

PEER REVIEWED

# Ocular Complications of Confirmed COVID-19 in a Systemically Asymptomatic Patient Using Telehealth: a Teaching Case Report and the Optometrist's Role in Culturally Competent Public Health

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## **Abstract**

*The rapid spread of novel coronavirus SARS-CoV-2 (COVID-19) ignited alarm nationally and globally. COVID-19 spreads via droplets transmitted into the air from coughing or sneezing, which can be attracted through the nose, mouth or eyes. Much remains unknown about this virus. Clinicians must be on high alert to detect potential ocular complications of systemic disease. This teaching case report outlines diagnosis, management, public health reporting and treatment of a patient with follicular conjunctivitis as a primary symptom of COVID-19 and highlights the importance of the clinician's role in using telehealth.*

**Key Words:** COVID-19, follicular conjunctivitis, telehealth, public health, cultural competence

## **Background**

Follicular conjunctivitis presents as a local host response to an exogenous substance or agent producing prominent subconjunctival lymphoid follicles. Viruses, chlamydia and other bacteria can produce the problem.<sup>1</sup> New cases of coronavirus disease 2019 (COVID-19) have escalated around the world. As local, state and national governments take extraordinary measures to limit its spread, uncertainty remains regarding how this virus may present in each organ system. There is known damage to the respiratory system, causing edematous mucous membranes, damaged alveoli, scar tissue, impaired oxygen flow and acute respiratory distress syndrome.<sup>1</sup> Experts have reported that organs other than the lungs can be affected by the virus, but data regarding ocular manifestations is limited.<sup>2</sup> Careful history, clinical examination and lab tests are required to diagnose COVID-19. This teaching case report is significant in that it highlights one of only a few reported ocular findings associated with COVID-19. It is intended for third- and fourth-year optometry students and all eyecare providers in clinical care.

## **Case Description**

A 48-year-old Hispanic male presented to a local hospital on April 27, 2020, with complaints of watery eyes, sensitivity to light and mild eye pain. He also reported his wife had been experiencing chest pain and breathing problems for two days. She was immediately referred to the emergency department and she tested positive for COVID-19. The patient had no systemic symptoms, but he also was administered a nasopharyngeal swab test for COVID-19, which returned positive. He reported being a construction

worker and disclosed no known history of exposure to others with COVID-19. His wife was a stay-at-home mom. He was sent home with the recommendation to quarantine for two weeks unless additional problems occurred.

The patient returned to urgent care two days later, on April 29, 2020, reporting chronic eye irritation. He tested positive a second time for COVID-19. His temperature was 98.6 degrees Fahrenheit, and physical examination showed normal findings except for tender pre-auricular lymph nodes on both sides. The patient's height was 5 ft. 11 in. and his weight was 170 pounds. His blood pressure was 115/78 mmHg. The primary care physician documented risk stratification as low based on respiratory rate, negative hypoxia, no change in mental state and no signs of being critically ill. Serology testing was ordered to determine whether the patient had antibodies for COVID-19 or false-positive previous test results. Additional blood work was ordered to assess D-dimer, ferritin and C-reactive protein (CRP) levels.

The patient was referred to primary care optometry the same day and examined via telehealth with the assistance of medical technology services using personal protective equipment. On admission to the eye service, a COVID-19 case history protocol was followed. History of present illness included foreign body sensation and watering in both eyes. The patient denied having similar eye problems in the past. He reported that he was not experiencing ocular burning, itching, flashes, floaters or fluctuations in vision. He stated he had not been rubbing or touching his eyes with his hands. His last comprehensive well care examination was five months prior. Periorbital pain scale evaluation was 4/10 for both eyes.



**Figure 1.** When the patient was admitted to the eye service, slit lamp examination revealed follicular conjunctivitis in the inferior fornix of both eyes (right eye shown). [Click to enlarge](#)



**Figure 2.** When the patient was admitted to the eye service, OCT showed no thinning of the retinal nerve fiber layer in either eye. [Click to enlarge](#)

Visual acuities were measured as 20/20 OD, 20/20 OS at distance and 20/30 OD, 20/30 OS at near without correction. Slit lamp examination revealed notable inferior conjunctival follicles in both eyes (**Figure 1**). Lids, lashes, cornea and anterior chamber were all unremarkable. There was watery discharge OD and OS. No mucopurulent discharge, injection or scarring was noted. Intraocular pressures, measured at 9 a.m. with iCare tonometry, were 14 mmHg OD and 11 mmHg OS. Conjunctival reverse transcription polymerase chain reaction (RT-PCR) testing for COVID-19 was performed (sterile swab, each fornix, without anesthesia).

