

Endogenous *Cryptococcus neoformans* endophthalmitis with subretinal abscess in a HIV-infected man

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To report a rare case of *Cryptococcus neoformans* endogenous endophthalmitis with subretinal abscess in a 36-year-old HIV-positive man, referred with progressive blurred vision in his right eye for the last 6 months. Vitreous biopsy followed by intravitreal ganciclovir did not result in significant improvement. Microbiology revealed the presence of *C. neoformans*, and intravitreal amphotericin B was then administered. The patient was treated aggressively with systemic and intravitreal antifungals but had a poor visual and anatomical outcome. A high degree of clinical suspicion combined with microbiological evaluation helped to arrive at an appropriate diagnosis.

Key words: *Cryptococcus*, endophthalmitis, immunocompromised, subretinal abscess

Endogenous endophthalmitis is a rare entity that accounts for 5%–7% of endophthalmitis cases.^[1] Fungal etiology is reported in 50%–62% of cases,^[2] with *Candida* being the most common isolate, followed by *Aspergillus* sp.^[2] *Cryptococcus neoformans* is ubiquitous-encapsulated yeast found in soil. Although various types of ocular cryptococcosis have been reported in the literature, in most cases, the diagnosis was made presumptively on clinical evidence or histopathological diagnosis.^[2,3] Definite microbiological identification was lacking in most of them, including direct microscopy of the vitreous sample.^[2] We report a case of *C. neoformans* endogenous endophthalmitis with subretinal abscess in a young immunocompromised male who was treated promptly based on positive microscopic examination of the vitreous.

Case Report

A 36-year-old patient was referred for painful gradual decrease of vision for 6 months in the right eye. There were no associated systemic complaints or any complaints in the left eye (OS). He was HIV seropositive for the last 15 years

with CD4 counts 105 cells/ μ L (normal 383–1347 cells/ μ L) and had taken highly active antiretroviral treatment for about 4 years and discontinued thereafter. On examination, the patient was denying light perception in the right eye with intraocular pressure 14 mm Hg in the right eye and 15 mm Hg in the OS. The conjunctiva showed congestion, and the pupil was round and mid-dilated with reacting relative afferent pupillary defect, Grade 2. Fundus examination revealed the presence of patches of retinal whitening, which were hazily seen. Retina appeared attached and optic disc was pale. A presumptive diagnosis of acute retinal necrosis or endogenous endophthalmitis of possible viral etiology with subretinal abscess was made, and a complete core vitrectomy was performed along with intravitreal ganciclovir (2 mg/0.1 mL), and oral valganciclovir (900 mg two times a day for 3 days) was administered. The vitreous biopsy sample was sent for microbiological investigation. Other investigations including hemoglobin, random blood sugar, blood urea, and serum creatinine were within normal limits. Postoperative B-scan ultrasound showed persistent moderate intensity echoes all throughout the vitreous cavity [Figs. 1].

The microbiological processing of the vitreous biopsy included direct microscopy with 0.1% calcofluor white, Gram and Gomori methenamine silver stains [Fig. 2a and b], and culture on 5% sheep blood agar, chocolate agar, thioglycollate broth, brain heart infusion broth, Sabouraud dextrose agar (SDA), and potato dextrose agar (PDA). All smears showed round, capsulated, budding yeast cells. Large, cream, mucoid, yeast-like colonies grew on blood agar, chocolate agar, SDA, and PDA after 72 h [Fig. 3a and b]. The fungus was later identified as *C. neoformans* using YST strip of VITEK 2 compact system. Molecular tests included polymerase chain reaction for eubacterial 16S rDNA^[4] and panfungal 28S rDNA as described earlier.^[5] Fungal DNA was detected in the vitreous sample of this patient [Fig. 4] and the sample was negative for bacterial DNA.

