



# Unilateral Endogenous Bacterial Endophthalmitis Post-Coronavirus Disease-19 in an Healthy Asian Indian Male

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## Abstract

Coronavirus disease 2019 (COVID-19) is associated with ocular involvement either during or after the infection. These include conjunctivitis, conjunctival hyperemia, chemosis, epiphora, reactivation of anterior uveitis, or presenting as anterior sclero-uveitis, cotton wool spots, retinal hemorrhages, retinal artery/vein occlusion, ophthalmic artery occlusion, panuveitis, papillophlebitis, central serous retinopathy, presumed fungal endophthalmitis, and multifocal chorioretinitis. A 47-year-old Asian Indian male was diagnosed with COVID-19 and had no other systemic history of note at the time of admission. Three weeks later, he developed sudden loss of vision in the right eye (OD). Visual acuity in OD was perception of light. OD had features of endophthalmitis. OD underwent pars plana vitrectomy with intravitreal antibiotics. Anterior chamber tap for fungal culture and polymerase chain reaction for panfungal genome was negative. Culture of ocular specimens did not reveal bacterial growth. Vitreous sample showed few Gram-positive cocci in singles and pairs with no evidence of fungal elements. Polymerase chain reaction for eubacterial genome was positive. He was treated with topical and systemic antibiotics and steroids. Final follow-up 6 weeks later, OD had a best-corrected visual acuity which was 20/200 with a quiet anterior chamber; cataract, with a macular traction and reduced sub retinal exudates and fluid. Post-COVID-19 sequelae causing sight-threatening manifestations as illustrated by this case report needs early recognition and prompt treatment to achieve a favorable visual outcome.

**Keywords:** Coronavirus disease-19, endogenous endophthalmitis, pars plana vitrectomy, polymerase chain reaction

## Introduction

Coronavirus disease 2019 (COVID-19) is associated with ocular involvement either during or after the infection. These include conjunctivitis, conjunctival hyperemia, chemosis, epiphora, reactivation of quiescent anterior uveitis, anterior

sclero-uveitis, cotton wool spots, retinal hemorrhages, retinal artery/vein occlusion, ophthalmic artery occlusion, panuveitis, papillophlebitis, central serous retinopathy, presumed fungal endophthalmitis, and multifocal chorioretinitis (1-11). We herein report a patient with unilateral presumed bacterial endogenous endophthalmitis 3 weeks after COVID-19.

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## Case Report

A 47-year-old Asian Indian male was diagnosed with COVID-19 pneumonia in the 1st week of October 2020 and was admitted in the hospital for more than 2 weeks. The course and details during his stay are mentioned in Table 1. Figure 1 shows the graph of inflammatory markers during his admission at a local hospital. He was administered systemic antibiotics and steroids during his stay at the local hospital.

The other details of the treatment was not available to us. Attempts to contact the hospital did not yield any results as the hospital did not provide any further information. We have included the investigation results which were available to us from the local hospital. There was no other systemic history of note at the time of admission for COVID-19.

This case report was a part of the study which was ethics approved vide Ethics Committee approval number: C/2020/09/09.

**Table 1.** The investigations done for the patient

### Investigations done at the time of diagnosis of COVID-19

Nasal swab was reverse transcriptase polymerase chain reaction (RT-PCR) for COVID-19 and severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) IgM were positive

Erythrocyte sedimentation rate (ESR) 62 mm/hour

Procalcitonin 1 ng/ml (0.5–2.0) indicative serious systemic infection (normal values <0.1 ng/ml)

C-peptide 8.62 ng/ml (1.1–5.0 ng/ml), 0.48–5.05 (fasting), and 0.5–8 (random) – consider MODY (Maturity Onset Diabetes of Young)/type 2 diabetes in young diabetes

Urine analysis done once during the early part of the hospital stay was normal

X-ray and computed tomography of the chest were not available

### Management at the local hospital during and after diagnosis of COVID-19

At the time of discharge, the patient was prescribed

T. Azithromycin 500 mg OD

T. Pantaprazole 40mg OD

T. Hydroxychloroquine 200 BD

T. Acebrophylline (200 mg)+Montelukast (10 mg)

T. Aspirin (75 mg) + Rosuvastatin (10 mg) + Clopidogrel (75 mg)

### At the time of discharge, his investigations were as follows

Severe acute respiratory syndrome coronavirus (SARS-CoV-2) negative by reverse transcriptase polymerase chain reaction (RT-PCR)

Lactate dehydrogenase (LDH) – 1068 IU/L (225–450)

CRP – 5.24 mg/L (<5)

Serum ferritin – 1040 ng/ml (30–220)

D-dimer – 1100 ng/ml (0–400)

### Investigations done during ocular management

RT-PCR for SARS-CoV-2 was negative both by nasal swab and the vitreous sample.

