

# Late Corneal Stromal Deposits After COVID-19

*Alicia Pareja-Ríos, PhD, MD,\* and Sergio Bonaque-González, PhD†*

**Abstract:** We present 2 cases of striking stromal corneal infiltrates months after COVID-19 infection. While we cannot prove that these infiltrates are caused by or directly related to COVID-19, we did not find any other plausible cause that could explain these ophthalmic signs. In these cases, the ongoing process was detected in relatively early stages due to scheduled visits with patients and responded positively to prednisolone acetate 1% ophthalmic suspension. However, we do not know the response to treatment in more advanced cases.

**Key Words:** cornea, COVID-19, stroma, deposits

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The medical community is still immersed in analyzing the consequences at a systemic level of the coronavirus disease 2019 (COVID-19). In relation to ophthalmology, it has been speculated that ocular surfaces may be a potential target for the invasion of this new coronavirus (severe acute respiratory syndrome coronavirus 2).<sup>1</sup> This was an initially controversial suggestion based on the report of conjunctivitis in some patients in the early stages of the disease.<sup>2</sup> Nevertheless, meta-analysis studies have reinforced this hypothesis, stating that conjunctivitis may represent a sign of COVID-19 infection associated with a more severe form of disease.<sup>3</sup> Keratitis has also been reported to be an associated sign.<sup>4</sup> For example, in a cross-sectional study conducted in Wuhan, China, keratitis cases were reported in 2.6% of patients infected with COVID-19.<sup>5</sup> Furthermore, severe acute respiratory syndrome coronavirus 2 ribonucleic acid has been detected in the tears,<sup>6</sup> although it is still unclear how its ribonucleic acid can end up there.<sup>7</sup> With the prevalence of keratitis and conjunctivitis low in the early stages of infection, it has been suggested that the tear film, in fact, protects the cornea and carries the virus to the nasolacrimal duct.<sup>8</sup> In this regard, it has also been reported that although the human cornea has receptors for this coronavirus, it does not replicate in it.<sup>9</sup> The findings do

not prove that all corneas are resistant, but all that were tested (n = 25) did not replicate COVID-19.

In this work, we present what we believe may be an unexpected late ophthalmic sign of COVID-19 infection that has not been previously described in the literature. In particular, we report 2 cases of striking stromal corneal infiltrates after COVID-19 infection, which cannot be explained by any other pathology or previous condition.

## PATIENT 1

A 60-year-old man presented with a general medical history of multinodular goiter under endocrinological observation and without current nonophthalmic treatment. Ophthalmically, the patient presented mild phacosclerosis justifiable by age. In addition, he suffered from open-angle glaucoma with retinal nerve fiber damage and visual fields within normality, which has been successfully controlled since 2018 with 2.0% dorzolamide and 0.5% timolol. The patient routinely uses eye lubrication to alleviate symptoms related to dry eye (unpreserved trehalose 30 mg/mL and sodium hyaluronate 1.5 mg/mL).

On January 17, 2020, the patient underwent a scheduled ophthalmic examination, showing no symptoms or signs of interest, apart from his controlled glaucoma. At that time, he presented intraocular pressure (IOP) values of 22.0 and 19.7 mm Hg for the right eye (OD) and left eye (OS), respectively. His best-corrected visual acuity (BCVA) was 20/20 in both eyes (AO). The manifest refraction was OD: +4.25 (−1.00) × 115 degrees and OS: +5.75 (−2.00) × 70 degrees. On June 1, 2020, the patient underwent a routine ophthalmic examination, with no symptoms or signs of interest, apart from his glaucoma, which did not show progression.

The patient was infected with COVID-19 probably in late February during a work trip. Of the 4 people who attended a meeting, 3 of them contracted the disease. The patient had no symptoms at any time. After knowing about the other 2 cases, a serological analysis was performed on June 15 in which it showed antibodies against COVID-19. When asked specifically about symptoms of conjunctivitis during this period, the patient remembers having red eyes for a few days, a condition that resolved spontaneously.

