



Endogenous Fungal Endophthalmitis in a Patient Admitted to Intensive Care and Treated with Systemic Steroid for COVID-19

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Abstract

A 61-year-old woman presented to our clinic with complaints of decreased visual acuity, pain, and redness in her left eye. Best corrected visual acuity (BCVA) was 20/20 in the right eye and counting fingers at 3 meters in the left eye. On slit-lamp examination, 1+ cells were detected in the anterior chamber. Fundus examination revealed 1+ haze in the vitreous and multiple creamy-whitish lesions in the retina and vitreous. Her history included a diagnosis of coronavirus disease 2019 (COVID-19) one month earlier, for which she was hospitalized in the intensive care unit for 20 days and received systemic corticosteroid treatment. Vitreous culture yielded *Candida albicans*. The patient's nasopharyngeal swab sample was positive for COVID-19 by reverse transcription polymerase chain reaction test. BCVA was improved to 20/40 after amphotericin therapy (via intravitreal injection and intravenous routes), and the vitritis and chorioretinitis lesion regressed after 2 weeks of treatment. Two weeks later, intravenous amphotericin was discontinued and oral fluconazole treatment was started at a dose of 400 mg/day. At 3-month follow-up, her BCVA was 20/25 and no inflammatory reaction was observed in the anterior chamber and vitreous.

Keywords: Endogenous endophthalmitis, posterior uveitis, endogenous fungal endophthalmitis, coronavirus disease 2019

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Introduction

Endogenous fungal endophthalmitis is a severe ocular inflammation that causes decreased visual acuity.¹ *Candida albicans* is the most common cause of endogenous fungal endophthalmitis, which is associated with predisposing risk factors such as an indwelling catheter, intravenous drug use, immunodeficiency, recent hospitalization, and use of corticosteroids or noncorticosteroid immunosuppressive agents.²

Coronavirus disease 2019 (COVID-19) is a global epidemic caused by a novel coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]).³ Herein, we aim to report a case of *Candida albicans* endogenous endophthalmitis in a patient who required intensive care admission and systemic steroid therapy due to COVID-19 infection. To the best of our knowledge, this is the first description of a case of endogenous fungal endophthalmitis that may be relevant to the current treatment of COVID-19 infection.

Case Presentation

A 61-year-old woman presented to our clinic with a 15-day history of progressively decreased vision, pain, and redness in her left eye. A month earlier, she had been hospitalized in intensive care for 20 days and received systemic steroid for the treatment of COVID-19. Her COVID-19 diagnosis was confirmed by reverse transcription-polymerase chain reaction test of a nasopharyngeal swab sample. The patient had no history of recent ocular trauma, intraocular surgery, or additional systemic disease (diabetes mellitus, malignancy). Systemic dexamethasone and favipiravir had been administered while she was in the intensive care unit.

At presentation, her best corrected visual acuity was 20/20 in the right eye and counting fingers at 3 meters in the left eye. Intraocular pressure was 15 mmHg measured by Goldmann applanation tonometry. On slit-lamp examination, 1+ cells were detected in the anterior chamber. Fundus examination revealed multiple creamy-white intravitreal lesions in the vitreous and retina (Figure 1). Examination of the right eye was normal.

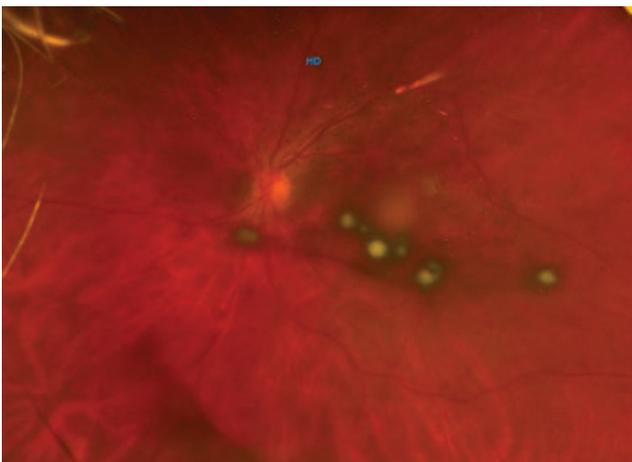


Figure 1. Widefield fundus image showing multiple creamy-white intravitreal lesions in the vitreous and retina

