

Coronavirus disease-19 disease in ophthalmology

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Since the outbreak of the severe acute respiratory syndrome (SARS) coronavirus 2 (CoV-2) pandemic, more than 29.6 million positive cases have been confirmed, 20.1 million people have recovered and nearly 1 million people have died. Mexico has reported 676,000 positive cases, 481,000 of these individuals have recovered and 71,678 deaths as of September 15, 2020. According to the World Health Organization (WHO), the most frequent clinical symptoms are fever (87.9%), fatigue (69.6%), dry cough (67.7%), anosmia and myalgia (34.8%), as well as dyspnea and conjunctivitis (10-20%). In more severe cases, pneumonia, SARS, multiple organ dysfunction syndrome, and death may occur^{1,2}.

Ophthalmological symptoms played a major role in the identification of this new disease as they were described for the first time in the world by Chinese ophthalmologist Li Wenliang (who unfortunately died from complications of the disease) in the community of Wuhan, China, in December 2019. Dr. Wenliang warned about a group of patients with atypical viral conjunctivitis associated with severe SARS-like respiratory symptoms that triggered the global epidemic in 2003³.

The WHO defined SARS-CoV-2 CoV disease (COVID) as a pandemic on March 11, 2020. CoVs are in the family Nidovirus. This subfamily of CoVs has four genera (alpha, beta, gamma, and delta). Alpha-CoVs and beta-CoVs infect humans; beta-CoVs are responsible for the Middle Eastern Respiratory Syndrome CoV and SARS-CoV and SARS-CoV-2.

All Coronaviridae are called enveloped viruses because of the lipid membrane that surrounds their crown-shaped capsid. They contain positive chain RNA as their genomic material, considered one of the largest (27-32 kb) among RNA viruses. This genome is protected inside the nucleocapsid, which is helicoidal when relaxed, and spherical when inside the virus. CoV RNA replicates in the cytoplasm of the host cell. The CoV genome encodes four proteins: spike (S), nucleocapsid (N), membrane (M), and envelope (E). The proteins of the nucleocapsid, membrane, and envelope are mainly involved in the formation and structuring of the virus, while the spike proteins are also involved in the binding of host cells.

SARS-CoV-2 is a highly infectious virus that can survive in the air from 2 to 9 h. Incubation time is approximately 4-8 days after infection. All age groups are vulnerable to infection and the main route of transmission of the infection is through airborne/throat spread or "respiratory route" through droplets or aerosols from an infected patient, contaminated dust, or liquids. The mode of transmission through the eye is by direct inoculation of drops onto the eye surface; in patients who already have respiratory disease, secondary ocular involvement is due to the virus migrating up the upper respiratory tract through the nasolacrimal duct. In addition, hematogenous infection of the lacrimal gland may also occur.

The presence of the SARS-CoV-2 virus on the ocular surface, corneal epithelium, conjunctival epithelium,

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and tear film as a potential portal of entry and transmission mechanism is currently under investigation as there are interesting data to be analyzed:

1. The ocular surface has the heparan sulfate receptor, which facilitates viral adhesion. However, this alone is not sufficient for a CoV infection. Moreover, the tear film has high concentrations of lactoferrin (2mg/ml), which prevents viral adhesion.
2. The ocular surface appears to possess the ACE2 (angiotensin-2 converting enzyme) receptor, but does not exhibit the serine protease, which is required for the SARS-CoV2 spike protein to bind to the ACE2 receptor.
3. The other CoV coreceptors (CD29, CD26, CD 13, and CD66e) have been found in fibroblasts and dendritic cells below the corneal and conjunctival surface. Therefore, data evidence suggests that the binding of the CoV to the ocular surface is unlikely for the onset of an infection. This reinforces the theory that the virus can be deposited on the ocular surface, mix with the tears, and travel with them through the tear duct (lacrimal points, canaliculi, and nasolacrimal duct) to the nasal mucosa where it is actually "adhered" by the cells of the respiratory tract.