At 1-week follow-up, the patient had no light perception, and fundus showed dense vitreous exudates with optic atrophy. The patient was started on systemic amphotericin B as well as intravitreal injection of amphotericin B 5 μ g/0.1 mL with close follow-up, and a repeat intravitreal antifungal (amphotericin B 5 μ g/0.1 mL) was administered after a gap of 2 weeks. Media cleared sufficiently and vitreous echoes were reduced but his best-corrected visual acuity remained no light perception in the right eye at the final visit at 1½ months. As the patient was comfortable, treatment was discontinued, and the extremely poor visual prognosis with risk of phthisis bulbi was explained.

Discussion

This case of endogenous cryptococcal endophthalmitis is noteworthy for the following reasons: It highlights the importance

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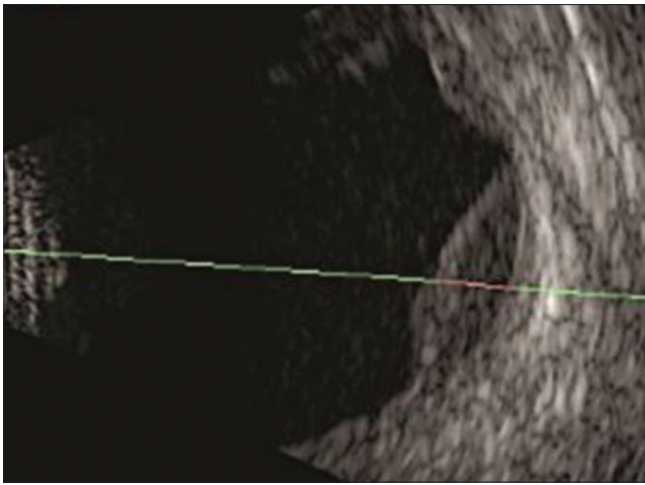


Figure 1: B-scan ultrasound showing low echo spike opacities in the vitreous cavity with localized elevations in all quadrants and submembranous opacities suggestive of exudates in the first visit

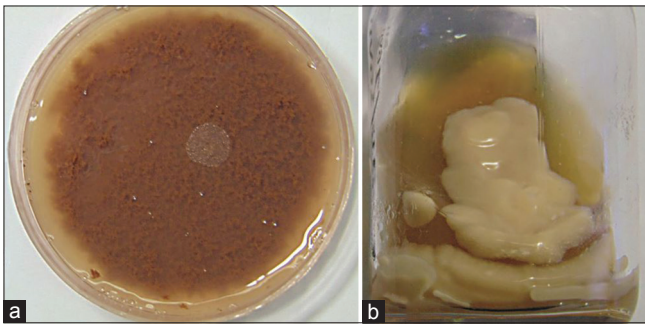


Figure 3: Photograph of (a) chocolate agar plate showing confluent growth of yeast-like colonies on the drop inoculum of vitreous sample after 48 h incubation at 37°C, (b) potato dextrose agar slant showing characteristic mucoid colonies after 10 days incubation which was identified as *Cryptococcus neoformans* by VITEK 2

of investigating vitreous biopsy including direct microscopy in the diagnosis of progressive endogenous endophthalmitis. Using simple Gram and GMS staining techniques, capsulated and budding forms were easily identified and were diagnostic of *Cryptococcus*. Given the difficulty of obtaining tissue from the intraocular space, clues to the cause of endogenous endophthalmitis will generally need to come from peripheral blood cultures and serum immunologic testing, in addition to urine and sputum culture. Most cases of confirmed cryptococcal endophthalmitis in the literature are from autopsy or enucleation,^[6,7] fine needle aspiration biopsy,^[8,9] and rarely after vitrectomy.^[6] Intraocular *Cryptococcus* may take the form of chorioretinitis, multifocal choroiditis, neuroretinitis, vitritis, uveitis, or endophthalmitis.^[4,6,8,9] Subretinal abscess formation in endogenous endophthalmitis is rare. *Aspergillus* was identified as the most frequent fungal cause of subretinal abscess.^[10] Cryptococcal endophthalmitis is an infrequent entity, and treatment usually consists of amphotericin B or flucytosine, with therapeutic failure or relapses being reported in approximately 33% of cases.^[8,9,11] There are some case reports of cryptococcal meningitis and endophthalmitis being successfully treated with voriconazole, especially to patients who had a treatment failure with amphotericin B alone or accompanied by fluconazole.^[12,13] Sheu *et al.*^[6] have reported

