

Case Report

A case of *Cryptococcus laurentii* meningitis in an immunocompromised patient: case report

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ABSTRACT

Cryptococcosis is an important opportunistic fungal infection among immunocompromised, AIDS patients and those under immunosuppressive therapy. While *C. neoformans* and *C. gattii* are the most common pathogens attributed to cryptococcosis, *C. laurentii* infections are also on the rise. Here, we report a case of meningitis caused by *C. laurentii* in an HIV infected, male patient with a low CD4+ T cell count. *C. laurentii*, though rare, has been reported as an etiological agent of cutaneous, pulmonary, disseminated and ocular infections in AIDS as well as HIV negative individuals. Species differentiation is necessary as *C. laurentii* has been reported to have higher resistance to azoles and flucytosine. Infections caused by *Cryptococcus* non-neoformans infection are rare and require extensive investigation to be substantiated. Increasing reports of infection caused by other cryptococcal species, can be attributed to the growing number of immunocompromised and debilitated patients with predisposing factors, improvements in their detection and identification, and enhanced awareness of such non-typical infections.

Keywords: *C. laurentii*, Cryptococcosis, Immunocompromised

INTRODUCTION

Cryptococcosis is an important opportunistic fungal infection among immunocompromised, AIDS patients as well as those under immunosuppressive therapy.¹ *Cryptococcus* species are encapsulated, basidiomycetes yeasts commonly found in the environment and known to cause opportunistic infections mainly in immunocompromised patients, though reports of the infection in immunocompetent patients have also been described.²

While *C. neoformans* and *C. gattii* are the main species causing cryptococcosis, infections caused by the other non-neoformans species are also on the rise.³ *C. albidus* and *C. laurentii* make up 80% of cryptococcosis caused by non- neoformans *Cryptococcus*.⁴

Cryptococcus laurentii is a saprobic, non- neoformans species which has been recovered from attics, dovecotes, house of pigeon fanciers, contaminated soil and droppings of birds.⁵ It has been reported to exhibit similar disease spectrum as *C. neoformans* and has been attributed as a rare causative agent of meningitis, skin infection, keratitis, peritonitis, lung abscess, fungemia and endophthalmitis.⁶ Predisposing risk factors include deficient immunity, presence of indwelling vascular catheter and HIV/AIDS disease.⁷

Here, we report a case of meningitis caused by *C. laurentii* in a 27-years-old, HIV infected, male patient.

CASE REPORT

A 27 years old HIV infected male, construction worker by occupation, was admitted with complaints of high-grade

fever, generalised weakness, vomiting, loss of appetite, altered sensorium since the last ten days and two episodes of unconsciousness on the day before admission.

On examination, patient was disoriented, irritable, violent and not following verbal commands. Neck rigidity and Kernig's sign were present. His eyes were sunken, skin turgor was lost, tongue was dry and bilateral periorbital swelling was observed. Vital signs were normal with SpO₂ of 98%, pulse rate of 69 bpm and blood pressure of 110/80 mmHg. Fundus examination revealed hypopigmented patch with well-defined margins, 1/3rd of disc size in supero-temporal quadrant suggestive of the choroid tubercle.

Patient had history of chronic alcoholism for more than 15 years. No history of tuberculosis, hypertension, diabetes mellitus, malignancy or other chronic illness present.

Patient being a construction worker, we assume that the exposure to pigeon droppings was the only risk factor.

Patient was started on inj. ceftriaxone, inj. vancomycin and inj. acyclovir empirically. Cerebrospinal fluid (CSF) and blood sample were collected before starting antimicrobials to be sent for investigations.

Investigations

Non-microbiological investigations

Complete blood count (CBC)-Hb=6.8 g/dL, platelet count=162×10⁹/L and leucocyte count=6.4×10⁹/L. CRP level- 14.3 mg/dL. Kidney function tests (KFT) and liver function tests (LFT)-normal limit. Computed topography (CT) scan of head-Encephalomalacic gliotic changes noted in left frontal lobe. Mucosal thickening seen in bilateral maxillary sinus. Age disproportionate generalised cerebral atrophy in the form of prominence of sulcogyral spaces and dilatation of ventricles. Ultrasonography (USG) of abdomen-borderline splenomegaly.

Microbiological investigations

Cerebrospinal fluid: CSF was centrifuged and processed as follows:

Wet film: Round yeast cells and leucocytes seen.

India ink: Encapsulated yeast cells observed.

Gram stain: Gram positive round, broad-based budding yeast cells and leucocytes seen.

Ziehl-Neelsen stain: No acid-fast bacilli seen.

Culture: CSF sample was inoculated: On SDA-A confluent growth of cream coloured, smooth, mucoid colonies were observed which appeared as gram positive budding yeast cells on Gram stain. On blood agar-small,

white, mucoid, smooth, circular, entire edge, easily emulsifiable, non - haemolytic colonies grown.

Biochemicals

Germ tube test-Negative, urea hydrolysis test-Positive. Carbohydrate assimilation test by KB006 HiCandida™ identification kit-Maltose, galactose, cellobiose, inositol, xylose, trehalose, melibiose and lactose were assimilated, confirming *C. laurentii*.

Vitek 2: Isolate was confirmed by Vitek 2 system as *Cryptococcus laurentii* with MIC <1 µg/mL for amphotericin B.

PCR for viral meningitis panel: CSF was negative for viral meningitis aetiology. PCR was done by DiaGSure Diagnostic kit detecting enterovirus, human adenovirus, herpes simplex virus (HSV) 1, HSV 2, Cytomegalovirus (CMV), Epstein Barr virus (EBV), Varicella Zoster (VZV) viruses causing meningitis.

Cartridge based nucleic acid amplification test (CBNAAT): Patient's CSF was tested to rule out tubercular meningitis which was negative for *M. tuberculosis*.