Aqueous tap

Culture did not reveal any bacterial growth

No evidence of fungal elements on potassium hydroxide mount

Fungal culture and polymerase chain reaction for panfungal genome were negative

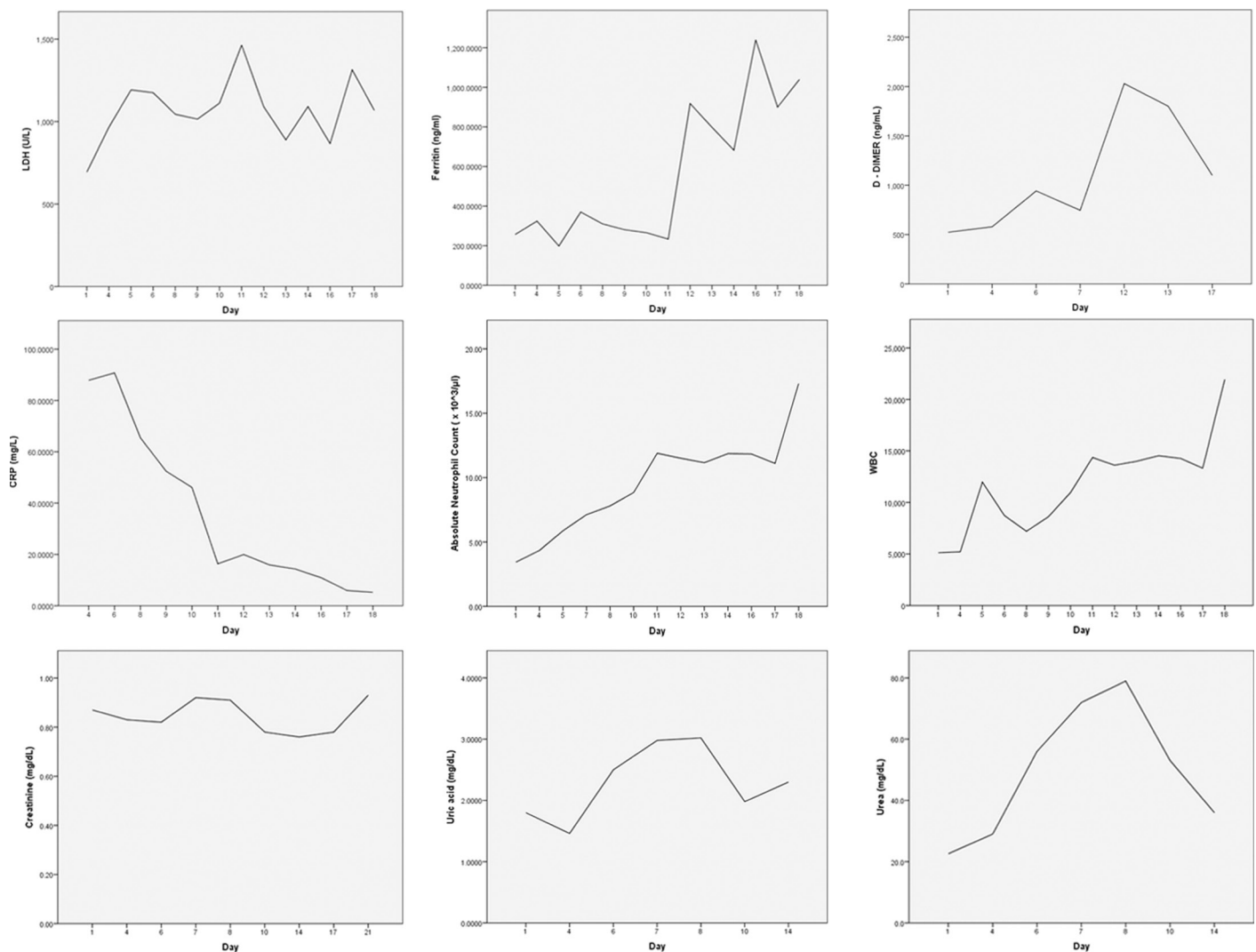
Polymerase chain reaction (PCR) for eubacterial genome was positive