On October 26, 2020, the patient underwent another routine ophthalmic examination to check his glaucoma status. The ophthalmic examination showed no progression in the glaucoma condition by means of retinal nerve fiber layer ocular coherence tomography (OCT), visual fields, and IOP (22.3 mm Hg OD and 18.3 mm Hg OS). The rest of the examination was strictly normal for BCVA (20/20 AO), retinal OCT, corneal

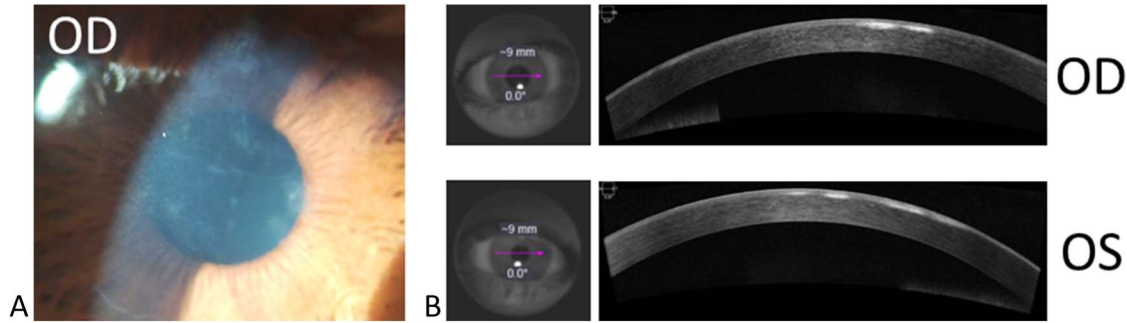
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From the \*Department of Ophthalmology, University Hospital of the Canary Islands, Santa Cruz de Tenerife, Spain; and †Wooptix, Santa Cruz de Tenerife, Spain.

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Correspondence: Alicia Pareja-Ríos, PhD, MD, Department of Ophthalmology, University Hospital of the Canary Islands, C/Ofra s/n San Cristóbal de La Laguna, Santa Cruz de Tenerife 38320, Spain (e-mail: aparejar@gmail.com).

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**FIGURE 1.** A, Slit-lamp photography of the right eye of patient 1. B, Corneal optical coherence tomography of both eyes of patient 1. (The full color version of this figure is available at [www.corneajrnl.com](http://www.corneajrnl.com).)

endothelium count, and fundus examination. However, the patient presented striking corneal stromal infiltrates in AO, without associated clinical symptoms, detected using a slit lamp (Fig. 1A). The stromal origin of these infiltrates was verified using a corneal OCT (Zeiss Cirrus 5000 HD-OCT; Carl Zeiss Meditec, Dublin, CA) (Fig. 1B). Given its morphological similarity to adenoviral conjunctivitis, treatment with preservative-free hydrocortisone of 0.335% drops was established.

On October 30, 2020, ophthalmic examination revealed no changes in stromal infiltrates. Thus, the previous treatment was replaced by prednisolone acetate ophthalmic suspension 1%. As of November 4, 2020, the deposits have decreased in size, presenting a more nummular shape and show signs of being in resolution.

## PATIENT 2

A 59-year-old woman presented with no relevant medical history, except for an episode of spontaneous uveitis resolved in 2016 and mild phacosclerosis justifiable by age. Her BCVA was 1.0 AO, with a refraction of OD: +1.00 OI +1.50, and a strictly normal fundus.

In late March 2020, she began a flu process with a headache, chest pain, dizziness, and anosmia. Her family doctor prescribed antibiotics. With no observing improvement, on April 10, 2020, a polymerase chain reaction test was performed with a positive result. On April 26, 2020, the polymerase chain reaction test was negative and serological tests confirmed the presence of antibodies against COVID-19. After that, she suffered from persistent fatigue, and was under observation by the internist, but

without pharmacological treatment. She did not recall having red eyes at any point in the process.

