Case Report

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Endogenous endophthalmitis in post-COVID-19 patients: a case report

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Introduction and importance: Ocular involvement in coronavirus disease 2019 (COVID-19) can be due to direct viral invasion or indirectly due to an immunosuppressed state. Prolonged hospitalization also makes them susceptible to various secondary infections. The purpose of this case report is to report two rare cases of endogenous endophthalmitis (EE) in COVID-19 recovered patients.

Case presentation: Two patients who were hospitalized and received treatment for COVID-19 pneumonia with remdesivir and systemic steroids presented with decreased vision. The first case had a severe anterior chamber reaction with a hypopyon and dense exudates in the vitreous. The second case had cells and flare in the anterior chamber and exudates in the vitreous. They were diagnosed with EE and underwent a diagnostic vitreous tap followed by pars plana vitrectomy and intravitreal antibiotic and steroid. The culture of vitreous fluid was negative for any bacteria and fungus in both cases. However, the first case demonstrated *Escherichia coli* in urine culture. The follow-up visual acuity was no perception of light and only perception of light in the first and second case, respectively.

Clinical discussion: Severe COVID-19 patients who are hospitalized, receive systemic steroid and have associated comorbidities like diabetes mellitus are at high risk of EE.

Conclusion: Delay in diagnosis and appropriate treatment in these patients leads to poor visual outcome.

Keywords: case study, endogenous, endophthalmitides, coronavirus disease 2019, SARS-CoV-2 virus

Introduction

The novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome (SARS) associated coronavirus 2 (SARS-CoV-2), has recently become a global pandemic[1]. SARS-CoV-2 primarily affects the respiratory system but may also affect multiple systems. Ocular involvement is not uncommon and various ophthalmic manifestations have been reported[1,2]. Anterior segment manifestations include conjunctival congestion, conjunctivitis, severe keratitis, and acute angle closure; uveal manifestations include anterior uveitis, panuveitis, reactivation of uveitis, retinal vasculitis, and chorioretinitis; retinal manifestations include microangiopathy, cotton wool spots, hemorrhages, central serous retinopathy, central retinal artery/vein occlusion, and Purtscher-like retinopathy; neuro-ophthalmic manifestations include optic neuritis, extraocular muscle palsies, and benign idiopathic intracranial hypertension with papilloedema; and orbital includes mucomycosis[1–6]. COVID-19 affects the retina possibly through viral invasion or immune-mediated inflammation, even after recovery[7]. Endogenous endophthalmitis (EE), one of a rare sight-threatening condition, has also been reported in some cases of COVID-19[8–10].

As patients with severe COVID-19 requires prolonged hospital stay, they are prone to various nosocomial and secondary infections[11]. In addition, these patients are immunocompromised as a result of the COVID-19 infection, and the steroids used for its management increasing their chances of getting these infections. EE can occur under such conditions due to the hematogenous spread of microorganisms from any primary focus in the body to the eye[12].

HIGHLIGHTS

- Endogenous endophthalmitis (EE) is a rare, sight-threatening, severe intraocular infection in which pathogens from a focus of infection within a body reach the eye via the bloodstream.
- EE can occur in patients with severe coronavirus disease 2019 infection as a result of systemic immunosuppression, prolonged hospital stay, the use of intravenous cannulas, associated systemic diseases like diabetes mellitus, and use of systemic medications like steroids.
- We have reported and discussed two cases of EE in coronavirus disease 2019 recovered patients, their management, and their poor outcome in our context.

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We would like to report two rare cases of EE with unusual manifestations and a poor prognosis in patients recovered from COVID-19 after hospital admission. To our knowledge, these are the first reported cases of EE following COVID-19 infection from our region. This case report has been reported in line with the Surgical CAse REport (SCARE) criteria[13].

Case 1

A call was received from a COVID ward for a 56-year-old male with the principal complaint of diminution of vision (DOV) of the right eye (OD) for 4 days. It was associated with redness, watering, and pain. The patient was hypertensive, under medication, and nondiabetic. He was diagnosed with COVID pneumonia and had been hospitalized 1 month back. He received ceftriaxone [1000 mg, intravenous (i.v.), twice daily (BD)], remdesivir (100 mg, i.v., OD), oral prednisolone (60 mg, OD, in tapering doses), and acetaminophen (500 mg, three times a day) during his hospital stay. His repeat SARS-CoV-2 polymerase chain reaction (PCR) report was negative on the 16th day of hospitalization. However, he had a urinary tract infection in the third week of admission and *Escherichia coli* was identified in the urine culture, which was sensitive to aminoglycoside antibiotics. At the time of the examination, he was receiving systemic steroid and steroid inhaler besides i.v. aminoglycosides. His regular check-up before COVID infection was unremarkable with his bilateral best corrected visual acuity (BCVA) of 20/20 and had corrective near vision spectacles for presbyopia.

