

# A Patient With Bilateral Conjunctivitis Positive for SARS-CoV-2 RNA in a Conjunctival Sample

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**Purpose:** To present a patient with bilateral conjunctivitis, testing positive for viral RNA of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in both nasopharyngeal and conjunctival samples.

**Methods:** A 40-year-old man with bilateral acute conjunctivitis and suspicious signs of coronavirus disease 2019 (COVID-19) presented to the hospital. A detailed ophthalmic examination was performed. Samples obtained from conjunctival and nasopharyngeal swabs were tested by reverse transcription PCR (RT-PCR) for the detection of SARS-CoV-2 virus. Ocular findings and duration of the presence of viral RNA in the conjunctival specimens were evaluated at follow-up visits.

**Results:** Slit-lamp biomicroscopy revealed bilateral acute follicular conjunctivitis. The RT-PCR assay demonstrated the presence of viral RNA in the nasopharyngeal and conjunctival specimens at the initial visit and at the 4-day follow-up. Conjunctivitis findings were decreased after 4 days and recovered completely without any sequelae within 10 days. The PCR results of both nasopharyngeal and conjunctiva specimens were negative for the viral RNA at 10 days.

**Conclusions:** Bilateral conjunctivitis is rare in patients infected with COVID-19. Although it is difficult to detect viral RNA from conjunctival swabs, conjunctival secretions may be a source of contamination, and protective measures must be taken.

**Key Words:** coronavirus, COVID-19, SARS-CoV-2, conjunctivitis  
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Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and is a potentially lethal disorder, which is a major concern for global public health. In December 2019, several patients with pneumonia of an unexplained etiology were

referred to hospitals in Wuhan, China.<sup>1</sup> All the initial cases were related to contact with a wild animal market, and patients presented with dry cough, dyspnea, fever, and bilateral pulmonary infiltrations on imaging. The causative agent was detected from throat swab samples, and the disease was named COVID-19 by the World Health Organization.<sup>2</sup> As of June 20, 2020, there were 8,912,552 infected patients and 466,205 deaths worldwide.<sup>3</sup>

The signs of COVID-19 infection occur after an incubation time of approximately 5.2 days.<sup>4</sup> COVID-19–infected patients may present with higher leukocytosis in a complete blood count, increased plasma proinflammatory cytokine levels, and abnormal respiratory findings. The most common symptoms are fever, cough, fatigue, headache, diarrhea, and dyspnea.<sup>5</sup> Ocular symptoms rarely occur and may be overlooked in COVID-19 patients. Several studies have demonstrated a relationship between coronaviruses and retinal diseases.<sup>6,7</sup> Scalinci et al reported conjunctivitis case series in 5 patients with no conjunctival swabs.<sup>8</sup> Few studies, however, have documented the ocular complications of COVID-19 disease.<sup>9,10</sup>

Here, we present a rare case of bilateral conjunctival hyperemia with mild systemic symptoms in a patient who tested positive for COVID-19 from both nasopharyngeal and conjunctival swab samples. This disease is highly contagious, and the present case report demonstrating the presence of the virus in conjunctival samples reveals another potential route of transmission.

## CASE REPORT

On April 13, 2020, a 40-year-old man was admitted to the hospital because of bilateral redness and stinging in both eyes for the 2 previous days. He reported having myalgia and a dry cough for 1 week but denied fever, dyspnea, and chest pain. He noticed a deterioration in taste and smell sensations that began 3 days before admission. The patient denied any underlying disease or drug use, and he had no significant family medical history. He had no history of smoking. He had no known interaction in the past 1 month with anyone diagnosed with COVID-19 and no recent travel history.

On ophthalmologic examination, his visual acuity was 20/20 bilaterally, intraocular pressure was 14/13 mm Hg, and slit-lamp biomicroscopy showed bilateral moderate to severe conjunctival injection and moderate follicles in the lower lids. The patient had no secretions, but there was mild epiphora. No subconjunctival hemorrhage or pseudomembrane was observed (Fig. 1). The cornea was clear, and no anterior chamber inflammation was detected. Fundus examination results were normal for both eyes. Bacterial culture and gram staining of the conjunctival fluid were performed.

