Fulminant fungal endogenous endophthalmitis following SARS-CoV-2 infection: A case report

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Systemic corticosteroids and immunocompromised state following SARS-CoV-2 infection can predispose individuals to endogenous endophthalmitis. A 66-year-old gentleman presented with complaints of diminution of vision and redness one week post discharge after hospitalization for COVID-19 infection. Clinical examination suggested fulminant endogenous endophthalmitis which responded poorly even after aggressive treatment requiring evisceration. Culture and gene sequenced analysis confirmed *Aspergillus fumigatus* to be the causative organism. A high degree of suspicion is warranted in the presence of recent onset of floaters in COVID-19-infected individuals to facilitate early diagnosis and outcomes.

Key words: Aspergillus fusarium, COVID-19 infections, endogenous endophthalmitis, fungus, SARS-CoV-2

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection affects different people in different ways. Although a majority of individuals recover after mild-to-moderate disease, some develop serious life-threatening complications requiring hospitalization and intensive critical care. Conjunctivitis has been reported as the most common ophthalmic manifestation of COVID19 disease.[1,2] Other less reported ophthalmic diseases include central retinal vein occlusion, central retinal artery occlusion, and acute macular neuroretinitis.[1-5]

Endogenous endophthalmitis, though relatively rare, is a potentially devastating intraocular infection if not treated promptly and adequately.[6] Risk factors include chronic diseases (for example, diabetes mellitus, renal failure), immunosuppressive state/treatment, invasive surgery, intravenous drug abuse, indwelling catheters, organ transplantation, and pregnancy.[6] The causative organism reaches the eye via the bloodstream from transient bacteremia or fungemia.

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There have been two recent reports of fungal endogenous endophthalmitis in COVID-19 infected individuals.[7,8] We here report a fulminant case of microbiologically culture-proven and gene sequenced fungal endogenous endophthalmitis which progressed to panophthalmitis requiring evisceration despite aggressive treatment. To the best of our knowledge, it is the second culture-proven case of Aspergillus endogenous endophthalmitis in post COVID-19 infection.

Case Report

A 66-year-old gentleman presented to our clinic with complaints of right eye redness and diminution of vision for four days. Systemic comorbidities included hypertension, coronary artery disease, and recently diagnosed diabetes mellitus on medications.

He had onset of cough, fever, and breathlessness three weeks prior and tested positive for SARS-CoV-2 (nasopharyngeal swab RT-PCR) with CT chest revealing a CO-RADS grade 5 [Fig. 1a]. During a 12-day stay in the critical care unit, he received systemic steroids (intravenous methylprednisolone 60 mg daily for 10 days initially and then oral prednisolone 50 mg for next two days) and respiratory support for severe respiratory distress. He was subsequently discharged on tapering dose of oral steroids over six weeks interval. His ocular complaints started two weeks after being discharged from critical care. He had undergone cataract surgery in the right eye eight years ago.

Visual acuity was perception of light and hand movements in right and left eye, respectively. Anterior segment examination of the right eye revealed eyelid edema, circumcorneal congestion, hypopyon, fibrinous exudates in the anterior chamber and posterior chamber intraocular lens [Fig. 1b]. The left eye was quiet with a total cataract with no view of the fundus. Ultrasonography B scan showed medium reflective dense echoes in the vitreous cavity [Fig. 2a] in the right eye with no evidence of T sign. Left eye B scan was normal.

A clinical diagnosis of acute endogenous endophthalmitis in the right eye was made. Examination by inhouse internist did not reveal any clinically evident systemic foci, specially of the oropharynx and paranasal sinuses. Blood and urine cultures were sent, but were unyielding. Immediately, a core vitrectomy with vitreous biopsy and intravitreal antibiotic injection (vancomycin, ceftazidime, and amphotericin B) was administered. Intraoperative patches of necrotic retina could be glimpsed through thick organized exudates, preventing a complete vitrectomy. Smear from the vitreous biopsy was positive for hyaline fungal filaments. Oral antifungals, voriconazole 200 mg BD were instituted immediately, and a repeat intravitreal injection (amphotericin B and voriconazole) was performed two days later.