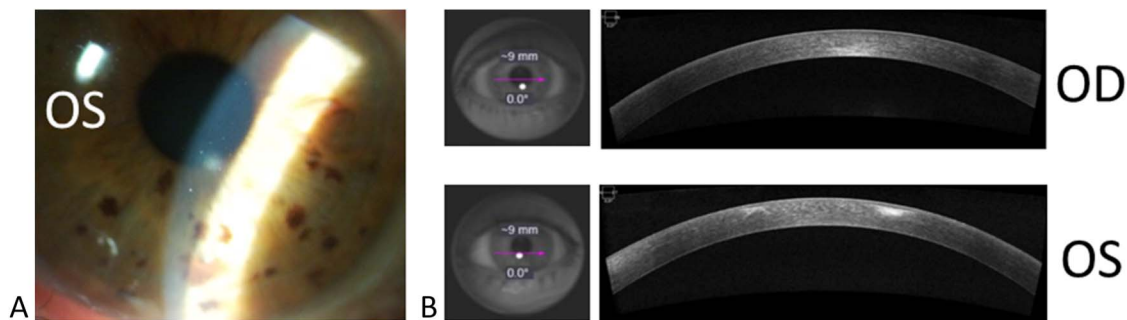
On October 28, 2020, she presented for her annual ophthalmic check-up without referring any ocular symptoms. The ophthalmological examination showed strictly normal for BCVA (20/20 AO), IOP (14.0 mm Hg OD and 14.7 mm Hg OS), retinal OCT, corneal endothelium count, and fundus examination. However, a series of corneal deposits were clearly visible with a slit lamp in OS (Fig. 2A). Its stromal origin was verified by corneal OCT (Fig. 2B), objectifying that the right eye also presented a very slight opacity in the deep stroma. Preservative-free hydrocortisone 0.335% was indicated on this visit.

On November 4, 2020, the patient showed no improvement and the treatment was changed to prednisolone acetate ophthalmic suspension 1%. On November 11, 2020, a slight improvement was observed in the size of the deposits.

## CONCLUSIONS

These findings are compatible with immune complex-like deposits. Approximately 30% to 50% of patients with epidemic keratoconjunctivitis (EKC) will develop similar infiltrates. They can persist for months or years after the resolution of an EKC, compromising the visual function of patients.<sup>10</sup>

In this report, we show 2 cases of corneal infiltrates in 2 patients who have suffered from COVID-19 with different severity, without ocular associated symptoms, and that seem to respond positively to treatment with prednisolone. It is



**FIGURE 2.** A, Slit-lamp photography of the left eye of patient 2. B, Corneal optical coherence tomography of both eyes of patient 2. (The full color version of this figure is available at [www.corneajrnl.com](http://www.corneajrnl.com).)

striking that in both cases, the process has occurred without previous episodes of conjunctivitis, in a binocular manner, and months after the resolution of the COVID-19 (in EKC, infiltrates usually appear between 2 and 5 weeks after infection<sup>10</sup>).

We did not find a plausible cause that could explain these ophthalmic signs, but nevertheless, we cannot prove that these infiltrates are caused by or directly related to COVID-19. We can only cautiously suggest that they could be related to exposure to COVID-19, which could have affected the cornea by an unknown mechanism. Given the response to steroids and the clinical similarities to EKC, perhaps these findings are immunologic-related. Hence, they could be totally casual but unusual findings related to EKC, herpes simplex virus and Epstein–Barr virus, which happened after the exposure to COVID-19 with an atypical and asymptomatic evolution.

In these cases, the ongoing process was detected in relatively early stages because of scheduled visits with patients. However, we do not know the response to treatment in more advanced cases. We believe that the ophthalmic community should be aware of this finding and pay special attention to processes of this nature in post-COVID-19 cases.

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