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The evidence of SARS-CoV-2 infection on ocular surface

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ABSTRACT

This is a cross-sectional study of patients who received a COVID-19 diagnosis between December 30, 2019 and February 7, 2020 at Tongji Hospital. A total of 102 patients (48 Male [47%] and 54 Female [53%]) with clinical symptoms, Rt, and chest Computed Tomography (CT) abnormalities were identified with a clinical diagnosis of COVID-19. Patients had a mean [SD] gestational age of 57.63 [14.90] years. Of a total of 102 patients identified, 72 patients (36 men [50%] and 36 women [50%]; mean [SD] age, 58.68 [14.81] years) were confirmed to have COVID-19 by laboratory diagnosis with a SARS-CoV-2 RT-PCR assay. Only two patients (2.78%) with conjunctivitis were identified from 72 patients with a laboratory confirmed COVID-19. Of those two patients, SARS-CoV-2 RNA fragments were found in ocular discharges by SARS-CoV-2 RT-PCR in only one patient. Our findings suspect the incidence of SARS-CoV-2 infection through the ocular surface is extremely low, while the nosocomial infection of SARS-CoV-2 through the eyes after occupational exposure is a potential route. To lower the SARS-CoV-2 nosocomial infection, all health care professionals should wear protective goggles. The inefficient diagnostic method and the sampling time lag may contribute to the lower positive rate of conjunctival swab samples of SARS-CoV-2.

A novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) associated with severe human infected disease (COVID-19) outbreak starting from January 2020, in China [1]. Most recently, Wang D et al. reported 138 hospitalized SARS-CoV-2 pneumonia cases with a hospital-associated transmission rate of 41%, among whom 70% were medical staffs [2]. To date, more than 100, 000 people have been infected by COVID-19, including over 3000 medical staffs. Therefore, in order to curb the spread of SARS-CoV-2, and reduce the nosocomial infection, the exact routes of transmission need to be further studied and confirmed. Like other highly contagious respiratory viruses, respiratory droplets are considered as the main route of SARS-CoV-2 transmission [3]. However, for the new outbreak of contagion, other ways of transmission should not be ignored. Until now, intensive work that has been focused on understanding the transmission of SARS-CoV-2, and limited investigations have been conducted to date into the clinical features of SARS-CoV-2 in the ocular surface. A recent research study has demonstrated that SARS-CoV-2 can be detected in the conjunctival sac of patients with COVID-19 patients or suspected [[4]]. However, none of these patients had ocular symptoms. We therefore conducted a study to describe the clinical spectrum of ocular symptoms and laboratory test in conjunctival swab samples. We found a rare case of nosocomial SARS-CoV-2 infection with conjunctivitis in a nurse, which suggests that ocular transmission may be a potential route of nosocomial transmission of the SARS-CoV-2.

Of a total of 102 patients identified, 72 patients confirmed by laboratory diagnosis. The time from the date of onset to the date of conjunctival sampling was 18.15 [7.57] days on average, ranging from 6 to 46 days. Only two patients (2.78%) with conjunctivitis were identified from 72 patients with a laboratory confirmed COVID-19. However, SARS-CoV-2 was found in ocular discharges by RT-PCR in only one patient. Briefly, a 29-year-old nurse working in the Emergency Department at Tongji hospital, Wuhan City, China was referred to the Department of Ophthalmology at Tongji Hospital on February 1st, 2020 due to excessive tearing and redness in both eyes. No other systemic symptoms were reported except for a moderate fever of 38.2 ˚C on January 31st, 2020. An ocular examination revealed conjunctival congestion and watery discharges in both eyes with normal best corrected visual acuity, normal corneal epithelium, quiescent anterior chamber, and no tenderness or enlargement of the preauricular lymph node (Fig. 1A). We therefore excluded the possibility of conventional conjunctivitis, such as bacterial conjunctivitis, hemorrhagic conjunctivitis, allergic conjunctivitis, according to her clinical symptoms and signs. The patient clarified that she continuously wore medical N95 respirator while working in the Emergency Department, but occasionally worked with a dislocated eye goggles touching her eyelids. Considering the occupational exposure by SARS-CoV-2, the related assay was arranged. Surprisingly, the chest CT showed multiple peripheral ground-glass opacities in both lungs (Fig. 1D). The conjunctival and oropharyngeal swabs tested for SARS-CoV-2 were both positive. The blood Rt showed initially normal lymphocyte count, followed with progressive lymphocytopenia. On the basis of her epidemiologic characteristics, clinical manifestations, chest images, and laboratory findings, this patient was diagnosed with SARS-CoV-2 infected acute viral conjunctivitis and pneumonia.