Gram stain of the vitreous sample showed plenty of pus cells, cellular debris, and few Gram-positive cocci in singles and pairs

Urine culture revealed *Pseudomonas* species – 100,000 CFU/ml of urine which was multidrug resistant and sensitive only to ciprofloxacin, amikacin, and gentamicin

Blood culture did not show any growth after 2 weeks of incubation for aerobic bacteria or fungus

SARS-CoV-2 RBD (receptor-binding domain) total (IgG and IgM) antibodies were 8.83 (positive) (<1.0)



**Figure 1.** The graphs of his systemic inflammatory markers during his admission at the local hospital. In the initial phases of his admission, there is elevation of lactate dehydrogenase, serum ferritin, and D-Dimer with peak levels between 11 and 14 days after diagnosis of COVID-19. Other parameters such as white blood count, absolute neutrophil count, urea, uric acid, and creatinine levels were also high except CRP which was lower during the same time.

All tenets of Helsinki Declaration were adhered to.

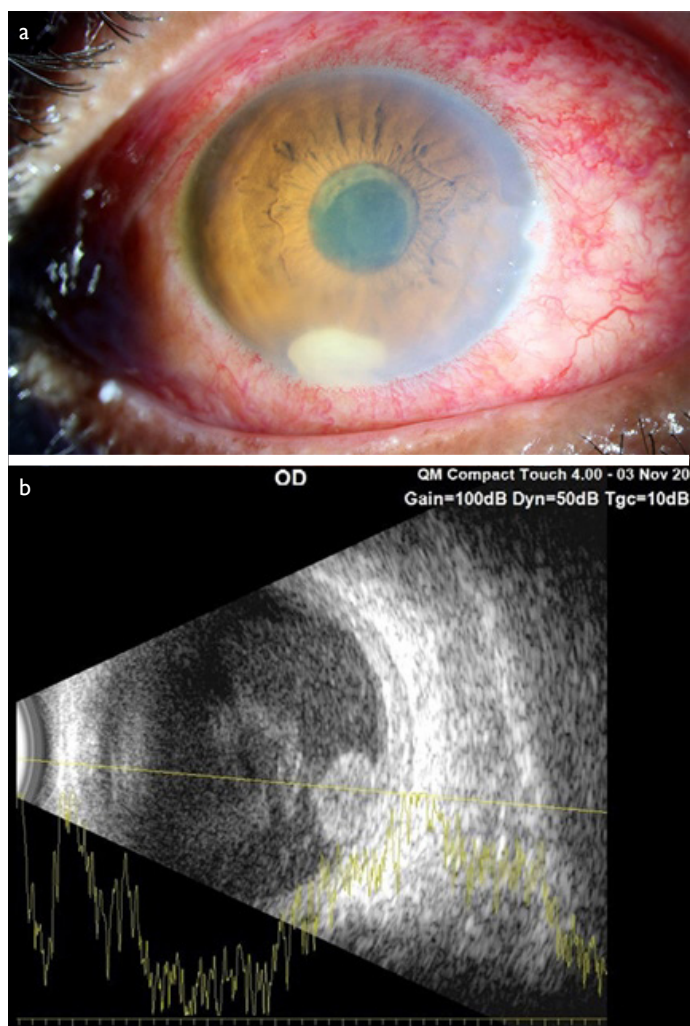
In the last week of October 2020, he developed sudden loss of vision in the right eye (OD). He was diagnosed as having endogenous endophthalmitis in OD and was referred to us for a second opinion after receiving a single dose of intravitreal vancomycin/ceftazidime and voriconazole.

On his ophthalmological evaluation at our tertiary center, his visual acuity in the OD was perception of light and 20/20 in the left eye (OS).