The ophthalmological implications of the disease have been updated continuously in the international literature. Follicular conjunctivitis is the most common ocular manifestation of the disease and can occur alone or associated with mild respiratory symptoms. Other ocular manifestations are chemosis, lacrimation, pruritus, hyperemia, ciliary injection, anterior uveitis, foreign body sensation, ocular pain, painful preauricular lymph nodes, decreased visual acuity, subconjunctival hemorrhage, and hyaline secretion. Some reports indicate the presence of vasculitis and retinal necrosis, associated with alterations in the central nervous system, in patients with severe COVID-19. However, it is not possible to directly assign the damage to the SARS-CoV-2 virus, as there are no studies of the damaged structures before the infection or the presence of concomitant diseases.

The SARS-CoV-2 virus has been shown to be found in the tears and conjunctival secretions of patients suffering from CoV pneumonia with conjunctivitis. However, the virus has not yet been detected in the tears or conjunctival secretions of patients without conjunctivitis. It has not been possible to establish whether the virus colonizes or actually invades the eye tissue, as screening tests by swabbing the palpebral sac and respiratory mucosa have not been positive in all cases. With regard to COVID-19 severity, patients with ocular

symptoms are more likely to have high leukocyte and neutrophil counts, high levels of procalcitonin, C-reactive protein, and lactate dehydrogenase.

A study conducted by Wu et al. in February 2020, reported that out of 38 patients studied, all of them of Asian origin, a third of them presented with ophthalmological manifestations. Another report by the WHO in China with 55,924 cases, reported that 0.8% of the patients presented with signs of conjunctivitis. However, in patients with severe pneumonia, this percentage increased to 10%⁴⁻⁷.

Three cases of pseudomembranous hemorrhagic conjunctivitis related to SARS-CoV-2 were recently described. One of them was a 63-year-old man admitted to an intensive care unit for SARS diagnosed 17 days before he presented ocular manifestations. The clinical signs were conjunctival follicles, petechiae, tarsal hemorrhages and chemosis, as well as pseudomembranes (thin translucent membranes that can be easily detached without bleeding) without identifying bacteria or viruses in the conjunctival secretion cultures. The other two cases were reported in a couple of passengers of the Diamond Princess Cruise with positive polymerase chain reaction (PCR) tests, who were asymptomatic⁸.

In May 2020 in China, a series of nine patients tested positive by PCR from nasopharyngeal swab specimens and other two patients tested positive by antibody test for COVID 19, with mild symptoms of fever, asthenia, and dyspnea. By means of optical coherence tomography (OCT) DRI: OCT Triton Swept Source and XR Avanti SD-OCT, they presented hyper reflective lesions at the level of the ganglion cell layer and more prominent internal plexiform layer in the papillomacular bundle region. Four patients had subtle cotton wool spots and micro-hemorrhages in the retinal arteries; being the first report of retinal findings associated with COVID-19 infection. As associated pathologies, endogenous endophthalmitis of very bad prognosis and the presence of fast-developing cataracts have been reported.

Treatment for SARS-CoV-2-associated conjunctivitis is mostly supportive. The use of topical anti-inflammatory drugs, such as 0.9% bromfenac is recommended, with a drop every 12 h for 10 days, as well as vasoconstrictors, lubricants, and cold compresses. Most cases are self-limited, hygienic measures should be strict (frequent hand washing, especially when applying the eye drops, suspended use of contact lenses, no touching or rubbing of the eyes, and constant change of bed covers and towels)^{3,9-12}.

Conjunctivitis or simple lacrimation may be the first manifestation of COVID-19. Although they are not as

frequent as cough, fever or headache, it is essential that physicians in any specialty consider this possibility and take proper personal protective measures to prevent spread, request confirmatory studies (PCR) and recommend immediate isolation. Conjunctivitis on its own is usually a self-limiting and benign condition.

Conflicts of interest

The author has no conflicts of interest.

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