The patient reported a 4-day history of persistent conjunctivitis and a 3-day history of fever from onset. Ganciclovir eye drops was used to treat her conjunctivitis on day 2 during home quarantine and she got cough from day 4–9 post of illness. Although the SARS-CoV-2 RT-PCR assays for both the nasopharyngeal and conjunctival swab were negative at day 10 post illness, a fever reappeared, and the chest CT showed

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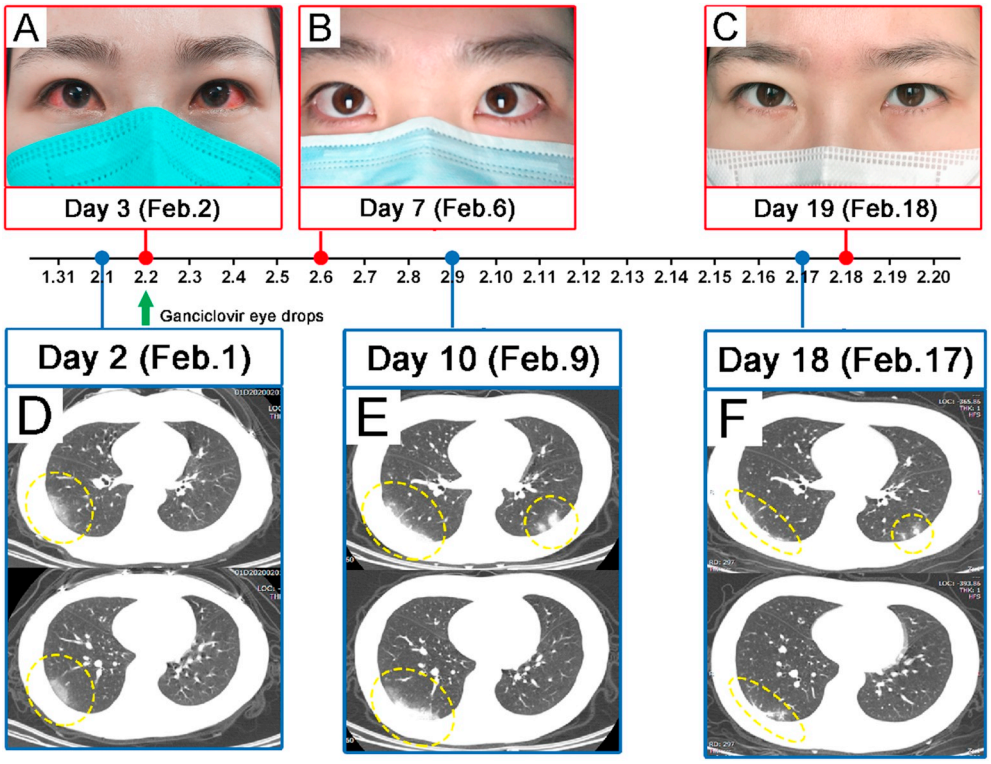

Fig. 1. Clinical photographs and chest CT of the patient with positive conjunctival swab: (A) clear binocular conjunctival congestion which is a classic sign for viral conjunctivitis; (B,C) conjunctivitis completely subsided and did not recur after 4 days following onset; (D–F) dynamic changes of peripheral ground-glass opacities in both lungs (yellow arrows) which illuminate the pneumonia caused by SARS-COV-2 infection.

that her pneumonia aggravated (Fig. 1E). She was transferred to the hospital, treated according to the guidance of CDC, and then discharged 11 days post hospitalization, accompanied with a slight cough, normal body temperature, normal conjunctival appearance, and regression of pulmonary lesions (Fig. 1 C and 1F).