The right eye had lid edema, ciliary congestion, corneal epithelial edema, Descemet's membrane folds, stromal edema, and anterior chamber had flare 3+, cells 3+ with a hypopyon of 2 mm with membranes in the pupillary area and over the lens (Fig. 2a). There was no view of the vitreous and fundus. The left eye examination was within normal limits. Ultrasound

B-scan of OD showed medium-high reflectivity echoes on vector A scan corresponding to dense vitreous debris predominantly in the middle and posterior vitreous cavity (Fig. 2b). There was organized vitreous inferiorly measuring 5.96 mm and 10.48 mm in its greatest dimensions, with subretinal fluid and no choroidal shadowing with vector A scan showing high reflectivity spikes. Anterior chamber and vitreous samples from OD were analyzed for Gram's stain, potassium hydroxide mount, aerobic/fungal culture, and polymerase chain reaction (PCR) for eubacteria and panfungal genome. Culture of blood and urine was done (Table 1).

Figure 3a shows nested PCR in 2% agarose gel with positive eubacterial genome in well 3 and 4. Figure 3b shows *Pseudomonas aeruginosa* colonies in nutrient agar showing greenish tinged colonies from the urinary sample.



**Figure 2.** (a) Diffuse slit-lamp view of the right eye showing circumferential congestion and chemosis, with hazy cornea, anterior chamber flare 4+ cells 3+, exudates, and 2 mm hypopyon, with exudates in the pupillary area. (b) Ultrasound B scan of the right eye shows medium reflective echoes with organized vitreous debris and membrane in the entire vitreous with a pre-retinal mass.

The right eye OD underwent synechiolysis, pars plana vitrectomy with fluid air exchange, and intravitreal antibiotics ceftazidime (2.25 mg/0.1 ml), vancomycin (1 mg/0.1 ml), and voriconazole (0.01 mg/0.1 ml). Silicone oil injection was done for a better post-operative monitoring and also to reduce the risk of post-operative retinal detachment.

Topical fortified vancomycin (50 mg/ml)/amikacin (40mg/ml)/prednisolone acetate 1% (2 hourly) and homatropine 2% twice daily were started. Oral ciprofloxacin 500 mg twice daily along with deflazacort 24 mg once daily in tapering dose over 4 weeks was prescribed.

He was reviewed at a local eye hospital every 3<sup>rd</sup> day and was given intravitreal injection of vancomycin and ceftazidime in OD.

Two weeks later at our tertiary center, vision in OD was counting fingers at 1 m. OD showed conjunctival congestion,

anterior chamber flare 2+, cells+, pigments, pigment clumps on the lens, vitreous haze 2+ cells +, pre-retinal exudate, subretinal fluid, and exudates in the macular area (Fig. 4a). A month later, after treatment with systemic, topical intravitreal antibiotics he had reduced pre-retinal exudates (Fig. 4b). Since aqueous and vitreous sampling did not yield any fungus, intravitreal dexamethasone was added to the treatment regimen. Spectral domain optical coherence tomography (SD-OCT) of OD showed pre-retinal hyper-reflectivity with shadowing of the retina and choroid, while adjacent area showed inner retinal swelling and mild subretinal fluid (Fig. 5a). SD-OCT a month later showed reduction in subretinal fluid and inner retinal swelling (Fig. 5b).

At his final follow-up 6 weeks later, his best-corrected visual acuity was 20/200 in the OD and had a quiet anterior chamber, cataract and showed a macular traction, with further reduction of subretinal exudates and fluid. Further intervention with pre-retinal exudate and silicon oil removal with excision of traction bands were due, but the patient was lost to follow-up. Repeat urine culture was not done.

