA: 2+ positive, ENA panel: Anti-Mi2 antibody – strong positive; Anti-Sp100 antibody – positive. Hematological, renal, and liver function monitoring: Within normal limits. CSF ADA and CBNAAT turned out to be negative and CD4 Count results showed a count of 9 cells/µL. Routine CSF cultures were negative and patient did not show clinical improvement. Fungal etiology was suspected and hence India ink stain stain was done which showed encapsulated fungal cells. CSF was sent for Fungal culture and sensitivity, Patient was started on Liposomal Amphotericin B 3-5mg/kg and and Flucytosine 25mg/kg four times a day. Patient did not show significant improvement. CSF culture sensitivity results were collected which showed Flucytosine resistance. Hence the patient was started on liposomal amphotericin B (4 mg/kg IV daily) along with oral fluconazole (800 mg/day). After six days of treatment, she demonstrated significant symptomatic improvement.

DISCUSSION

Clinical Presentation in Severe Immunosuppression

Cryptococcal meningitis remains a leading cause of morbidity and mortality in people living with HIV/AIDS (PLHA)[5], particularly those with advanced immunosuppression. In this case, the patient presented with a CD4 count of just 9cells/µL, placing her at the highest risk for opportunistic CNS infections. While the classic presentation often involves fever, headache, and neck stiffness, immunocompromised patients may present with atypical or insidious symptoms. This patient presented with a chronic, intermittent holocranial headache of three months' duration and significant weight loss, but lacked other signs of raised intracranial pressure such as vomiting or papilledema. The presence of neck stiffness on examination, however, was a crucial clinical clue that warranted immediate investigation for meningitis.

Diagnostic Confounders: The Role of Autoimmune Markers

A unique and confounding aspect of this case was the presence of positive autoimmune markers, including ANA (2+), anti-Mi2 (strong positive), and anti-Sp100 antibodies. These findings initially raised concerns for autoimmune overlap syndromes or connective tissue disorders, potentially diverting focus from an infectious etiology. HIV infection is known to cause polyclonal B-cell activation, which can lead to the production of autoantibodies and false-positive serological markers. This case illustrates the critical importance of interpreting autoimmune serology with caution in PLHA. Clinicians must prioritize ruling out opportunistic infections—specifically Cryptococcus and Mycobacterium tuberculosis before attributing neurological symptoms to autoimmune pathologies, even when serology is suggestive.[7]

Therapeutic Challenges and Antifungal Resistance

Standard guidelines typically recommend induction therapy with amphotericin B and flucytosine for HIV-associated cryptococcal meningitis. However, this case highlights the growing challenge of antifungal resistance in resource-limited settings. Following the confirmation of Cryptococcus via India ink staining and culture, the patient initially showed no clinical improvement on the standard regimen. Sensitivity testing subsequently revealed resistance to flucytosine.

The management was promptly adjusted to a regimen of Liposomal Amphotericin B (4 mg/kg IV daily) combined with high-dose oral fluconazole (800 mg/day).[8] This alternative regimen proved effective, with the patient demonstrating significant symptomatic improvement after six days. This clinical course underscores the necessity of obtaining fungal culture and sensitivity reports early in the treatment of non-responders. It further supports the efficacy of Amphotericin B plus Fluconazole as a viable alternative induction strategy when Flucytosine is ineffective due to resistance or unavailability.

CONCLUSION

This case emphasizes the need for a high index of suspicion for cryptococcal meningitis in PLHA presenting with chronic headache, even when confounding factors such as positive autoimmune markers are present. It further demonstrates that while standard protocols exist, successful management of fungal CNS infections in the severely immunocompromised often requires tailored therapy based on microbiological sensitivity patterns.

Patient Consent

Informed consent was obtained from the patient for publication of this case report.

Declarations

Conflict of interest: None.

Funding: None.

Ethical approval: Not required for a single case report as per institutional policy.

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