Dilated fundus examination showed cup-to-disc ratios of 0.6 OD and 0.6 OS. Optical coherence tomography (OCT) scans (Zeiss Cirrus, optic disc cube 200x200) of both eyes, with reliable signal strengths, showed retinal nerve fiber layer thickness within normal limits (**Figure 2**). Fundus photographs (Zeiss Clarus 500 v1.0) were unremarkable with no signs of thrombosis OD or OS (**Figure 3**). The patient was instructed to use artificial tears four times per day and warm compresses three to four times per day. He was scheduled for a follow-up visit in two weeks and released to continue self-quarantine.



**Figure 3.** Initial fundus photographs of each eye. Dilated fundus exam showed cup-to-disc ratios of 0.6 OD and 0.6 OS and no specific areas of concern.

[Click to enlarge](#)

Two weeks later, on May 13, 2020, the patient participated in a telehealth home visit and reported intermittent relief. He was informed that the previously performed fornix swab testing was positive for COVID-19, consistent with his serological test results, which showed positive antibodies for the virus. Results of the other previously performed blood tests showed D-dimer, ferritin and CRP within normal ranges. Positive tests were reported to the department of public health. Exam findings were consistent with findings two weeks prior except the patient reported photophobia on this particular day. Supportive treatment was continued.

Two weeks later, on May 27, 2020, during a home telehealth phone consultation, the patient reported he had been free of all ocular symptoms for the past 24 hours. With asymptomatic systemic COVID-19 infection, he continued home isolation and monitoring and the recommended ocular support care for another two weeks. Three other members of the household — two teenage children and the patient's mother-in-law — had tested positive for COVID-19 via nasopharyngeal swab tests over a period of four weeks. The teenagers' only symptoms were loss of taste and sense of smell. The patient's mother-in-law was hospitalized due to breathing problems and chest pain. All members of the family recovered (**Figure 4**).



**Figure 4.** Timeline of patient's COVID-19 exposure, quarantine, positive test results and ocular symptoms.

[Click to enlarge](#)

## Education Guidelines

### *Key concepts*

1. Follicular conjunctivitis has a viral component; therefore, differential diagnoses should include COVID-19. This may help eyecare providers in recognizing COVID-19
2. A multispecialty medical team, which includes eyecare professionals, is an essential standard of care for optimal patient outcomes
3. When cases of COVID-19 are diagnosed in eyecare practice, public health reporting systems are a key component of completing the public health triad of test, treat and trace
4. Telehealth is a useful component of patient care in optometric practice and may help with cultural understanding and communication and effectively increase interaction with patients across cultures, especially those with disparities in eye health

### *Learning objectives*

At the conclusion of this case discussion, participants should be able to:

1. Understand both the current definition of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as well as the disease name COVID-19 as outlined by the International Committee on Taxonomy of Viruses (ICTV)
2. Develop a case history protocol for diagnosing COVID-19 patients under investigation (PUI) who are symptomatic or asymptomatic in eyecare practice
3. Recognize systemic and ocular findings associated with COVID-19 including follicular conjunctivitis
4. Understand ocular tests, lab tests and ancillary tests and how they can be used to diagnose and manage COVID-19 patients
5. Understand public health reporting and the triad of test, treat and trace to mitigate disease spread
6. Provide culturally competent patient education including co-management with other specialists,