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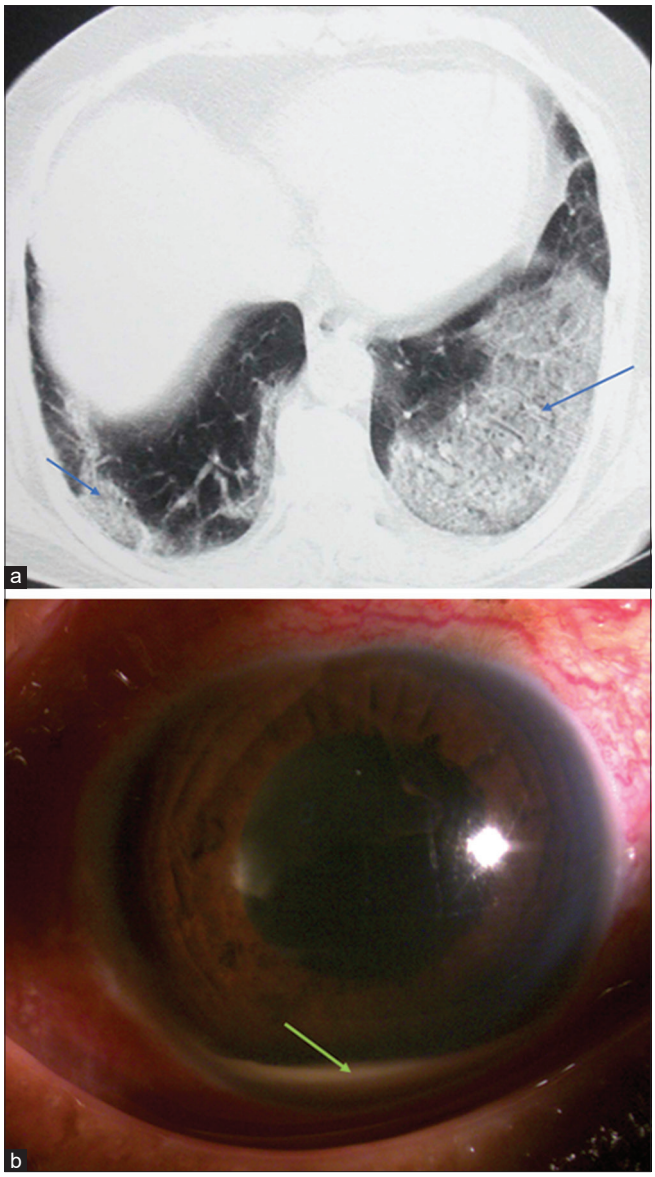

Figure 1: (a) CECT thorax scan images showing ground glass opacities (blue arrow) with interstitial thickening bilaterally with CT severity score of 15/25 and CO-RADS grade 5; (b) Anterior segment slit lamp photograph showing congestion with few Descemet membrane folds, fibrin in pupillary region, inferior hypopyon (green arrow) with an IOL *in situ*

