

Endogenous fungal endophthalmitis treated with intravitreal caspofungin in a COVID-19 recovered patient: A case report

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We present a case of endogenous fungal endophthalmitis in a nondiabetic, nonhypertensive patient who recovered from COVID-19 infection. Endogenous fungal endophthalmitis in an immunocompetent individual is quite uncommon. The organism in our patient was resistant to amphotericin and voriconazole and was successfully treated with intravitreal caspofungin. The rarity of an opportunistic nosocomial infection in an immunocompetent person with a drug-resistant organism prompted us to write this report.

Key words: COVID-19, endogenous endophthalmitis, fungal endophthalmitis, hospital-acquired infections

As the pandemic of SARS-COV-2 (COVID-19) surges, it has revealed unique pulmonary and extrapulmonary manifestations of COVID-19. Prolonged hospitalization along with heavy doses of systemic steroids and immunosuppressive drugs present some real risks of secondary nosocomial infections in patients. Ocular surface involvement due to the novel coronavirus disease 2019 (COVID-19) manifesting as ocular pain, discharge, redness, and follicular conjunctivitis has been reported in the literature.^[1] Posterior segment involvement seen as central retinal vein occlusion^[2] and endogenous fungal endophthalmitis following severe COVID-19 disease have also been reported.^[3] We discuss endogenous fungal endophthalmitis in a recovered COVID-19 patient.

Case Report

A 45-year-old nondiabetic, nonhypertensive male had been hospitalized in an ICU setting for COVID-19. During his 3-week hospital admission, he was treated with multiple drugs, including intravenous and oral steroids.

One week after his discharge, he complained of difficulty in vision in his left eye. On ocular examination, his left eye had

a vision of CF 1 m. On examination, the eye had circumcillary congestion and grade 1 anterior chamber cells and flare. There was grade 1 vitritis with vitreous exudates and a creamy white retinitis patch on the macula [Fig. 1a]. The right eye was quiescent with 6/6 vision at all visits during the course of his follow-up and treatment.

A presumptive diagnosis of infective endophthalmitis in the left eye was made. An OPD-based aqueous tap was collected and intravitreal vancomycin and ceftazidime were injected. The aqueous sample was sent for Grams and Giemsa staining and bacterial and fungal culture. Blood and urine cultures were ordered, which returned negative. The aqueous tap did not yield any organism; thus, a presumptive diagnosis of endogenous fungal endophthalmitis was made on clinical grounds and the patient was shifted to intravitreal voriconazole (50 mcg/0.1 ml) which was repeated every 48 hours.

At 1-week post injections, the eye did not show a favorable response. The vitritis worsened and the patient's vision dropped further to HMCF. The patient then underwent a core vitrectomy and the undiluted vitreous sample was sent for microbiological testing (smear and culture) for bacteria and fungi.

The vitreous sample was positive for yeasts and grew *Candida Tropicalis* on culture. Antimicrobial sensitivity tests were performed using the broth dilution technique on a VITEK-2 system.

The isolates were resistant to fluconazole, voriconazole, and amphotericin B. They were sensitive to caspofungin and micafungin. Based on the susceptibility pattern, the patient was counseled for treatment with systemic and intravitreal caspofungin. After informed consent, the patient was given the drug intravitreally (50 mcg/0.1 cc, every 48 hours) and intravenously for 14 days.

The patient showed a gradual improvement [Fig. 1b]. The vitritis and the size of the retinitis patch gradually decreased. The patient received around six intravitreal injections of caspofungin over 2 weeks. After 3 months from presentation, the eye was quiescent with a clear vitreous cavity [Fig. 1c]. The vision had stabilized at 6/12 N10 with a slight subjective distortion revealed on Amslers' chart.

Discussion

The COVID-19 pandemic has revealed a few extrapulmonary and multisystem manifestations that can cause significant morbidity. Prolonged hospitalization and ICU stay with multiple indwelling catheters is a pertinent risk factor for developing opportunistic nosocomial infections.