using telehealth when necessary

*Discussion points*

1. Knowledge and concepts required for critical review of the case:
  - a. What virus name, virus classification and disease name have been specified for COVID-19?
  - b. What pertinent questions should be included in the case history protocol for COVID-19 PUI to improve clinical decision-making and identification of risk factors?
  - c. What organ systems are known to be affected by COVID-19?
  - d. What are the current known ocular manifestations of COVID-19?
2. Differential diagnosis:
  - a. What are the differential diagnoses of follicular conjunctivitis?
  - b. What is the purpose of test, treat and trace for COVID-19?
  - c. How is reporting done for confirmed cases of COVID-19?
  - d. What tests are available for systemic and ocular complications of COVID-19?
3. Disease management:
  - a. How would you manage follicular conjunctivitis as an ocular complication of COVID-19?
  - b. How would you utilize a multispecialty team to treat a COVID-19 patient?
  - c. Describe the role of telehealth in the management of COVID-19 patients
4. Patient education:
  - a. What role does cultural competence play in COVID-19?
  - b. How would you educate the patient regarding this diagnosis?
  - c. What other important outcomes should be discussed?
5. Critical thinking:
  - a. What personal protective equipment is needed to examine PUI for COVID-19?
  - b. How can digital tools be used in contact tracing for confirmed cases of coronavirus?
  - c. What role does quarantine play in this case?

**Discussion**

Coronaviruses are not new pathogens. They were first isolated from chickens in 1937. Human coronaviruses were identified in the mid-1960s.<sup>3</sup> On Dec. 31, 2019, the World Health Organization (WHO) China Country Office was notified about several cases of pneumonia of unknown etiology in Wuhan City, China. Immediately following, China's National Health Commission reported that the

outbreak had been traced to a seafood market in Wuhan. Later, metagenomic next-generation sequencing technology was used to identify a novel coronavirus in a bronchoalveolar lavage fluid sample from the Wuhan Seafood Market.<sup>3,4</sup> Scientific authorities isolated and identified this novel coronavirus and shared its genetic sequence on Jan. 12, 2020.<sup>4</sup>

Coronaviruses belong to the *Coronaviridae* family of viruses. All viruses are named based on their genetic structure to facilitate the development of diagnostic tests, vaccines and medicines. Virologists and the wider scientific community name viruses according to standards set by the ICTV. The ICTV announced SARS-CoV-2 as the name of the newly discovered virus on Feb. 11, 2020. This name was chosen because the virus is genetically related to the coronavirus responsible for the SARS outbreak of 2003. While related, the two viruses are different. Also on Feb. 11, 2020, WHO announced COVID-19 as the name of the disease caused by SARS-CoV-2.<sup>4</sup> Members of the *Coronaviridae* family are enveloped, positive-sense, single-stranded RNA viruses.

The phylogenetic analysis of coronaviruses classifies them into four genera:  $\alpha$ ,  $\beta$ ,  $\gamma$ , and  $\delta$ . The coronaviruses of the  $\alpha$  and  $\beta$  genera generally infect mammals and humans, while the coronaviruses of the  $\gamma$  and  $\delta$  genera mainly infect birds. SARS-CoV-2 is a novel coronavirus of the  $\beta$  genus. It is round or oval with a diameter of 60-140nm and a crown-shaped appearance under electron microscopy.<sup>5</sup> Seven types of coronaviruses are known to infect humans: 229E (*alphacoronavirus*), NL63 (*alphacoronavirus*), OC43 (*betacoronavirus*), HKU1 (*betacoronavirus*), MERS-CoV (*betacoronavirus*), SARS-CoV (*betacoronavirus*), and the most recent SARS-CoV-2.<sup>5</sup> It is widely agreed that these viruses cause respiratory tract infections, and patients can present with a wide spectrum of manifestations. A protein sequence analysis showed that the amino acid similarity of the seven conserved nonstructural proteins between SARS-CoV-2 and SARS-CoV was 94.6%, suggesting that they might belong to the same species. The homology between the SARS-CoV-2 genome and the bat SARS-like coronavirus [Bat-CoV (RaTG13)] genome is 96%.<sup>6</sup>

In addition to causing human respiratory tract infection, coronaviruses can cause animal intestinal infection. The process of infection requires the participation of receptors on the surface of the host cell membrane. The S protein on the surface of coronaviruses can recognize and bind to the receptor and then invade the host cell through clathrin-mediated endocytosis.<sup>7,8</sup> Different coronaviruses can use different cell receptors to complete the invasion. The severe immune injury COVID-19 can cause has been attributed at least partially to the overactivation of T cells (manifested by an increase in Th17 cells), which play a role in defense against extracellular pathogens by mediating the recruitment of neutrophils and macrophages, coupled with high cytotoxicity of CD8 T cells.<sup>9</sup>

One study revealed that SARS viral detection peaks at two weeks. The incubation period is 1-14 days with an average of 3-7 days. The main routes of transmission are respiratory droplets and articles contaminated with virus droplets. Asymptomatic patients may also be a source of infection.<sup>9</sup> Another study showed that SARS-CoV-2 nucleic acid can be detected in the feces and urine of patients with COVID-19, suggesting that the virus may be transmitted via the fecal-oral route.