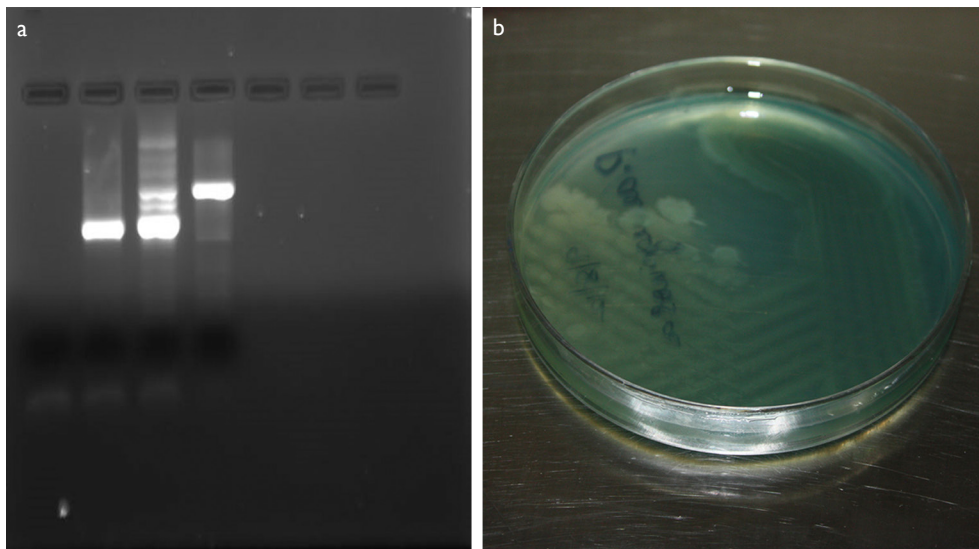
Another characteristic feature in our patient at the time of ocular presentation was the presence gangrene at the root of the nose (vertical stout down arrow (Fig. 6a)) and presence of purpuric rash beneath it suggesting inflammation (block red arrow) and eschar-like lesions on the forehead (hollow red arrow). Financial circumstances of the patient prevented further dermatology/infectious diseases referral or work-up. Figure 6b shows healed gangrene and reduction of eschar a month later.

## Discussion

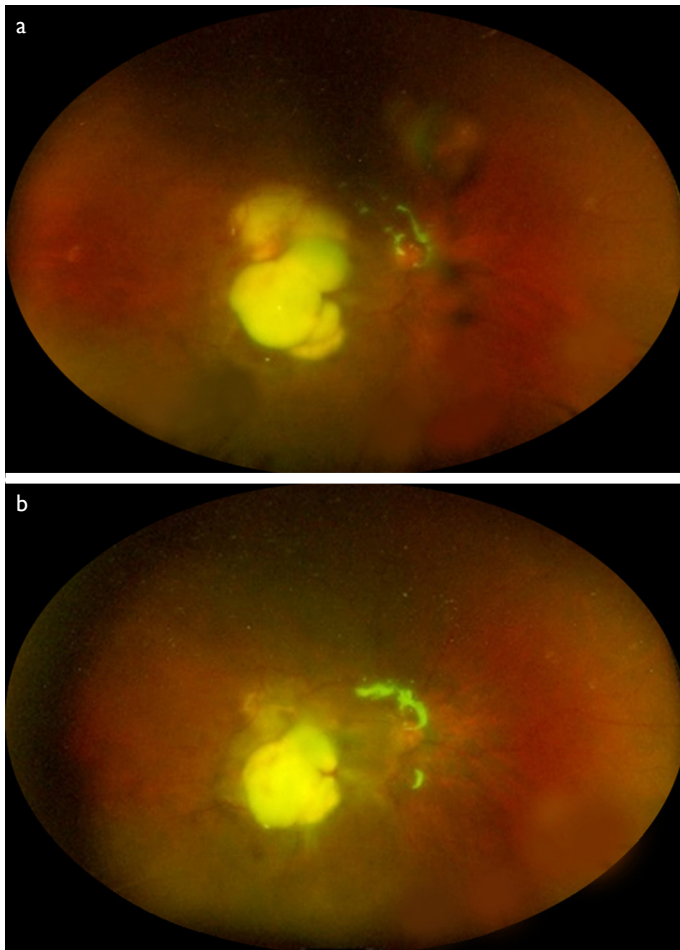
It is possible that our patient developed urinary infection during his stay at the local hospital and was possibly not recognized which could have caused his endogenous endophthalmitis post-COVID-19. Endogenous endophthalmitis is exceedingly rare in immunocompetent patients. Its presence should prompt an immunologic work-up to exclude underlying immune deficiencies, which was negative for our patient. The presence of *Pseudomonas* urinary infection in patients with immune deficiencies or debilitating disease is a well-known risk factor for endogenous endophthalmitis and would explain both the mucosal lesions at the nose and the eye involvement. The presence of COVID-19, might as well be a fortuitous phenomenon. We cannot, however, conclude that intraocular inflammation may be related to the COVID-19 despite the fact that patient otherwise had no systemic illness. The patient did not have any symptoms suggestive of urinary tract infection.

In a series of fungal endogenous endophthalmitis, five of the seven eyes grew fungus as the causative organism (*Candida* spp. in four eyes and *Aspergillus* spp. in one eye) (10).