Systemic physical examination revealed a body temperature of 37.2°C, blood pressure of 120/70 mm Hg, heart rate of 80 beats

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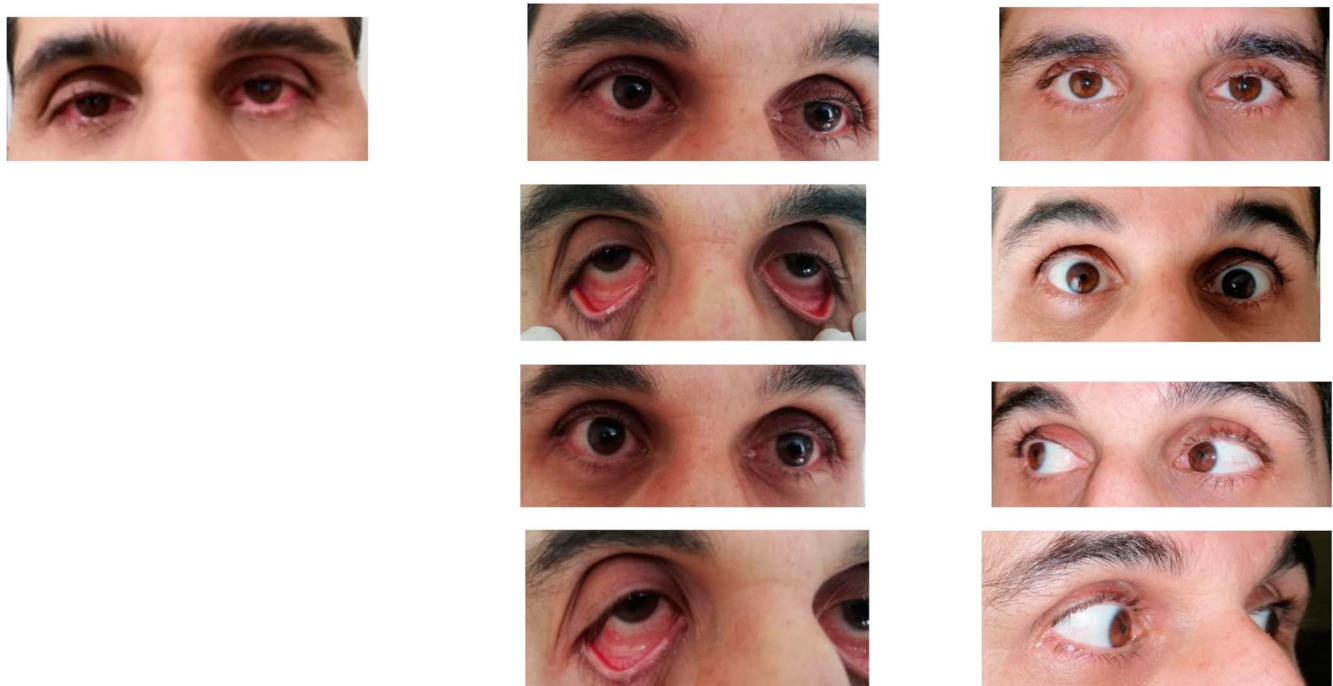
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April 13, 2020

April 17, 2020

April 23, 2020



**FIGURE 1.** The course of conjunctivitis in the patient's 10-day follow-up. Conjunctivitis findings completely healed at the 10-day follow-up.

per minute, respiratory rate of 20 breaths per minute, and oxygen saturation of 98% while breathing ambient air. Thorax computed tomography findings were unremarkable (Fig. 2). Blood tests revealed normal blood cell counts, and serum parameters showed only a slight increase in C-reactive protein levels (1.44 mg/L; Table 1).

Because of suspicious systemic symptoms for COVID 19, nasopharyngeal and conjunctival swab samples were obtained from the patient. Conjunctival swabs were taken from the lower fornix of each eye. The swab specimens were tested by real-time reverse transcriptase–polymerase chain reaction (rRT-PCR) assay. Both swab samples were positive for SARS-CoV-2 nucleic acid 1 day later. The patient was therefore diagnosed with COVID-19.

After consulting with infectious disease specialists, he was treated with ganciclovir ophthalmic gel 0.15% (Virgan; Thea Pharmaceuticals, Clermont-Ferrand, France) 4 times daily, polyvinyl alcohol+ povidone ophthalmic drops (Refresh; Allergan PLC, Dublin, Ireland) 3 times daily, and oral hydroxychloroquine 200 mg (Plaquenil; Sanofi-Aventis, Bridgewater, NJ) twice daily. Because the patient's vital signs were within normal limits and no lung involvement was detected, the patient was placed in airborne infection isolation in the hospital and followed up.