The main symptoms of COVID-19 caused by SARS-CoV-2 are fever (87.9%), dry cough (67.7%), fatigue (38.1%), sputum production (33.4%), shortness of breath (18.6%), sore throat (13.9%), headache (13.6%), myalgia or arthralgia (14.8%), chills (11.4%), nausea or vomiting (5.0%), nasal congestion (4.8%), diarrhea (3.7%), hemoptysis (0.9%) and conjunctivitis or conjunctival congestion (0.8%).<sup>10</sup>

Serious cases of COVID-19 may progress rapidly to acute respiratory distress syndrome, coagulation dysfunction and septic shock.<sup>13-16</sup> Mild cases tend to involve low fever and slight fatigue but no pneumonia. Most patients have a good prognosis, but some have severe morbidity and higher mortality. Risk factors for higher mortality include asthma, cerebrovascular disease, cystic fibrosis, hypertension, HIV, dementia, liver disease, pregnancy, pulmonary fibrosis, smoking, thalassemia, history of blood

clots, type I diabetes and advanced age.<sup>11-14</sup>

Also of concern is the presence of the virus in ocular tissue. In 2004, tear samples collected from 36 suspected SARS-CoV patients were sent for RT-PCR testing. The SARS-CoV RNA was identified in three of the patients. Out of the three, one patient had the RNA identified not only in tear samples but also in stool samples and respiratory swab samples. One patient had RNA identified in stool and tear samples, but the respiratory swab was not sent. The third patient had RNA identified in tear samples only while stool samples were negative, and the respiratory swab was not sent. The findings of this study suggested that SARS-CoV can be present in tears and emphasized the need for appropriate precautions to prevent transmission through ocular tissues and secretions.<sup>15</sup> As of this writing, it remains unclear how SARS-CoV can end up in tears. Theories include that the conjunctiva is the direct inoculation site of SARS-CoV from infected droplets, the upper respiratory tract infection migrates through the nasolacrimal duct, or viral infection of the lacrimal gland is hematogenous.<sup>16</sup> In this case report, acute viral follicular conjunctivitis was the clinical presentation. Swab testing confirmed COVID-19. While COVID-19 has been documented in the tears, ocular complications of SARS-CoV2 follicular eye disease is still not fully understood especially in terms of possible transmission.

### *Differential diagnosis*

There are a multitude of ocular conditions that present with follicular conjunctivitis. The follicles appear as gray-white, round-to-oval elevations measuring 0.5-1.5 mm in diameter. From an epidemiological perspective, ocular follicular conjunctivitis caused by viruses accounts for up to 80% of all cases of acute conjunctivitis.<sup>17</sup> The rate of clinical accuracy in diagnosing viral conjunctivitis is less than 50% compared with laboratory confirmation.<sup>17</sup> Many cases are misdiagnosed as bacterial conjunctivitis.<sup>17</sup> Between 65% and 90% of cases of viral conjunctivitis are caused by adenoviruses,<sup>17</sup> and they produce two of the common clinical entities associated with viral conjunctivitis, pharyngoconjunctival fever and epidemic keratoconjunctivitis.<sup>17</sup>

Follicular conjunctivitis may present as an acute or chronic disease. Acute cases are commonly associated with viral ocular disease (epidemic keratoconjunctivitis, herpes zoster keratoconjunctivitis, infectious mononucleosis, Epstein-Barr virus infection) or chlamydial infections (inclusion conjunctivitis). Chronic follicular ocular disease may be caused by chronic chlamydial infection (trachoma, lymphogranuloma venereum) or as a toxic or reactive inflammatory response to topical medications and molluscum contagiosum infection. Secondly, symptoms of hyperemia, chemosis, watery discharge, photophobia and periorbital pain are associated signs of viral conjunctivitis. Based on extensive patient history, COVID-19 should be added to the list of differential diagnoses for patients presenting with follicular viral conjunctivitis. Treatment should be based on ocular signs and symptoms as well as any systemic disease.<sup>18</sup>