On ocular examination, BCVA in OD was finger count close to the face and 6/12, N/6 in the left eye (OS). OD examination revealed circumcorneal congestion, the pupillary reaction was slow but without a relative afferent pupillary defect, cells (4 +) in the anterior chamber, and a hypopyon of 1 mm (Fig. 1A, B). The lens was clear, but the media was hazy with 4 + vitreous cells throughout the cavity that obscured the view of the fundus. Intraocular pressure (IOP) was 12 mmHg with a pneumotonometer (NT-530). The OS findings were unremarkable. Ultrasound B-Scan (Compact Touch, Quantel Medical) of OD revealed dense heterogeneous opacity in the entire vitreous cavity persisting up to 90 dB, suggestive of severe vitritis (Fig. 1C). A provisional diagnosis of endophthalmitis most likely endogenous secondary to urinary tract infection/pneumonia was made in this post-COVID patient.

The patient was shifted to the ophthalmology ward. A diagnostic vitreous tap was performed, followed by intravitreal injection of vancomycin 1 mg/0.1 ml, ceftazidime 2.25 mg/0.1 ml, and dexamethasone 0.4 mg/0.1 ml. Postoperatively, he received topical prednisolone acetate two hourly, moxifloxacin eye drop two hourly, and atropine three times a day. Oral prednisolone was continued.

Gram's stain, Giemsa stain, and potassium hydroxide (KOH) mount were carried out in the vitreous sample where plenty of pus cells were noted in the Gram's stain but no organism was isolated. Even the vitreous tap culture was sterile with no growth of organisms. There was no improvement in signs and symptoms of the patient even on day 3; hence, a three-port 23-gage pars plana core vitrectomy (PPV) (Faros, Oertli) with intravitreal antibiotics (vancomycin 1 mg and amikacin 0.4 mg) and triamcinolone (4 mg) was performed by Dr Sagun Joshi. Intraoperatively, the retina was pale and ischemic with necrosis in the upper and lower quadrants and retinal detachment in 5–7 clock hours. The antigen test of the aspirated vitreous for SARS-CoV-2 was negative.

Regular reviews during the hospital stay did not show a significant improvement in vision; however, pain and photophobia were reduced. His retina on the first postoperative day of vitrectomy showed necrosed peripheral retina similar to acute retinal necrosis with decreased IOP. By the fourth week, BCVA was the perception of light with an inaccurate projection of the rays, the retina was detached inferiorly, the intraocular pressure was 8 mmHg and the eye appeared to be in the state of atrophic bulbi. Therefore, we could not preserve the anatomical or physiological integrity of the eye of this recovered patient with COVID. The patient was not happy with the visual outcome.

Case 2

A 79-year-old male presented with sudden onset painful DOV of OS for 6 weeks. There was no history of trauma or a history of similar disease in the past. He was under medication for diabetes and hypertension for the past 10 years. He and his whole family were tested positive for COVID-19 positive 3 months back and he had recovered from bilateral pneumonia after 21 days of hospital admission but his wife could not survive. He received ceftriaxone (1000 mg, i.v., BD), remdesivir (100 mg, i.v., OD, and oral prednisolone (60 mg, OD) during his hospital stay. The blood and urine culture were negative. He had tested negative for SARS-CoV-2 PCR on the 20th day.

The patient's ocular symptoms developed 3 weeks after his COVID diagnosis and he had chosen ophthalmic consultation elsewhere, where it was diagnosed as panuveitis and kept on topical steroids and mydriatics without significant improvement. Because of his progressive DOV, he visited us with BCVA of 6/18, N/8 in OD and perception of light with inaccurate projection of rays in OS. OD ocular findings were not remarkable and in OS, circumcorneal congestion was present with diffuse fine keratic precipitates, 3 + cells and 3 + flare in the anterior chamber (Fig. 2A, B). There was no hypopyon. Grade II nuclear sclerosis was present and 4 + cells with exudates and degenerations were observed in the vitreous. The details of the fundus could not be elucidated. IOP were 15 and 8 mmHg in OD and OS, respectively, with the pneumotonometer. Ultrasound B-Scan of OS revealed heterogeneous opacity throughout the vitreous cavity persisting up to 90 dB, suggestive of dense vitritis with a flat retina but thickened retinochoroidal complex (Fig. 2C).