A comprehensive uveitis screening was performed, including chest X-ray, hemogram, biochemical investigations (plasma creatinine, potassium, sodium, C-reactive protein, erythrocyte sedimentation rate, urinary albumin to creatinine ratio, aspartate aminotransferase and alanine aminotransferase, alkaline phosphatase, and γ -glutamyl transferase), serology for *Toxoplasma*, venereal disease research laboratory pathogens, human immunodeficiency virus, hepatitis C and B virus, Epstein-Barr virus, cytomegalovirus, and varicella zoster virus. The results of all tests were normal or negative. In light of her medical history and clinical findings, we suspected endogenous endophthalmitis, and performed a vitreous tap of her left eye with intravitreal injection of empirical amphotericin (0.005 mg/0.1 mL), vancomycin (1 mg/0.1 mL), and ceftazidime (2.25 mg/0.1 mL). The vitreous specimen was plated directly onto chocolate agar, 5% sheep blood agar, and Sabouraud agar. Sabouraud agar was incubated at 35 °C for 72 hours and then at 25 °C for up to 2 weeks. The plate was examined daily for the detection of fungal growth. Colonies suggestive of fungal growth were evaluated by Giemsa and calcofluor white stains and with slice culture to detect microscopic morphologic features and characteristic conditions. The vitreous culture result was positive for *Candida albicans* (Figure 2). PCR test of the vitreous sample was negative for SARS-CoV-2. After culture positivity, a second dose of intravitreal amphotericin was administered and an intravenous form of the drug was added to treatment at 3 mg/kg/day. She also received routine topical uveitis treatment (prednisolone acetate 0.1% and cyclopentolate hydrochloride 1.0%) for her left eye. Visual acuity improved to 20/40, and after 2 weeks of treatment there were no signs of vitreous infiltrates and the chorioretinitis lesion has regressed (Figure 3). Intravenous amphotericin was stopped 2 weeks after admission and treatment was continued with oral fluconazole 400 mg/day. Best corrected visual acuity was 20/25 at 3-month follow-up and no inflammatory reaction was observed in the anterior chamber or vitreous.

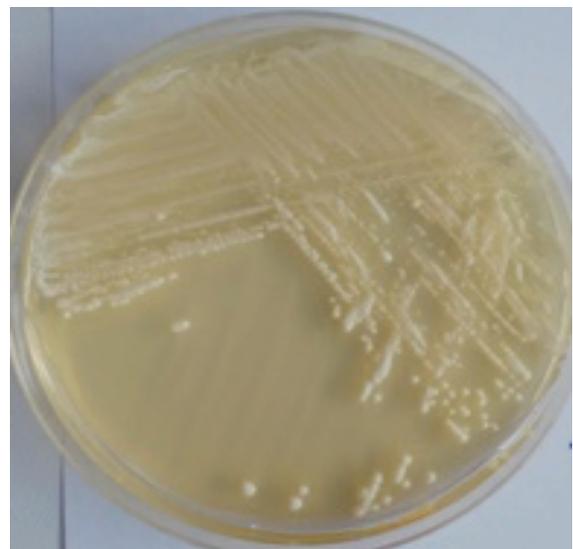


Figure 2. *Candida albicans* isolated by vitreous culture on Sabouraud agar



Figure 3. Widefield fundus image 2 weeks after intravenous amphotericin treatment

Discussion

Endogenous fungal endophthalmitis would be expected in an immunosuppressed patient with risk factors such as chronic immune-compromising disease, intravenous catheters, use of broad-spectrum antibiotics, immunosuppressive agents, or steroids, and diabetes mellitus.^{1,4} As COVID-19 is a new disease, there is still limited evidence about it and the outcomes of treatment.⁵ Hospitalization and systemic steroid use may be required during the treatment and management of COVID-19.⁶ Presented here is a case of endogenous fungal endophthalmitis in a patient who required intensive care admission and systemic steroid use for the treatment of COVID-19.

Endogenous fungal endophthalmitis generally begins with choroidal spread and eventually invades the vitreous. In candidemia, the incidence of chorioretinitis is 11%, while that of endophthalmitis is only 1.6%.⁷ It progresses slowly, some cases are clinically silent at the early stage, and symptoms usually increase after notable vitritis. Some patients develop subretinal abscess, which generally has a poor visual prognosis. Subretinal abscess is often associated with mold rather than yeast endophthalmitis.⁸

There is still controversy regarding the ophthalmological effects of SARS-CoV-2 and whether transmission can occur via ocular tissues (tears). In the studies and case reports in the literature, SARS-CoV-2 was detected in ocular samples in a very small proportion of patients who were positive for COVID-19.⁹ It was also reported that SARS-CoV-2 has a lesser tropism for ocular tissue than the respiratory tract.¹⁰ Gupta et al.¹¹ reported a case of atypical acute retinal necrosis in a COVID-19-positive immunosuppressed patient, but PCR test of a vitreous specimen was negative for SARS-CoV-2. Furthermore, in-vivo animal experiments on this subject have shown that coronaviruses can increase blood-retinal barrier destruction.^{5,12} Perhaps the fact that the patient was positive for COVID-19 in our case caused a breakdown of the blood-retinal barrier, facilitating the development of endogenous fungal endophthalmitis.

The pandemic has spread rapidly, and it is important to report cases associated with COVID-19. Further studies may show how the SARS-CoV-2 virus and treatment of COVID-19 interact with ocular tissue. The treatment of COVID-19 may lead to other opportunistic infections for reasons such as hospitalization, intravenous drug administration, and broad-spectrum antibiotic and systemic steroid use. We recommend that endogenous endophthalmitis be kept in mind in patients who present with complaints of decreased visual acuity and have a history of systemic steroid therapy and hospitalization for COVID-19.

Ethics

Informed Consent: Obtained.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: S.T.K., A.K., B.E.Ç., Concept: S.T.K., A.O.S., Design: S.T.K., A.K., B.E.Ç., A.O.S., Data Collection or Processing: S.T.K., A.K., B.E.Ç., Analysis or Interpretation: S.T.K., A.K., A.O.S., Literature Search: S.T.K., A.K., Writing: S.T.K., A.K.,

Conflict of Interest: No conflict of interest was declared by the authors.

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