### *Role of case history protocol*

Standard case history plus additional historical data are important during an outbreak or epidemic even in low prevalence areas as predictive values may change. One tool for collecting the relevant information is the *Human Infection with 2019 Novel Coronavirus Case Report Form*.<sup>19</sup> This COVID-19 questionnaire includes exposure query regarding domestic and international travel, cruises, family gatherings, workplace gatherings, adult congregate living facilities (nursing, assisted-living or long-term care facilities), school gatherings, correctional facility visits, community events, healthcare worker exposure or exposure to persons known to have COVID-19. Based on symptoms and case history, the triad of test, treat and trace is the standard of care that should be initiated.

### *COVID-19 testing*

Currently, follicular conjunctivitis is the most reported ocular manifestation of COVID-19. However, given the higher number of thrombotic episodes reported in the literature for COVID-19, it is also considered a prothrombotic disease.<sup>20</sup> Thorough ocular posterior segment examination with the aid of OCT and fundus photos is beneficial in ocular thrombotic evaluation. The COVID-19 RT-PCR test is a real-time test for the qualitative detection of nucleic acid from SARS-CoV-2 in upper and lower respiratory specimens (such as nasal, nasopharyngeal or oropharyngeal swabs, sputum, lower respiratory tract aspirates, bronchoalveolar lavage, and nasopharyngeal wash/aspirate or nasal aspirate) collected from individuals suspected of infection with COVID-19 by their healthcare provider. Individuals may also self-collect nasal swab specimens for this test at home when a healthcare provider deems it appropriate based on results of a COVID-19 questionnaire.

Viral loads are high at symptom onset with a viral detection peak at two weeks after onset. Blood/serology testing for COVID-19 is also available, but blood tests are not intended for diagnosis of recent or active disease. Testing of this nature is useful for confirming prior infection by detection of an immune response to COVID-19 in individuals who are at least 14 days post-symptom onset or following exposure to individuals with confirmed COVID-19. Some studies have shown that blood tests revealing higher levels of D-dimer, ferritin and CRP indicate more severe disease.<sup>21,22,23</sup> Follow-up with local and state departments of public health for confirmed positive results is required.

### *COVID-19 treatment and prevention*

At the time of this writing, no vaccine or treatment specific to COVID-19 is available. Most people who become ill with COVID-19 recover at home. Treatment for severe cases is aimed at mitigating symptoms. On March 24, 2020, the U.S. Food and Drug Administration (FDA) began allowing convalescent plasma to be used in patients with serious or immediately life-threatening COVID-19 infections.<sup>24</sup> This treatment is still considered experimental. Convalescent plasma has been used for years, with intermittent success. Currently not much is known about its effectiveness for COVID-19. There have been reports of success from China, but no randomized, controlled studies have been done. Experts also have not determined the best time during the course of the illness to administer convalescent plasma. A recent report by the Center for Evidence Based Medicine cited a clinical trial that showed the corticosteroid dexamethasone decreased the risk of dying in extremely ill hospitalized COVID-19 patients. The report was released prior to publication of the study indicating that the research results have not gone through peer review. Early reports from China and France suggested that patients with severe symptoms of COVID-19 improved more quickly when given chloroquine or hydroxychloroquine. Some doctors were using a combination of hydroxychloroquine and azithromycin with some positive effects, but evidence-based clinical trials have yet to support this.<sup>25</sup>