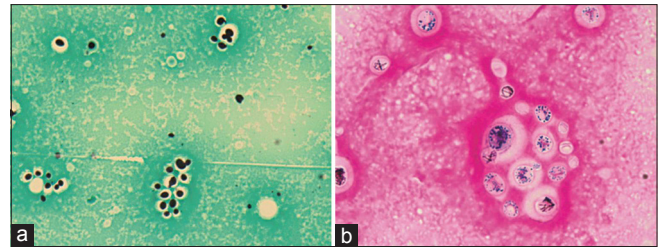


Figure 2: (a) Direct smear prepared from the vitreous biopsy examined after staining with Gomori Methenamine Silver stain demonstrates characteristic budding yeast cells and unstained capsule (x400), (b) Gram-stained smear of vitreous biopsy showing encapsulated budding yeast cells engulfed within a macrophage (x1000)

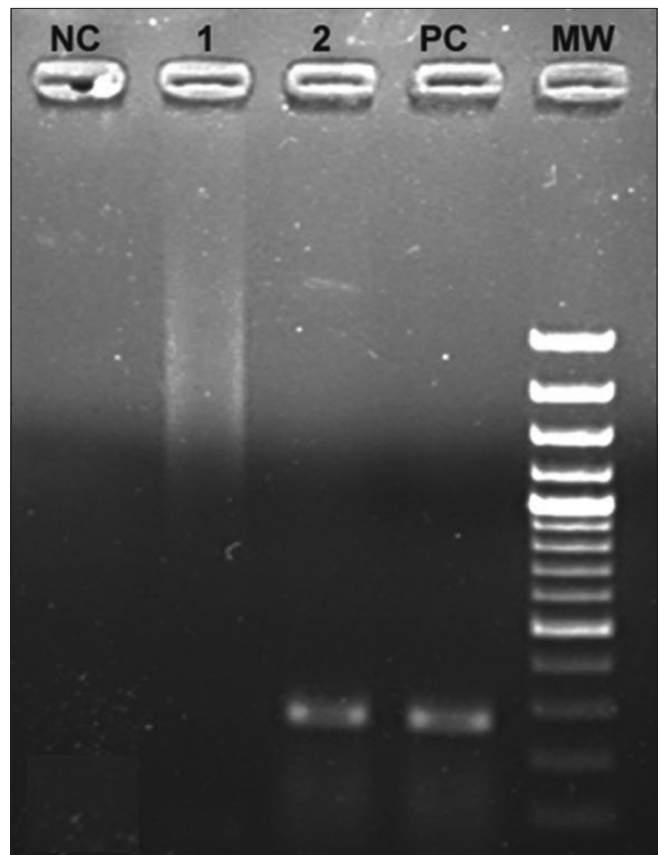


Figure 4: Agarose gel showing amplicon of 259 bp obtained with the polymerase chain reaction of the vitreous sample (target: 28S rRNA gene). NC: Negative control; Lane 1: Negative another patient sample; Lane 2: Current patient sample (positive); PC: Positive control; MW-100 base pairs-molecular weight ladder

that systemic amphotericin B-fluconazole and two doses of intravitreal amphotericin B injection eliminated the cryptococcal infection successfully; however, in our case, in spite of a quick microbiological diagnosis and aggressive medical and surgical management, there was a poor visual and anatomical outcome possibly due to the immune status of the patient as well as late presentation to the clinic.

Conclusion

Although endogenous *C. neoformans* endophthalmitis is commonly considered as a possible etiology in

immunocompromised hosts, it should also be included in the differential diagnosis of endophthalmitis with subretinal abscesses. Late presentation by the patient may lead to extensive inflammation and heavy load of organisms may account for poor outcome despite specific treatment.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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