**Figure 3. (a)** Nested polymerase chain reaction in 2% agarose gel showing four wells from left to right, Well 1 – negative control; Well 2 – sample showing positive; Well 3 – second round positive control; and Well 4 – first round positive control. **(b)** *Pseudomonas aeruginosa* colony growth in nutrient agar showing greenish tinged colonies.



**Figure 4. (a)** Wide angle fundus images of the right eye (top) 2 weeks after surgery showing pre-retinal exudates and subretinal fluid in the macular area and (down), **(b)** 1 month later showing reduction of the pre-retinal exudates.

Celiker and Kazokoglu in a 5-year retrospective study of endogenous endophthalmitis from Türkiye found that 40% of the patients had diabetes mellitus. The microorganisms isolated were predominantly *Candida* species (71.4%). Fungemia (76.2%) was seen with predominant yeast cells (12).

Endogenous endophthalmitis due to *Aspergillus* species may be challenging to diagnose as blood cultures, serological tests, and pulmonary radiography may be negative. The best diagnostic approaches in these instances would be cultures of pars plana vitrectomy specimens and examination of Gram- or Giemsa-stained smears as aspergillosis clinically presents with deep retinitis and/or choroiditis (13).

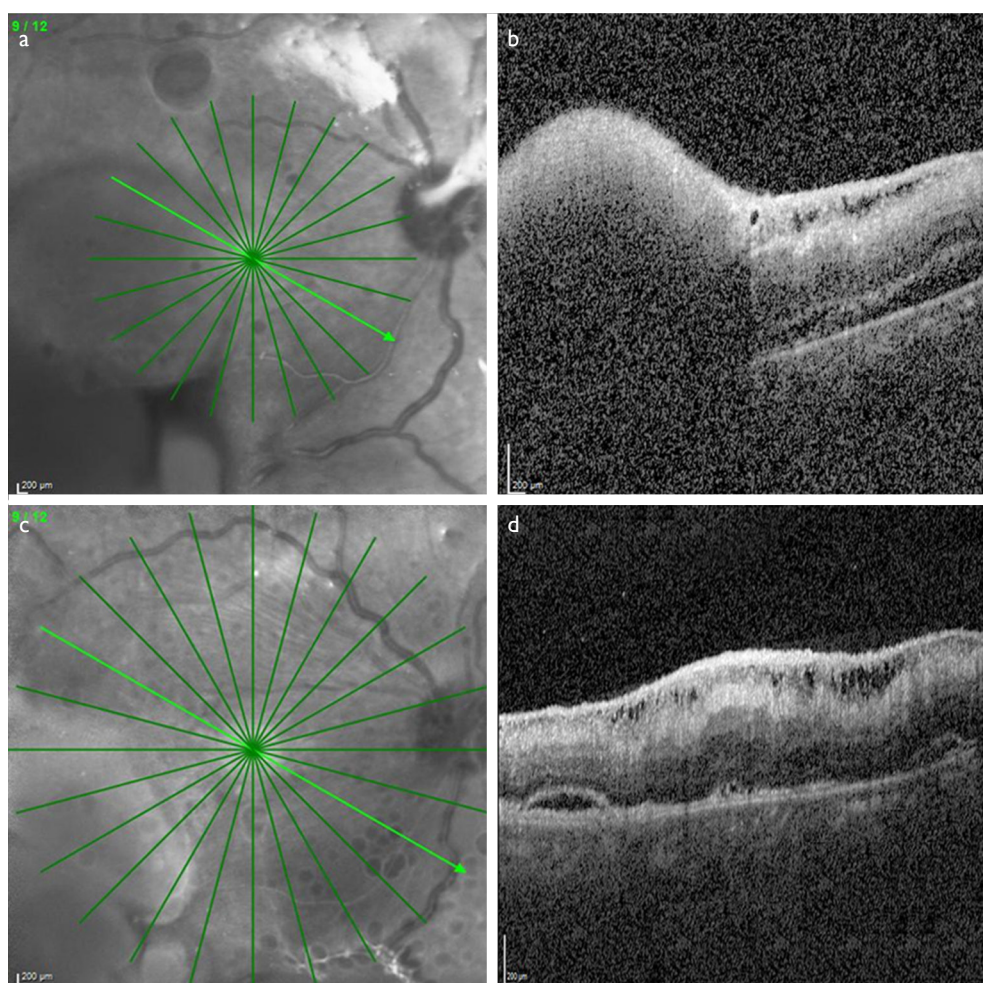
COVID-19 patients who have multifocal pneumonia were more likely to be treated with systemic steroids than no steroid group at admission (14). Furthermore, it was noted that the steroid group had higher rates of bacterial infection (25% vs. 13.1%,  $p=0.041$ ) and fungal infection (12.7% vs. 0.7%,  $p<0.001$ ) during hospital course (14). This may be a possible reason in our patient.