Serology: Patient was found to be reactive for HIV 1 and his CD4 count was 34 cells/µL.

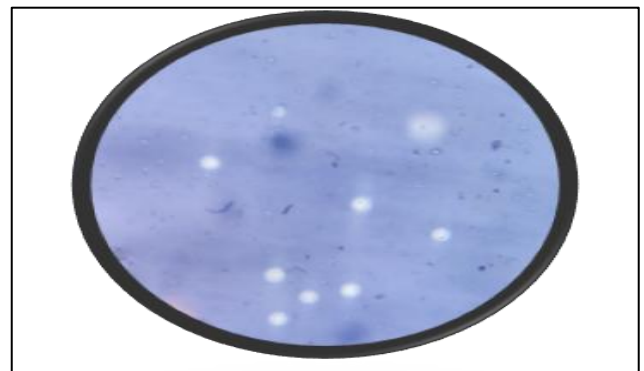


Figure 1: Capsule of *C. laurentii* seen in India ink preparation.

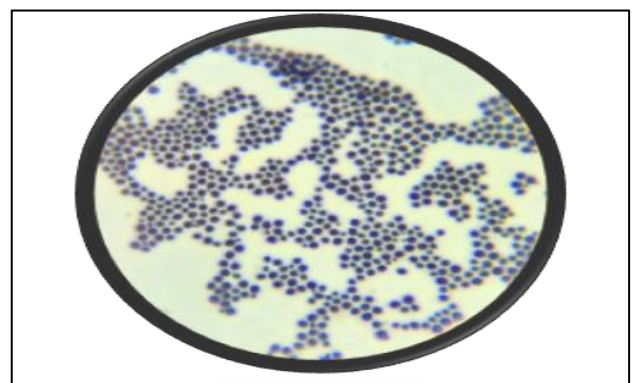


Figure 2: Gram positive broad based budding yeast cells seen.



Figure 3: Mucoïd colonies of *C. laurentii* on Sabouraud's dextrose agar.



Figure 4: Carbohydrate assimilation test reaction of *C. laurentii* as per KB006 HiCandida™ identification kit.

*U-Urea hydrolysed, Mel-Melibiose (Positive), L-Lactose (Positive), Mal-Maltose (Positive), S-Sucrose (Positive), G-Galactose (Positive), C-Cellobiose (Positive), I-Inositol (Positive), X-Xylose (Positive), D-Dulcitol (Positive), R-Raffinose (Negative) and T-Trehalose (Positive).

Treatment

Patient was started on Inj. liposomal amphotericin B and oral fluconazole as soon as presence of encapsulated yeasts was reported on India Ink preparation. Patient's clinical condition improved three days after targeted therapy was initiated and treatment was continued for a period of 14 days.

DISCUSSION

C. laurentii, formerly considered as a non-pathogenic saprophyte, is a psychrophilic yeast which grows at an optimal temperature of 15°C-30°C, and is commonly found in the tundra, Antarctica, the Himalayas, Caribbean regions and prairie soils.¹ Though rare, it has been reported as an etiological agent of cutaneous, pulmonary, disseminated and ocular infections.⁸

The first case of meningitis caused by *C. laurentii* in an AIDS patient, was reported in Greece, in a 34 years old male patient, by Kordossis et al.⁹ Zulfikar et al (Pakistan, 2023) reported *C. laurentii* meningitis with an unusual neurological presentation of cryptococcomas and leptomeningitis.¹⁰

In India, Mittal et al isolated *C. laurentii* from a case of fatal meningitis in a post-partum immunocompetent woman.¹¹

Here, we reported a case of meningitis due to *C. laurentii* in a HIV infected male with CD4 count below 50 cells/μL.

Diagnosis of non-neoformans *Cryptococcus* species can be challenging due to factors such as poor sensitivity of antigen testing and not so widely used conventional methods for their diagnosis.⁷ There are limited guidelines regarding the significance of a culture growing these species.³

Cryptococcal meningitis are associated with a low CD4 cell count. Studies from the Sub-Saharan Africa, reported a CD4 count of less than 100 cells/μL in 75% of HIV patients with meningeal cryptococcosis.¹² According to Tugume et al prognosis of cryptococcal meningitis in patients with CD4 count of less than 50 cells/μL is poorer than those with higher cell count.¹³ Both these findings are comparable with the present study where CD4 count of the patient was below 50 cells/μL, but the patient in this study recovered from the infection and had a better outcome.

C. laurentii isolates have been reported to exhibit different degrees of susceptibility to different antifungals, and various studies have showed this yeast to have higher resistance to azoles and flucytosine, which is the standard regimen for *C. neoformans* and *C. gattii* infections.¹⁴ This emphasizes the importance of identification of cryptococcus upto species level as well as performing antifungal susceptibility test on the isolates. Ryder et al reported that MIC range of seven isolates for fluconazole ranged between 1 to 4 mg/L while higher MIC ranges were reported by Johnson et al (8-16 mg/L) and Averbuch et al (>50 mg/L). Various studies showed MIC range towards amphotericin B to be below 1μg/L similar to our case.¹⁵

In our case, patient responded well to combination of amphotericin B and fluconazole. To the best of the author's knowledge, this is the first case of meningitis due to *C. laurentii* in an HIV positive patient from India.

CONCLUSION

Though rare, non-neoformans *Cryptococcus* species cannot be ruled out as a cause of meningitis in HIV patients with a low CD4 count. Identification till species level is important in case of cryptococcal meningitis since resistance pattern of neoformans and non-neoformans *Cryptococcus* species may vary. Automated identification systems play a great role in identification of such rare

pathogens which might be missed by conventional methods. Early identification can lead to proper treatment and better patient outcomes.

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