Like other highly contagious respiratory viruses, respiratory droplets are considered to be the main route of SARS-CoV-2 transmission [3]. However, other possible transmission routes should be taken into account. A recent bioinformatics analysis study analyzed 4 datasets with single-cell transcriptomes of lung, oesophagus, stomach, ileum and colon, and SARS-CoV-2 was found in stool samples of patients with abdominal symptoms [5]. Moreover, Lofy KH et al. also detected the SARS-CoV-2 in a patient's stool, which warns us of the risk of fecal oral transmission [6]. Similarly, SARS-CoV-2 was also directly detected in the oesophageal erosion and bleeding site in a case with severe peptic ulcer symptom reported by Zhong et al. [7] With multiple potential routes of transmission already confirmed, hand-eye contact such as eye rubbing should also be further studied and confirmed.

In our current study, SARS-CoV-2 was found in ocular discharges by RT-PCR only in one COVID-19 patient. Although the incidence of conjunctivitis is extremely low, these results demonstrate that SARS-CoV-2 has shown a capacity to use the eye as a portal of entry and cause ocular disease. To our knowledge, several anatomical and mucosal immune properties permitted the eye as both a potential site of virus infected site as well as a gateway for respiratory infection [8,9]. Sun and colleagues found that ACE2 is expressed in human cornea and conjunctival tissues [10]. In addition, transmission from hand-eye contact (such as eye rubbing, etc.) has been reported in nosocomial infection of epidemic keratoconjunctivitis, which provides evidence supporting our standpoint [11]. In consistence with our result, Dr. Guangfa Wang, a member of the national expert panel on COVID-19, reported that he was infected by SARS-COV-2 during the inspection in Wuhan, through unprotected eye exposure [12]. Similarly, an anesthesiologist with insufficient eye protection confirmed with COVID-19 also presented conjunctivitis as the initial symptom. The laboratory test revealed that the nasopharyngeal swab was positive while the conjunctival swab was negative [4]. On the contrary, our case initially presented similar conjunctivitis with a positive conjunctival PCR result. Considering conjunctivitis as the same initial symptom for Dr. Wang, the anesthesiologist and the nurse with positive conjunctival PCR result in our case, and the SARS-COV-2 infected mechanism, we believe that ocular transmission of SARS-CoV-2 must be seriously considered, especially in health care professionals.

The negative results of conjunctival sac in other 71 patients, may be owing to the lower viral concentration, the sampling time lag, and the lower positive rate of the inefficient diagnostic method. Ziad and colleague found that tracheal aspirates yielded significantly higher SARS-CoV loads, compared with the nasopharyngeal swab and sputum specimens [13]. This suggests that the viral concentration and genome fraction is diverse in different sites. In consideration of the fact that the ocular surface is an open microenvironment, and that the viral may transport to the inferior meatus of the nose rapidly [14], the SARS-CoV-2 concentration in ocular surface is likely to be very low. We also found that suspected patients often had 2–3 repeated tests of nasopharyngeal swabs before the positive result confirmed SARS-CoV-2 infection. The sampling time lag and the inefficient diagnostic method may contribute to this lower positive rate of SARS-CoV-2. de Wit and colleagues demonstrated that, in the rhesus macaque model, another type of coronavirus named MERS-CoV RNA could be detected in the conjunctiva, but the viral loads could no longer be detected in the conjunctiva 6 days post infection [15]. The earliest time for conjunctival sampling is 6 days after onset in our present study which may lead us to miss the high replication period of virus. Another consideration is that the lower positive rate of RT-PCR makes diagnosis of SARS-CoV-2 in ocular surface a challenge.

In conclusion, our findings imply the incidence of SARS-CoV-2 infection through the ocular surface is extremely low in the general population. However, we highlight that ocular transmission is a potential way of occupational exposure for medical staff. To lower the risk of SARS-CoV-2 nosocomial infection, protective goggles should be worn by all the health care professionals, especially who work in the Fever Outpatient and Infection Wards. Patients with conjunctivitis in the

epidemic area should also be treated seriously to rule out presence of COVID-19. The negative conjunctival sac PCR results should be further re-evaluated using more sensitive detection methods.

Declaration of competing interest

All authors report no relevant conflicts of interest, financial or otherwise.

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