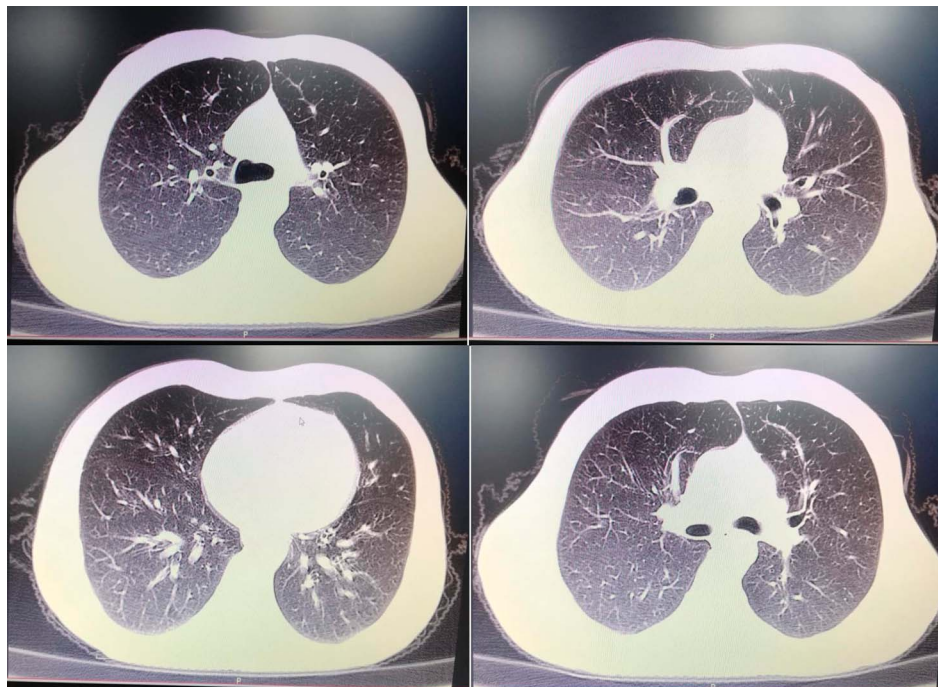
On April 17 (4 days after hospital admission), his general condition was good. Systemic physical examination revealed a body temperature 36.6°C, blood pressure of 115/75 mm Hg, heart rate of 72 beats per minute, respiratory rate of 18 breaths per minute, and oxygen saturation of 98%. In addition, he had no cough, dyspnea or diarrhea, and no complaints of fatigue. Control laboratory results were within normal limits (Table 1). In both eyes, the redness was reduced, visual acuity was 20/20, intraocular pressure was 14/14 mm Hg, and slit-lamp biomicroscopy revealed mild conjunctival hyperemia and a quiet anterior chamber (Fig. 1). He stated that the ocular symptoms had resolved. Nasopharyn-

geal and conjunctival swab samples were again collected for SARS-CoV-2 testing. Both samples were positive for SARS-CoV-2 virus nucleic acid by rRT-PCR. Initially requested bacterial culture and Gram staining tests were negative. Medical treatment for an additional week and continued isolation was recommended.

On April 23 (10 days after hospital admission), the general condition of the patient was good, and he had no complaints. His body temperature was 36.0°C, blood pressure was 120/70 mm Hg, heart rate was 72 beats per minute, oxygen saturation was 98%, chest radiography was normal, physical examination was unremarkable, and laboratory results were within normal limits (Table 1). Visual acuity was 20/20, intraocular pressure was 15/14 mm Hg, and slit-lamp biomicroscopy revealed complete resolution of the conjunctival hyperemia (Fig. 1). Nasopharyngeal and conjunctival swab samples were obtained, and both samples tested negative for SARS-CoV-2. Those who had been in contact with the patient were informed about the exposure and followed up clinically by Department of Infectious Diseases and Clinical Microbiology.

## DISCUSSION

In this case report, we detected SARS-CoV-2 nucleic acids in nasopharyngeal and conjunctival swab samples obtained from a patient presenting with conjunctival hyperemia in both eyes. He responded to topical ganciclovir treatment within 4 days and recovered. The patient was followed up in the hospital for 10 days and exhibited no systemic findings. Interestingly, the virus was isolated in both nasopharynx and conjunctiva during the patient's asymptomatic period.