Remdesivir, an investigational nucleotide analog with antiviral activity, was compared with placebo in more than 1,000 people hospitalized with COVID-19. In this analysis, patients who received remdesivir recovered more quickly than those who received placebo (a median of 11 days for remdesivir vs. a median of 15 days for placebo).<sup>26</sup> The difference was statistically significant. Remdesivir was less effective in sicker COVID-19 patients, including those on a ventilator or on a heart-lung machine. In early May 2020, the FDA issued an emergency use authorization for remdesivir in adults and children hospitalized with severe COVID-19 illness.<sup>23</sup> Finally, vitamins C and D may protect against COVID-19.<sup>26</sup> Vitamin D may help boost the body's natural defense against viruses and bacteria. Second, it may help prevent an exaggerated inflammatory response, which has been shown to contribute to severe illness in some people with COVID-19.<sup>27</sup> The idea that high-dose IV vitamin C might help in overwhelming infections is not new. A [2017 study](#) by Marik et.al. found that high-dose IV vitamin C treatment (along with thiamine and corticosteroids) appeared to prevent deaths among people with sepsis, a form of overwhelming infection causing dangerously low blood pressure and organ failure, which has been seen in COVID-19 patients.<sup>28,29</sup>

Treatment for the relatively newly discovered ocular complications of COVID-19 is also aimed at mitigating symptoms. Follicular conjunctivitis is typically self-limiting. Treatment targets the underlying condition and includes support therapy such as artificial tears. Doctors in China treated follicular conjunctivitis in a patient with severe systemic COVID-19 with ribavirin eye drops, which gradually improved the patient's symptoms.<sup>30</sup> As in all cases of viral conjunctivitis, patients should discontinue contact lenses wear and use spectacles if needed. In cases of disease or non-disease, non-pharmaceutical interventions are highly effective in mitigating the spread of COVID-19 and include social distancing, wearing face masks in public, and frequent hand-washing. These measures hold promise for ocular prevention as well.

### *Cultural competence in public health optometry*

Evidence-based research supports collaborative multispecialty medicine for better patient outcomes.<sup>31</sup> Pandemics often provide opportunity for healthcare professionals at every level to elevate multidisciplinary approaches to mitigate disease. In the most severe cases of COVID-19, patients are hospitalized. Given that symptoms may range from zero to life-threatening, optometrists are in a unique position to identify and treat ocular symptoms and refer as needed. When COVID-19 is suspected based on exposure and symptoms, telemedicine is an appropriate integrative choice for improving public health. From telephone calls to apps, telehealth has been widely used in the current climate. Patient education is a key factor for helping to prevent spread of the virus when disease is found.

The concept of cultural competency is broad and used to describe a multitude of interventions that aim to improve access and effectiveness of healthcare services for all minority groups.<sup>32</sup> Minorities have been affected by COVID-19 at alarmingly higher rates, and awareness is key to mitigation.<sup>33</sup> This teaching case report illustrates two important aspects of cultural competence, increased access and communication, as positive interventions in public health practice.

### **Assessment of Learning Objectives**

1. Students can be tested on the definition and ICTV name of COVID-19 and how the current definition applies clinically to the ocular complications of systemic disease including follicular conjunctivitis
2. Students presented with a routine or urgent ocular case can be evaluated on the development of a more comprehensive historical account of the case, which can be accomplished using a series of questions based on the Centers for Disease Control and Prevention's *Human Infection with 2019 Novel Coronavirus Case Report Form*.<sup>19</sup>
3. Based on PowerPoint slide quizzes, students should be able to develop a differential diagnosis for all follicular conjunctivitis diseases, which includes how to rule out bacterial vs. viral and acute vs. chronic follicular conjunctivitis as well as current potential systemic findings associated with COVID-19.
4. Students should be evaluated on their knowledge of the lab tests available for detecting active systemic COVID-19 infection, previous exposure to the virus, and SARS-CoV-2 in the eye and how to use them
5. To foster continuity of care, a list of co-managing physicians, hospital referral contacts and telehealth options could be written up as an information brochure for low- to no-symptom patients suspected of having COVID-19
6. Clinical-thinking skills regarding education for PUI for COVID-19 and protocols for testing, treating, and tracing can be practiced in small groups

### **Conclusion**

Optometrists play an important role in public health surveillance and diagnosing and managing ocular

complications of COVID-19. Outbreaks, especially of novel pathogens, create a pressing need to collect data on diagnostics and treatment and organ systems, including ocular clinical characterization, to inform rapid public health response. Optometrists' can increase cultural competence with awareness of healthcare disparities and by improving access and providing caring communication related to COVID-19.

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