

Commentary: The daunting enigma of post-COVID-19 endogenous endophthalmitis

Visual deterioration following COVID-19 virus-related ocular involvement has been responsible for reduced mobility, increased dependence, and subsequent deterioration in the quality of life for patients after being discharged from intensive care units.^[1]

Sight-threatening COVID-19-related ocular involvement (CROI) can be classified broadly under two categories: a) noninfectious retinochoroidal involvement led by COVID-19 inflammatory syndrome and b) nosocomial/opportunistic infections. Both remain a sequel to the primary disease process rather than a direct manifestation.^[1,2] For the former, COVID-19 inflammatory syndrome can present with inflammatory blood dyscrasia responsible for retino-optic vascular thrombosis or may even present with features of posterior uveitis such as retinitis, choroiditis, and vasculitis.^[2,3]

The second subset of patients consists of those who are at the risk of developing secondary infectious diseases due to long-term hospital stays, prolonged parenteral therapy, and extended use of systemic steroids in a nosocomial setting of a critical care unit. The altered consciousness and the vegetative state of patients in critical care units make them not only vulnerable but also less aware of the ocular symptoms in the early stage of the disease.^[1] Of the known sight-threatening manifestations developing in patients admitted for assisted ventilation, exposure keratopathy and secondary infectious keratitis-associated visual impairment are reported to be the most common, followed by endogenous endophthalmitis.^[1]

Patients developing endogenous endophthalmitis have been reported to present with symptoms within a minimum of 6 days following discharge. Although the presence of vitreous exudates and yellow-white subretinal granulomas are more

consistent for the diagnosis of endophthalmitis, the variable grades of anterior segment inflammation and vitritis are the common presenting nonspecific features, which are often misleading and can be confused to be a sterile inflammatory response in the absence of any specific clinical finding.^[4] This often leads to a delay in diagnosis as well as providing appropriate intervention.^[5]

Of note is that all the reported cases of endophthalmitis in COVID-19-infected individuals share a common ground of prolonged hospital admission (>2 weeks) and the use of systemic steroids for more than 10 days.^[4-6] Though both bacteria and fungi have been reported to cause post-COVID-19 endophthalmitis, fungal isolates such as candida, aspergillus, and mucormycosis have been more commonly reported. The resurgence of fungal endogenous endophthalmitis in the COVID-19 era can be well attributed to the extended use of steroids and broad-spectrum antibiotics along with the constitutional immunosuppression and neutrophil dysfunction levied by the COVID-19 virus.^[7]

Neutrophils are known to be the first line of defense against fungal infections. Although patients with COVID-19 infection have neutrophilia with lymphopenia unlike other viral infections, the neutrophils are not competent to neutralize the bugs; this puts the patient at greater risk of secondary fungal infections.^[8]

Khalid *et al.*^[9] in their study evaluating the role of fundus examination in patients with fungemia noted that retinal examination could detect ocular involvement in 12.5% of the cases, of which only 1/3 were symptomatic. For patients at risk of developing fungemia/bacteremia, it is important to understand the following points. 1) Not all cases with bacteremia or fungemia may develop endophthalmitis despite being at risk. 2) Asymptomatic diseases in the early phases can only be picked up by thorough fundus evaluation and should be considered for all high-risk cases admitted in critical care units during their stay and following their discharge.

3) Similarly, all high-risk patients must undergo fundus examination at the slightest of doubt during the follow-up visit, even if the initial examination at the time of discharge is negative for endogenous endophthalmitis.

A recent series on endogenous endophthalmitis in COVID-19 patients requiring hospitalization showed rapid progression of the endophthalmitis with loss of functional vision over 7 days after the onset of symptoms.^[6] Due to availability and logistics-related challenges, it might not always be possible for all admitted patients to undergo a dilated fundus examination. However, a simple test of bedside visual acuity evaluation during admission and at the time of discharge can assist in the early identification of visual symptoms wherein timely intervention can provide an opportunity to salvage vision.

In compendium, the learning from the existing literature on post-COVID-19 endophthalmitis highlights three essential aspects.

1. Even though systemic steroids are required to reduce the mortality of COVID-19-related respiratory distress for patients requiring oxygen support, extending its usage beyond the recommended 10-day regimen can have detrimental effects and can increase the vulnerability toward opportunistic infections.
2. The diagnosis of endogenous endophthalmitis should be considered for patients presenting with any form of intraocular inflammation and having a history of prior hospitalization and steroid therapy.
3. Bedside fundus examination should be considered in high-risk cases for hospital-acquired infections, which include patients with prolonged duration of admission, intravenous line, and those who received systemic steroids for more than 10 days.

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