Endophthalmitis in times of COVID-19 pandemic has been described (10, 15-17). However, in all these cases, they were not able to conclusively prove if it was due to bacteria or fungal infections after COVID-19.

In our patient blood, vitreous sample did not yield any bacterial/fungal growth and PCR for viruses and panfungal genome was also negative. Our patient's urine culture yielded *Pseudomonas* which was resistant to almost all antibiotics.

In another series, patients had clinical features of fungal endophthalmitis but no organism was isolated (18).

COVID-19 causing virus is either not detected or detected in a very low percentage in the ocular samples (19). This



**Figure 5.** (a) SD-OCT of the right eye (top) 2 weeks after surgery showing pre-retinal hyper-reflectivity with shadowing of the retina and choroid, while adjacent to it shows inner retinal swelling and mild subretinal fluid and (b) (down) 1 month later showing reduction in the same.



**Figure 6.** (a) Gangrene at the root of the nose (vertical stout down arrow Figure 6a) and presence of purpuric rash beneath it suggesting inflammation (block red arrow) and eschar-like lesions on the forehead (hollow red arrow). (b) Healed gangrene and reduction of eschar a month later.

statement obviously has to take in to account the limitations of all the laboratory tests conducted. This further supports the possibility that the virus seems to have less tropism for

ocular tissues (19).

Skin manifestations have been reported with COVID-19 and have been classified into the following patterns in a re-



cently published review article. They are (i) urticarial rash, (ii) confluent erythematous/maculopapular/morbilliform rash, (iii) papulovesicular exanthem, (iv) chilblain-like acral pattern, (v) livedo reticularis/racemosa-like pattern, and (vi) purpuric “vasculitic” pattern (20).

Our patient had purpuric vasculitic pattern at the root of his nose.

Limitations of this report include inability to culture an organism and bacterial detection was limited to only PCR from the ocular specimens. We were also not able to isolate severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from ocular specimens to conclusively prove it occurred due to COVID-19. Intravitreal antibiotics were continued even in the absence of bacterial growth and there was improvement in the condition. *Pseudomonas* was not isolated from the ocular specimens, and there is a possibility that the endophthalmitis may not have been due to *Pseudomonas* and could be due to a different organism. However, in the absence of any other systemic risk factor except administration of steroids, detection of *Pseudomonas* on urinary culture, and presence of high levels of SARS-CoV-2 antibodies at ocular presentation, we can presume that this condition was aggravated by post-COVID-19 inflammatory status.

## Disclosures

**Informed consent:** Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Concept – S.S., P.M.; Design – S.S., B.P., P.M.; Supervision – S.S., B.P.; Resource – S.S., B.P., R.S.; Materials – S.S., B.P., A.K., E.S., V.C.N.; Data collection and/or processing – S.S., B.P., V.C.N., A.K., R.S., P.M.; Analysis and/or interpretation – S.S., A.K., P.M.; Literature search – S.S., A.K., P.M.; Writing – S.S., P.M.; Critical review – S.S., A.K., P.M.