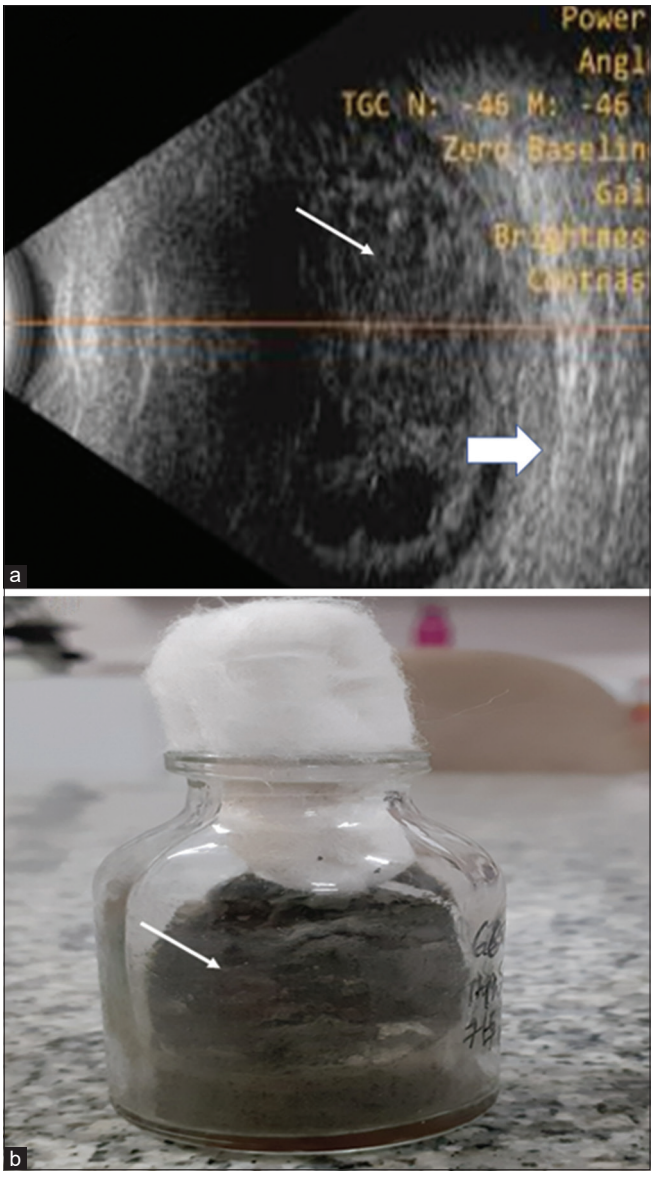

Figure 2: (a) Ultrasound B scan transverse section, showing moderately reflective dense echoes in the vitreous cavity (white arrow) with thickened chorioretinal complex (white thick arrow); (b) Sabouraud Dextrose Agar bottle showing the confluent growth of fungus (white arrow)

However, there was clinical worsening with proptosis and limitation of extraocular movements on the third day, with questionable perception of light present. Given an extremely poor visual prognosis, the options of vitreous lavage with repeat intravitreal injections versus evisceration were discussed with the patient and his family.

The patient opted for evisceration because of the fulminant course and multiple comorbidities. Evisceration (with PMMA implant) under local anesthesia was done. On the day of discharge, the socket was healthy with conformer *in situ*. At final follow-up three months after presentation, he awaits a left eye cataract surgery for visual rehabilitation.

Culture reported growth of fungus on SDA agar [Fig. 2b]. Gene sequencing of the fungus allowed for a precise species identification of *Aspergillus fumigatus* with GenBank accession number MZ576859.

Discussion

COVID-19 infection can predispose one to endogenous endophthalmitis in multiple ways: One, intensive critical care with multiple invasive procedures during hospital stay; two, prolonged and sometimes overzealous systemic corticosteroid therapy; three, compromised immune system modulated by COVID-19 virus itself; and four, presence of other systemic comorbidities like diabetes and hypertension which also predispose to fulminant respiratory disease. White *et al*.[9] reported an incidence of 26.7% of systemic fungal disease in patients infected with COVID-19 disease

requiring critical intensive care. Intensive critical care needs multiple invasive procedures. These could possibly introduce nosocomial pathogenic organisms into the bloodstream which subsequently seed in multiple organs including the sino-nasal, orbital, and ocular structures.[10]

Fungal endogenous endophthalmitis usually has a protracted indolent course with poor outcomes despite the best medical care. A delayed ophthalmic consultation in the setting of serious life-threatening COVID-19 disease, travel restriction hindering accessible specialized medical care, and immunocompromised state may further dismay prognosis in the present COVID-19 pandemic. Poor outcome even after aggressive therapy based on culture report in our present case possibly reflect advanced disease state at presentation, multiple systemic comorbidities, and highly virulent causative organism, that is, *Aspergillus fumigatus*. Silicone oil injection could have possibly salvaged globe with some functional outcomes.

The first case series by Shah *et al*.[7] reported four cases of presumed fungal endogenous endophthalmitis in post-COVID-19 patients. However, their study had a limitation that a microbiological diagnosis remained unproven. Shroff *et al*.[8] published the first case series of microbiology-proven fungal endophthalmitis in COVID-19-infected patients. Of the five cases with microbiology proven fungal diagnosis, only one case had Aspergillus species infection which fared poorly.

We here report the second case of microbiology-proven fungal endogenous endophthalmitis post COVID-19 infection. The strength of the present case is the use of molecular diagnosis in the identification of Aspergillus species isolated from culture. Unfortunately, despite the best of our efforts, vision and globe salvage could not be achieved.

Conclusion

Our case highlights the need for a high index of suspicion for endogenous endophthalmitis in COVID-19 infected patients complaining of new-onset visual symptoms, especially in the setting of comorbidities like diabetes mellitus and recent use of corticosteroid. A prompt ophthalmic cross-consultation can lead to early diagnosis and prompt intervention.

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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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Conflicts of interest

There are no conflicts of interest.

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