A diagnosis of EE was made and the patient underwent three-port 23-gage PPV with intravitreal antibiotics (vancomycin 1 mg/0.1 ml and ceftazidime 2.25 mg/0.1 ml) and dexamethasone 0.4 mg/0.1 ml with silicone oil injection by Dr Pratap Karki. Intraoperatively, areas of retinal necrosis and thinning with inferior retinal detachment were observed as suggestive of endophthalmitis. The grams stain of the vitreous sample showed pus cells (1–2/high power field), fungal elements were not seen and there was no culture growth within 48 h. The vitreous antigen test for SARS-CoV-2 was also negative in this case.

At 1 month of follow-up, BCVA was PL with an inaccurate projection of rays. Silicone oil was present in the vitreous cavity with minimal reaction. IOP was maintained. Retina was attached

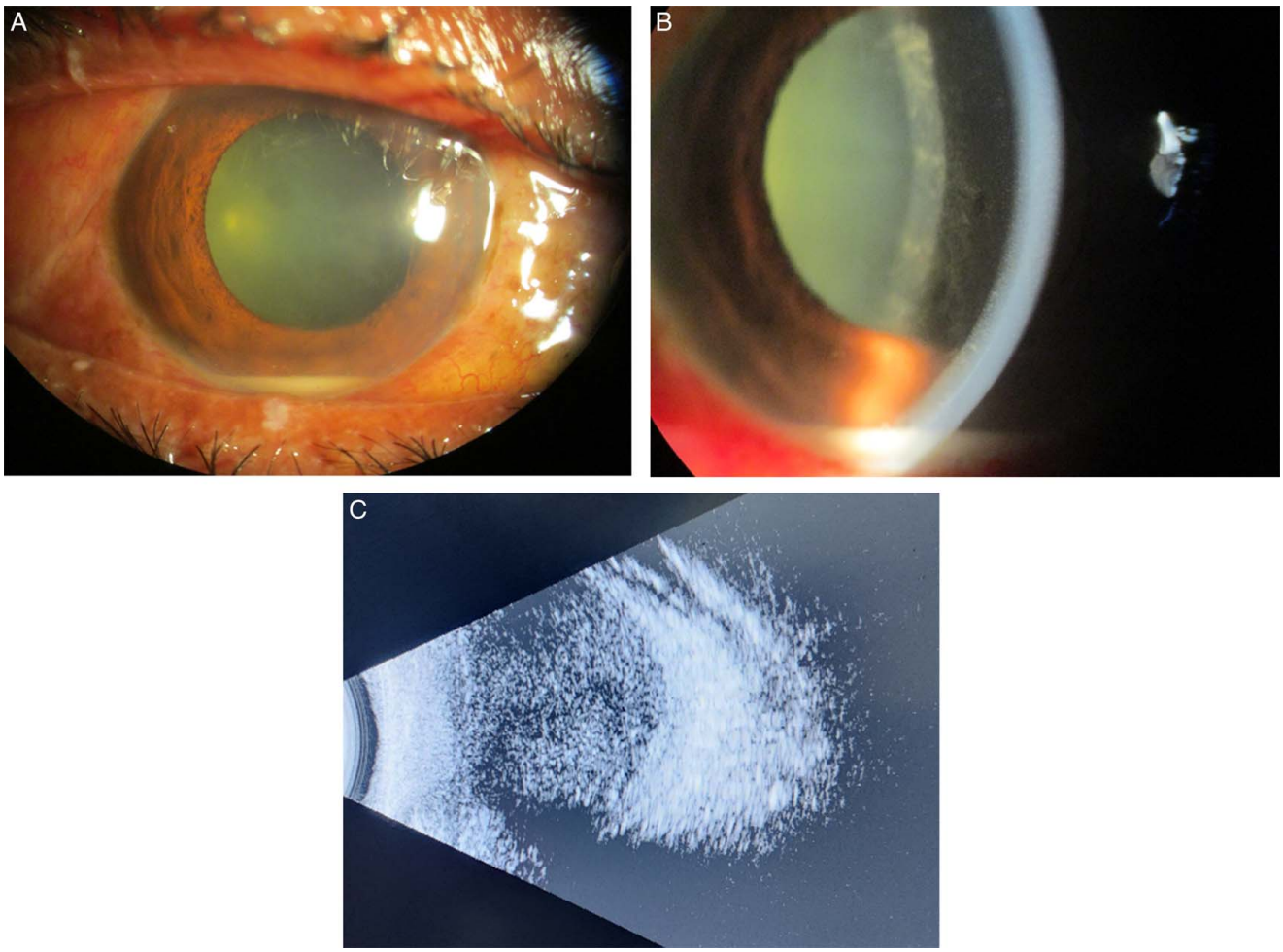

Figure 1. Clinical photograph of OD showing (A) circumcorneal congestion with hypopyon (B) cells 4 + and flare 4 + in the anterior chamber (C) Ultrasound B-Scan showing heterogenous opacity in entire vitreous persisting up to 90 dB suggestive of exudate in vitreous cavity.