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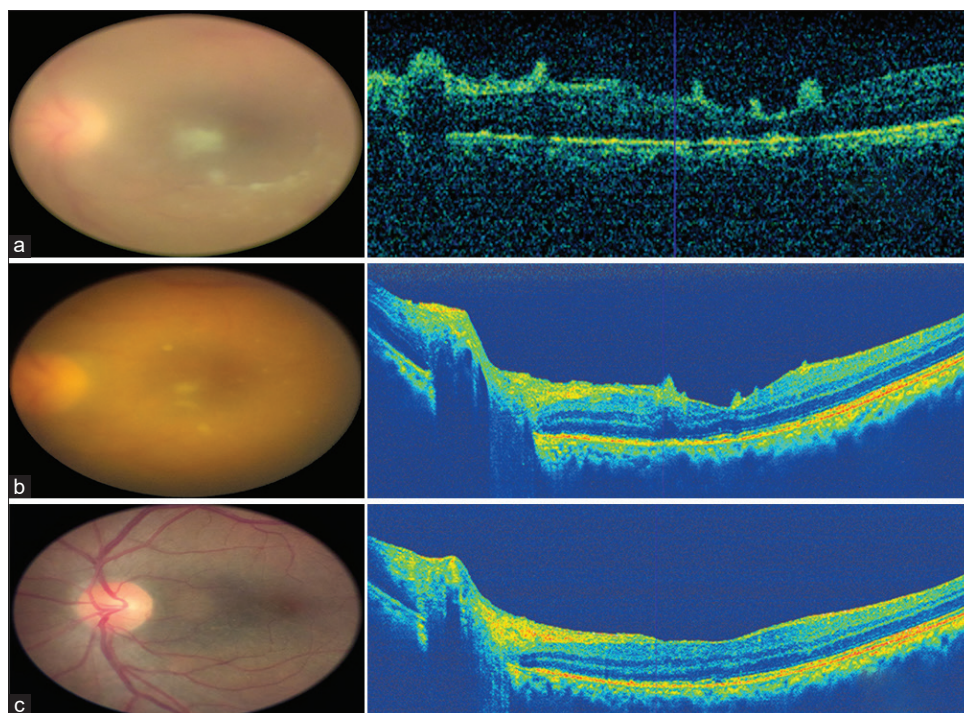


Figure 1: (a) Retinitis patch at the macula with grade 1 vitritis. (b) Post-core vitrectomy with the patient receiving intravitreal Caspofungin injections. The size of the retinitis patches is noted to be decreasing. (c) - Completely resolved macular retinitis with a clear vitreous cavity

Endogenous fungal endophthalmitis (EFE) is one such entity that can have a devastating effect on the patient's eye and vision. These blood-borne metastatic infections are more commonly seen in diabetics, hypertensives, and immunosuppressed patients.^[4] However, our patient despite not having any of these comorbidities developed EFE.

Clough *et al.*^[5] documented a fivefold increase in the incidence of candidemia in an ICU setting during the COVID-19 pandemic. COVID-19 results in substantial neutropenia along with reduction of peripheral CD4 and CD8 T cells.^[6] Although systemic corticosteroids are extremely important in the management of COVID-19, they may also contribute to immunosuppression.^[7] These factors may have promoted fungemia and may have been causal in the occurrence of fungal endophthalmitis in our patient.

C. Tropicalis is a part of the normal human microbiota and is normally present on the skin, GI tract, and respiratory tract of humans.^[8] The strain isolated in our patient was resistant to voriconazole and amphotericin B. Thus, therapy was switched to caspofungin (50 µg/0.1 ml, intravitreal). Caspofungin is an echinocandin antifungal drug that inhibits β -D-glucan synthase an enzyme needed for fungal cell wall synthesis.^[9] It is efficacious even against pathogens resistant to azoles and amphotericin B. This drug has been used as an off-label agent for the treatment of EFE^[10] with drug-resistant organisms. The effective control of infection in our case shows the promising role of this drug in managing such patients.

Conclusion

EFE, though rare, can have a devastating effect on the vision. Caregivers in the ICU setting must keep in mind the possibility

of candidemia and blood-borne metastatic infections. Bedside monitoring of vision and funduscopic examination of at-risk patients should be recommended wherever possible. Patients who have recovered from COVID-19 should be taught and explained self-monitoring of vision. They should be instructed to report to the ophthalmologist if they have any visual symptoms.

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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Conflicts of interest

There are no conflicts of interest.

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