

Clinical manifest of post COVID-19 syndrome on ocular surface and cornea

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Abstract: Coronavirus disease (COVID – 19) was one of the most severe pandemics that the world has ever seen. The infection ranges from asymptomatic, mild to life threatening respiratory distress. It can affect almost every organ of the body, including the organ of vision. Ophthalmic manifestations may be present in the course of COVID-19 infection or they may develop later in rehabilitation period. The aim of the research is to facilitate the diagnostics and initiation of comprehensive therapy of pathological eye conditions of ocular surface and cornea that occur in coronavirus disease.

The coronavirus global pandemic has caused significant negative effect on lives of millions with diversity of clinical features and life and sight – threatening consequences. The full spectrum of the disease is yet to be unraveled. A simple search of 'COVID-19 Ophthalmic manifestation ' in search engines throws up over 100 publications. We believe it is important for ophthalmologists to have knowledge about the ophthalmic manifestations of the novel viral infection in order to suspect, diagnose, refer and treat the conditions with skills, machinery, and drugs that we already possess. This article gives an overview of the ophthalmic conditions that have been associated with the virus, directly or indirectly. We have also tried to categorize the manifestations into the phase of the coronavirus disease-19 (COVID-19) when they are most likely to present.

Methods

Literature research has been made in PubMed for 'COVID-19 ocular surface and cornea'. Articles in the English language, published between January 1, 2020 to January 31, 2020, were studied, analyzed and presented in the given article. All the cases were diagnosed as COVID-19 based on nasopharyngeal or oropharyngeal swabs or antibody titers.

Ocular surface and cornea

Our literature research has resulted in findings of various types of corneal, conjunctival and scleral inflammatory process that are reported in the following list.

Follicular conjunctivitis

Conjunctivitis is the most common ophthalmic manifestation documented in COVID-19 patients. In a large series of cases with mild COVID-19 infection, Sindhuja *et al.* reported that 11/127 (8.66%) patients had conjunctivitis. All symptomatic patients gave a history of redness of one or both eyes. Presence of respiratory tract symptoms were associated with conjunctival congestion. A positive history of hand-eye contact was elucidated in four patients; however, this did not attain clinical significance as a risk factor.[¹] This was different from the results of a cross-sectional study performed by Chen *et al.* in 535 cases of COVID-19 patients which showed that hand-eye contact was independently correlated to the presence of conjunctival congestion amongst patients.[²]

Chen *et al.* suggested that ocular manifestations are more common in the middle phase of the disease based on their findings of bilateral acute follicular conjunctivitis in a patient on the 13th day of the illness. [Fig. 1] The conjunctival swab remained positive for five days, though with progressively increasing cycle threshold (Ct) values.[³] Nayak *et al.* reported delayed onset of follicular conjunctivitis four weeks after severe COVID-19 infection in a 65-year-old male with diabetes, hypertension, and asthma. The conjunctival swab did not reveal any bacterial or fungal infection. The conjunctivitis resolved in two weeks with lubricants and preservative-free moxifloxacin eye drops. The authors also concluded that virus shedding in the conjunctiva may persist even after the nasopharyngeal swab becomes negative for SAR-

CoVvirus.[4]

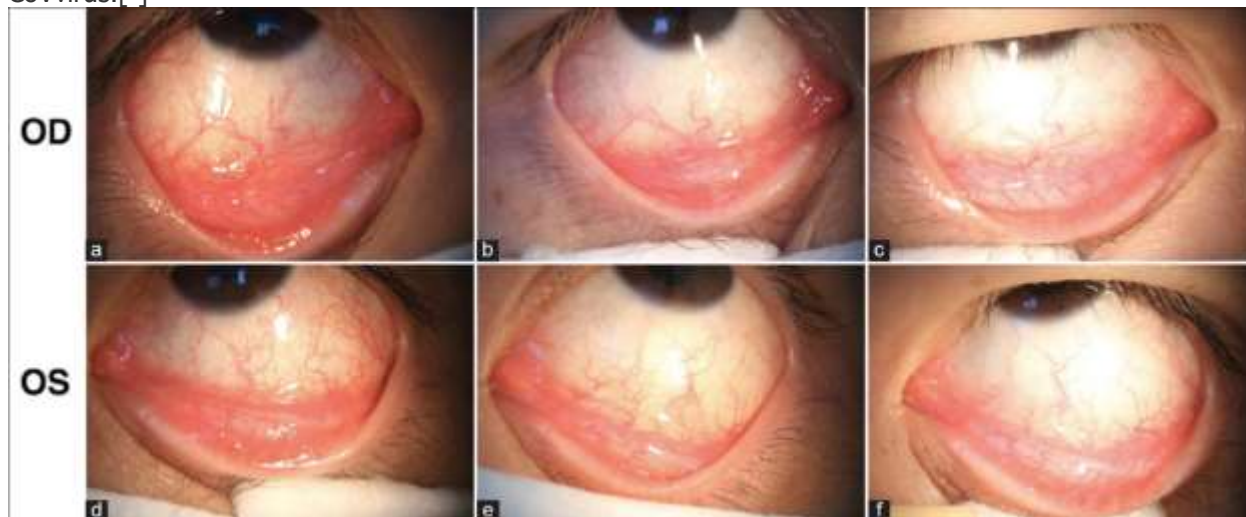


Figure 1:

Follicular conjunctivitis following COVID-19: A 30-year-old man developed bilateral follicular conjunctivitis 13 days after mild COVID-19 infection. Slit lamp examinations showed evidence of acute viral conjunctivitis. (a and d)The examination on illness day 13 showed moderate conjunctival injection and inferior palpebral conjunctival follicles. (b and e) Examinations on illness day 17 and (c and f) illness on day 19 demonstrated that treatment with ribavirin eye-drops gradually improved the patient's symptoms. (Reproduced with permission from Chen L, Liu M, Zhang Z, Qiao K, Huang T, Chen M, Xin N, Huang Z, Liu L, Zhang G, Wang J. Ocular manifestations of a hospitalised patient with confirmed 2019 novel coronavirus disease. *Br J Ophthalmol.* 2020;104:748-51)

Viral keratoconjunctivitis

Keratoconjunctivitis as the initial presentation in a patient with mild respiratory symptoms has been reported by Cheema *et al.* The patient presented with redness, discharge, and photophobia and was treated as herpetic keratoconjunctivitis, and later, as epidemic keratoconjunctivitis with oral valacyclovir and topical moxifloxacin. SARS-CoV-2 testing was done only in view of updated guidelines for testing patients with travel history in Canada. The nasopharyngeal and conjunctival swabs both turned out to be positive. This case highlights the importance of considering conjunctivitis as a presenting symptom of COVID-19.[5]

In a case report from China, Guo *et al.* reported a patient with moderate-severe COVID-19 infection with left eye conjunctivitis developing ten days after COVID-19 symptoms. In the first episode, the cornea was clear, and patient had viscous discharge. Conjunctival swab was positive for SARS-CoV-2 virus ribonucleic acid (RNA) by reverse transcriptase polymerase chain reaction (RT-PCR) but not for herpes simplex virus (HSV) or adenovirus and this was repeated daily. On the second day after initiation of treatment with topical levofloxacin and sodium hyaluronate, the swab became negative. Patient recovered well within a week but presented with a relapse and peripheral corneal staining in both eyes after five days. This time the conjunctival swab was negative for both SARS-CoV-2 and HSV. However, the interleukin-6 (IL-6) levels showed ten-fold elevation in the left eye. With an immune-mediated pathogenesis in mind, topical fluoromethalone was started and patient responded well with complete resolution. Since SAR-CoV-2 virus was detected in the conjunctiva, the first episode of conjunctivitis was attributed to local invasion and inflammation of the ocular surface caused by the virus. It was localized to the left eye with resolution within a week. The relapse, with more widespread bilateral manifestation, on the other hand, was presumed to be due to a cytokine surge caused by an autoimmune response mediated by the virus. A longer follow-up with proper use of topical glucocorticoid is recommended by some to diminish the risk of immune-mediated keratoconjunctivitis.[6]

Hemorrhagic and pseudomembranous conjunctivitis

Navel *et al.* in France reported a case of a 63-year-old male patient with severe COVID-19 infection, admitted in intensive care unit (ICU), developing hemorrhagic and pseudomembranous conjunctivitis 19 days after the onset of systemic symptoms. Treatment was with azithromycin and dexamethasone drops and daily debridement of pseudomembrane.[7]

Conjunctivitis in children

A 30 fold increase in the incidence of Kawasaki disease-like condition has been reported in children in some parts of Italy with strong association with COVID-19. This atypical presentation is known as multisystem inflammatory syndrome in children (MIS-C).[8] Kawasaki disease, a form of self-limiting vasculitis, is associated with iridocyclitis, punctate keratitis, vitreous opacities, papilloedema, subconjunctival hemorrhage and conjunctival injection.[9] In the literature

available on MIS-C, the ophthalmic manifestations have mainly been in the form of conjunctivitis.^[8] MIS-C is commonly being noted to have serological positivity for SARS-CoV-2 than on nasopharyngeal swab indicating it to be a manifestation of delayed immunological response to COVID-19. Treatment is directed towards suppressing the systemic inflammation. Corticosteroids, intravenous immunoglobulin (IVIG) and aspirin have been used in the cases reported.^[8]

Episcleritis

A case of episcleritis as the initial manifestation of COVID-19 has been described in a 29-year old male by Otaif *et al.* Patient had history of foreign body sensation in the left eye and examination revealed nasal conjunctival and episcleral congestion with blanching with phenylephrine. He developed mild viral infection with symptoms appearing three days after the ocular signs.^[10] Managna *et al.* reported another case of episcleritis which developed seven days after the onset of symptoms of COVID-19 infection. Most cases of episcleritis are idiopathic and self-limiting. About a third of them may be associated with viral infections including ebola, HSV and hepatitis C and now possibly, SARS-CoV-2 virus.^[11]

Conclusion

The prevalence of ophthalmic manifestations among COVID-19 patients ranges from 2-32%.^[12] The given complications certainly deteriorate the life quality of individuals with COVID-19 infection. Thus it is crucial for eye-care specialists to get familiarized with the data provided in fresh researches carried out worldwide as well as in the given literature review and to be able to recognize and address them with sophisticated knowledge.

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