**FIGURE 2.** Chest computerized tomography images on April 13, 2020, showing no pathological findings.

The number of cases of SARS-CoV-2 infection with ocular involvement is limited. To date, very few cases in which COVID-19 clearly caused conjunctivitis have been reported.<sup>10,11</sup> Zhang et al<sup>12</sup> found that only 2/72 (2.78%) laboratory-confirmed COVID-19 patients with conjunctivitis and conjunctival samples from only 1 of these patients tested positive for the virus by RT-PCR. Guan et al reported conjunctival congestion in 9 (0.8%) of 1099 COVID-19 patients. The conjunctival mucosa is directly exposed to infectious particles during close contact with patients or when

infected hands touch the eye.<sup>13</sup> SARS-CoV-2 has a similar receptor-binding pattern as SARS-CoV, which enables it to infect host cells through angiotensin-converting-enzyme 2. The binding capability and expression of the virus in the conjunctiva is very low compared with the lung. In addition, lactoferrin and secretory IgA have protective effects, and the rinsing effect of tears reduce the binding of the virus to the conjunctiva. Further studies are needed to investigate the theory of SARS-CoV-2 ocular infection by angiotensin-converting-enzyme 2.

The potential for infection by ocular secretions is currently uncertain, and how SARS-CoV-2 accumulates in ocular secretions remains unclear. Possible hypotheses involve direct inoculation of the ocular tissues from respiratory droplets or viral aerosolized particles, migration from the nasopharynx through the nasolacrimal duct, or even hematogenous dissemination through the lacrimal gland. Given the connection of the conjunctiva with the nasolacrimal duct or the proximity to the nasopharynx, transmission to other regions of the body is possible. Zhang et al presented a case with bilateral conjunctivitis, for whom conjunctival and oropharyngeal swab samples tested positive for SARS-CoV-2. They reported hand-eye contact, such as eye rubbing, as a possible route of transmission.<sup>12</sup>

The viral load found in nasal and throat samples is increased for approximately 2 weeks from the onset of COVID-19 symptoms.<sup>14</sup> De Wit et al<sup>15</sup> showed that another form of coronavirus, MERS-CoV RNA, could be identified in the conjunctiva in a rhesus macaque model, but viral loads could no longer be identified in the conjunctiva 6 days after infection. It is recommended that conjunctival samples be obtained within 6 days of symptoms first presenting, but the result may be negative because of a low concentration in RT-PCR. Chen et al,<sup>10</sup> however, isolated the virus in the

**TABLE 1.** Follow-up Laboratory Measurements of the Patient

	April 13, 2020	April 17, 2020	April 23, 2020
White blood cell count, 10 <sup>9</sup> /L	5.48	5.26	5.50
Neutrophil count, 10 <sup>9</sup> /L	2.69	2.63	2.70
Lymphocyte count, 10 <sup>9</sup> /L	2.15	2.08	2.12
Platelet count, 10 <sup>9</sup> /L	199	206	202
Red blood cell count, 10 <sup>12</sup> /L	5.44	5.42	5.32
Hemoglobin, g/dL	15.9	15.5	15.3
C-reactive protein, mg/dL	1.44	1.12	1.08
Procalcitonin, µg/L	0.020	0.018	0.019
International Normalized Ratio	1.18	1.12	1.10
D-dimer, µg/mL	53	45	46
Creatine kinase, U/L	65.8	60.8	62.1
Lactate dehydrogenase, U/L	148.5	145.2	147.6
Alanine aminotransferase, U/L	18	20	19
Aspartate aminotransferase, U/L	24	25	23
Creatinine, mg/dL	0.75	0.88	1.02

conjunctiva 13 days after disease onset, and PCR of conjunctival samples was positive up to day 19. They reported that the virus remained for 5 days, and a conjunctival swab was not a reliable method for early detection of COVID-19. The viral load found in asymptomatic or minimally symptomatic patients is reported to be similar to that in symptomatic patients.<sup>14</sup> Detection by SARS-CoV-2 rRT-PCR in conjunctival samples is very low, with a sensitivity ranging from 50% to 60%.<sup>13</sup> It should be noted that PCR results will be negative in the late phases of viral infection. Wu et al<sup>9</sup> reported that white blood cells, neutrophils, and C-reactive protein are increased in patients with ocular symptoms. In our patient, however, this was not the case. We think that larger samples are needed to guide the laboratory findings, and corollary studies to elucidate the underlying mechanism are warranted.

In conclusion, conjunctivitis is a rare condition in patients with COVID-19. The ocular surface is open to the environment and allows for viral entry into the body. Hand-eye contact (such as eye rubbing) is a potential problem for disease transmission and can cause conjunctivitis. Ophthalmologists may be the first point of contact in the healthcare sector for patients with potential COVID-19 and no characteristic symptoms. It is important to take protective measures during an ophthalmological examination to prevent transmission of the virus.

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