A case series of presumed fungal endogenous endophthalmitis in post COVID-19 patients

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The novel coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2, has challenged the medical community. Several ocular manifestations secondary to COVID-19 have been documented. Prolonged hospitalization exposes the patient to various multiresistant bacteria making them prone to various secondary infections. This case series describes four cases of presumed fungal endogenous endophthalmitis in patients who recovered from COVID-19.

Key words: COVID-19, endogenous endophthalmitis, nosocomial fungal infection, SARS-CoV-2

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The novel coronavirus disease 2019 (COVID-19) has been studied in great detail and respiratory complications of the disease are well known.\(^1\) Ocular involvements are not uncommon and reports of ocular complications in patients recovering from Covid infections are on the rise.\(^{1,2}\) In addition to that, a prolonged hospital stay may make these patients vulnerable to various nosocomial infections. Endogenous endophthalmitis (EE) is one such rare sight-threatening infection that can result from the hematogenous spread of the microorganisms to the eye from a primary focus elsewhere in the body.\(^3\) We describe herein four cases of presumed fungal EE in patients who recovered from COVID-19.

## Case Reports

### Case 1

A 61-year-old male patient presented with diminution in vision and ocular pain in OS. He had contracted COVID and was admitted in a hospital for 14 days. He was a known diabetic, hypertensive and suffered from coronary heart disease in the past. On examination, the best-corrected visual acuity (BCVA) in OD was 20/30 and that in OS was CF 1 meter. Fundus examination of OD [Fig. 1] revealed subretinal exudate nasal to the disc, and a large subretinal exudate clump under the fovea in OS with vitreous exudates forming a string of pearl-like appearance. A clinical suspicion of fungal EE (OU) with subretinal abscess was made and the patient started on oral ketoconazole 200 mg BD. In spite of extensive investigations and a thorough evaluation by an internist, no systemic focus of infection could be found. Intravitreal voriconazole was administered and repeated twice at 72-h intervals. Once the lesion started reducing in size, the patient was continued on oral ketoconazole and is currently undergoing treatment.

### Case 2

A 55-year-old male presented with complaints of a central scotoma in OS for 15 days. He gave a history of contracting COVID-19 1½ months back with hospitalization for a month. He was diagnosed as post COVID retinitis elsewhere and subsequently treated with three doses of intravenous corticosteroid followed by a tapering schedule of oral corticosteroid. On examination, BCVA in the OD and OS was 20/20 and CF 1 feet, respectively. Fundus examination in OD [Fig. 2] revealed subretinal exudate superior and temporal to fovea, and a large subretinal abscess under the fovea with overlying retinal necrosis and localized vitritis in front of the lesion was noted in OS. A clinical suspicion of fungal EE was made and the patient started on oral itraconazole 200 mg BD as his LFT was deranged. No systemic focus of infection was noted, and blood and urine culture were negative. As the lesion appeared to enlarge during the follow-up visit, OS vitreous biopsy was performed and intravitreal vancomycin, ceftazidime, and voriconazole combination was administered. However, the culture from vitreous aspirate failed to yield any organism. In the follow-up visit, the patient developed ball-like vitreous exudates. Hence, intravitreal voriconazole was administered repeatedly for four times, whereas oral itraconazole was continued. The subretinal lesions in OD resolved and the size of the subretinal exudate reduced significantly. BCVA in the last follow-up was 6/6 in OD and CF 2 m in OS.
Case 3
A 64-year-old male reported to us with complaints of a black dot seen in OS for 15 days. A known diabetic and hypertensive, he was diagnosed to have COVID-19 in the previous month and had been admitted for over 20 days. On examination, BCVA in OD was CF 3 m and that in OS was 20/20. Fundus examination in OD [Fig 3] revealed subretinal exudate adjacent to fovea, whereas OS showed vitreous haze and few vitreous balls. The patient was started on oral itraconazole 200 mg BD and intravitreal voriconazole was administered in OS subsequently. The blood and urine culture were negative and systemic evaluation was noncontributory.

Case 4
A 54-year-old male patient presented with complaints of diminution of vision in OU for 20 days. The patient was a known diabetic and was diagnosed to have COVID-19 1 month back. His BCVA was the perception of light in OD and CF close to face in OS. A hypermature cataract was seen in OD and OS was pseudophakic. Slit-lamp examination of OS revealed fibrin over IOL and 1+ cells in AC. The vitreous cavity showed dense vitritis with fluffy snowballs in the vitreous cavity precluding the view of the retina. B scan [Fig. 4] revealed few dot echoes in vitreous and thickened membrane echo not attached to disc s/o posterior vitreous detachment in the OS, whereas OD vitreous was clear. The patient underwent vitrectomy with silicone oil injection in OS and vitreous biopsy was sent for microbiological evaluation, which did not yield any organism. The patient was started on oral ketoconazole and was followed up closely. After 1 month of OS surgery patient also underwent OD cataract surgery. At final follow up the BCVA in OD had improved to 6/9 and OS had a visual acuity of CF 1 meter.

**Discussion**
EE is a well-described nosocomial infection. Risk factors such as prolonged hospital stay, long-dwelling intravenous cannulae make patients with COVID-19 infection vulnerable for EE. Additionally, a large proportion of these patients may have preexisting comorbidities like diabetes mellitus. A sustained and substantial reduction of the peripheral lymphocyte counts, mainly CD4 T and CD8 T cells, has been observed in COVID-19 patients. High-dose intravenous corticosteroid therapy as part of the management of COVID-19 may contribute to systemic immunosuppression. Thus, opportunistic infections in these patients are not uncommon. Candidemia in patients with COVID-19 following prolonged intravenous therapy has been recently reported. An etiological diagnosis may be reached by testing ocular fluid(s) as well as blood, urine, etc. However, the yield of culture from ocular fluid in EE is low (14–43%). The authors agree that isolating organism on culture could have helped manage the cases better. However, an exact microbiological diagnosis could not be obtained in any patient even with a vitreous biopsy. Although all patients ended up receiving empirical treatment, they showed improvement in the clinical picture. Visual outcome in our series depended principally on the location of the lesion (macular versus extramacular) and response to therapy.

Another danger is that such lesions could be entirely misdiagnosed as retinitis or being immune-mediated, as in patient 2. Inadvertent treatment with local or systemic immunomodulators would be devastating.

**Conclusion**
We believe that this index case series will help raise awareness among ophthalmologists of endogenous endophthalmitis in post COVID-19 patients.

**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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