## References

- Wu P, Duan F, Luo C, Liu Q, Qu X, Liang L, et al. Characteristics of ocular findings of patients with coronavirus disease 2019 (COVID-19) in Hubei Province, China. *JAMA Ophthalmol* 2020;138:575–8. [CrossRef]
- Acharya S, Diamond M, Anwar S, Glaser A, Tyagi P. Unique case of central retinal artery occlusion secondary to COVID-19 disease. *IDCases* 2020;21:e00867. [CrossRef]
- Insausti-García A, Reche-Sainz JA, Ruiz-Arranz C, López Vázquez Á, Ferro-Osuna M. Papillophlebitis in a COVID-19 patient: Inflammation and hypercoagulable state. *Eur J Ophthalmol* 2022;32:NPI68–72. [CrossRef]
- Landecheo MF, Yuste JR, Gándara E, Sunsundegui P, Quiroga J, Alcaide AB, et al. COVID-19 retinal microangiopathy as an in vivo biomarker of systemic vascular disease? *J Intern Med* 2021;289:116–20. [CrossRef]
- Dumitrascu OM, Volod O, Bose S, Wang Y, Biousse V, Lyden PD. Acute ophthalmic artery occlusion in a COVID-19 patient on apixaban. *J Stroke Cerebrovasc Dis* 2020;29:104982. [CrossRef]
- Ortiz-Seller A, Martínez Costa L, Hernández-Pons A, Valls Pascual E, Solves Alemany A, Albert-Fort M. Ophthalmic and neuro-ophthalmic manifestations of coronavirus disease 2019 (COVID-19). *Ocul Immunol Inflamm* 2020;28:1285–9. [CrossRef]
- Sanjay S, Srinivasan P, Jayadev C, Mahendradas P, Gupta A, Kawali A, et al. Post COVID-19 ophthalmic manifestations in an Asian Indian male. *Ocul Immunol Inflamm* 2021;29:656–61.
- Sanjay S, Gowda PB, Rao B, Mutalik D, Mahendradas P, Kawali A, et al. “Old wine in a new bottle” post COVID-19 infection, central serous chorioretinopathy and the steroids. *J Ophthalmol Inflamm Infect* 2021;11:14. [CrossRef]
- Sanjay S, Mutalik D, Gowda S, Mahendradas P, Kawali A, Shetty R. “Post coronavirus disease (COVID-19) reactivation of a quiescent unilateral anterior uveitis”. *SN Compr Clin Med* 2021;3:1843–7. [CrossRef]
- Shroff D, Narula R, Atri N, Chakravarti A, Gandhi A, Sapra N, et al. Endogenous fungal endophthalmitis following intensive corticosteroid therapy in severe COVID-19 disease. *Indian J Ophthalmol* 2021;69:1909–14. [CrossRef]
- Sanjay S, Kawali A, Agrawal S, Mahendradas P. Unilateral acute anterior sclero-uveitis preceding Corona virus disease (COVID-19). *Pan Am J Ophthalmol* 2022;4:26.
- Celiker H, Kazokoglu H. Ocular culture-proven endogenous endophthalmitis: A 5-year retrospective study of the micro-organism spectrum at a tertiary referral center in Turkey. *Int Ophthalmol* 2019;39:1743–51. [CrossRef]
- Comez AT, Komur B, Akcali A, Otkun MT. Ocular aspergillosis: Obtaining a specimen is crucial for diagnosis. A report of three cases. *Med Mycol Case Rep* 2012;1:39–41. [CrossRef]
- Obata R, Maeda T, Rizk D, Kuno T. Increased secondary infection in COVID-19 patients treated with steroids in New York City. *Jpn J Infect Dis* 2021;74:307 15. [CrossRef]
- Available from: <https://www.aao.org/newsroom/news-releases/detail/study-finds-link-between-eye-infection-coronavirus>. Accessed Jan 28, 2022.
- Pirraglia MP, Ceccarelli G, Cerini A, Visioli G, d’Ettorre G, Mastroianni CM, et al. Retinal involvement and ocular findings in COVID-19 pneumonia patients. *Sci Rep* 2020;10:17419. [CrossRef]
- Verma S, Walinjar JA. A case of endogenous endophthalmitis in COVID-19 pandemic. *Apollo Med* 2020;17:229–32. [CrossRef]
- Shah KK, Venkatramani D, Majumder PD. A case series of presumed fungal endogenous endophthalmitis in post COVID-19 patients. *Indian J Ophthalmol* 2021;69:1322–5. [CrossRef]
- Seah IY, Anderson DE, Kang AE, Wang L, Rao P, Young BE, et al. Assessing viral shedding and infectivity of tears in coronavirus disease 2019 (COVID-19) patients. *Ophthalmology* 2020;127:977–9. [CrossRef]
- Genovese G, Moltrasio C, Berti E, Marzano AV. Skin manifestations associated with COVID-19: Current knowledge and future perspectives. *Dermatology* 2021;237:1–12. [CrossRef]