with decreased intensity of retinal ischemia. At 2 months of follow-up, the anatomical integrity of his left eyes was maintained with an attached retina, but vision had not improved probably due to damage to the retinal tissues due to long-standing retinal necrosis. The patient was relieved of the pain but was not satisfied with his vision.

Discussion

In our case study, both the patients presented with endophthalmitis following the COVID-19 infection. They underwent PPV with intravitreal injections. However, the visual outcome was poor. EE is a rare, sight-threatening, severe intraocular infection in which pathogens from a focus of infection within a body reach the eye via the bloodstream. This can be caused by patients own flora in an immunocompromised state or the reactivation of a pathogen in a host. Prolonged hospital stay and the use of i.v. cannulas make patients with severe COVID-19 infection, especially those with comorbid conditions such as diabetes mellitus and hypertension prone to EE[14]. Systemic immunosuppression by sustained and significant reduction in lymphocyte counts, decreased production of CD4 and CD8 T cells and stimulation of cytokines during COVID-19 infection also predispose these patients to secondary opportunistic infections[15]. This state of immunosuppression is further increased by the use of systemic steroids that are currently being used as part of the management of severe COVID-19 infection[16]. As a result of immunosuppression during, the microorganisms could reach the eye from the focus of infection through the hematogenous route leading to endophthalmitis[17].

EE is a clinical diagnosis and treatment should be started empirically till the causative organism is isolated[18]. Organisms can be isolated by culture of ocular fluids as well as blood, urine, etc. However, the culture may not always be positive as the yield of the ocular fluid culture in EE is only 14–43%[14]. Although vitreous cultures in our cases were negative, *E. coli* was isolated from the urine culture in our first case. This could be the focus of infection for the development of EE. Though blood and urine culture in the second case were negative, pharyngeal swab culture could have helped us to identify possible sources of endophthalmitis in our second case. The antigen tests of vitreous samples for SARS-CoV-2 were negative. However, the PCR for SARS-COV-2 and other common viral microorganisms of the vitreous sample could not be performed, which is the limitation of our study.

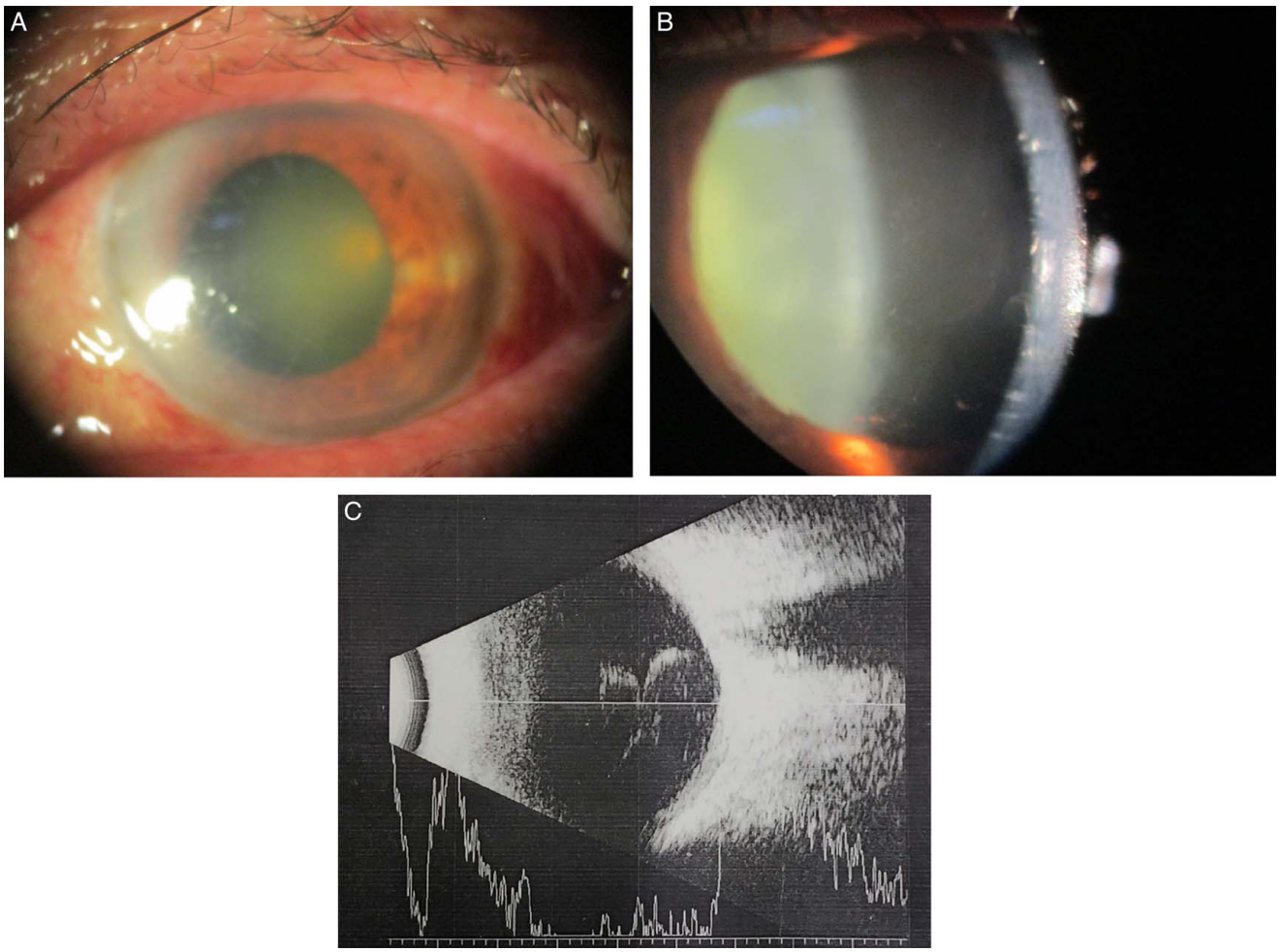

Figure 2. Clinical photograph of OS showing (A) conjunctival edema with circumcorneal congestion (B) cells 4 + and flare 4 + in the anterior chamber without hypopyon (C) Ultrasound B-Scan of showing heterogenous opacity in mid and posterior vitreous persisting up to 90 dB suggestive of exudate.

Various authors have reported cases of EE in the setting of COVID-19[8–11,19]. Bilgic *et al.*[10], in a series of three cases of EE, had COVID-19 pneumonia and received remdesivir and systemic steroids. All the patients underwent vitrectomy and intravitreal antibiotic injection. Agarwal *et al.*[8], in a report of six patients with EE as a complication of COVID-19 infection, two patients had bilateral involvement, four were diabetics, and five patients received systemic corticosteroid. Two of the six vitreous samples showed fungi, two showed bacteria, and two were culture negative. Similarly, Shah *et al.*[11] and Shroff *et al.*[19] have reported cases of fungal EE. All of those cases were hospitalized for severe COVID-19 pneumonia and received systemic steroid therapy.

Bilgic *et al.*[10] reported good results in all cases after early intervention. Agarwal *et al.*[8] had good visual results in four out of six patients. The outcome was very poor in a case of Klebsiella endophthalmitis associated with diabetes who underwent delayed PPV[9]. In our cases, despite intravitreal injections of antibiotics, endophthalmitis continued to progress until PPV was performed. Our first case required multiple intravitreal antibiotic injections. In both of our cases, the intervention was delayed and had a poor visual outcome. Therefore, these cases also highlight the importance of early intervention in EE.

Conclusion

EE in the setting of COVID-19, though rare, is a possible and potentially devastating complication. The use of systemic corticosteroids and associated comorbidities in hospitalized patients may increase the risk of EE. Therefore, a high index of suspicion with a detailed fundus evaluation must be carried out in all cases with visual diminution in patients with COVID-19. Delayed intervention in these cases leads to a poor visual outcome.

Ethical approval

None.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by Editor-in-Chief of this journal on request.

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Conflicts of interest disclosure

The authors declare no conflicts of interest.

Author's contribution

S.C.: concept, design, literature search, manuscript preparation, edit, and finalize; R.K.S.: concept, design, manuscript revision, edit, and finalize; P.K.: design, manuscript revision, edit, and finalize; S.N.J.: design, manuscript revision, and finalize.

Research registration unique identifying number (UIN)

1. Name of the registry: not applicable.
2. Unique identifying number or registration ID: not applicable.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): not applicable.

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Data availability statement

Data sets were not generated or analyzed during the current study.

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