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CASE REPORT

Immune-Related Peripheral Keratopathy in Post-COVID-19 Syndrome

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Background: Post-COVID-19 Syndrome, marked by systemic immune dysregulation, has been linked to various ocular manifestations, including conjunctivitis, anterior uveitis, and vitritis. Emerging evidence highlights the role of inflammatory mediators, cytokines, and abnormal immune cell activation in post-viral complications, which may contribute to corneal damage. This case report describes immune-related peripheral keratopathy in a patient with Post-COVID-19 Syndrome, emphasizing that it may influence the ocular surface immune microenvironment.

Case Presentation: We describe a woman in her 30s who has a history of mild dry eye disease. After her third COVID-19 infection, she experienced eye redness, dryness, and a foreign body sensation. Ophthalmic examination revealed a corneal ulcer at the limbal region in both eyes. Treatment with topical antibiotics, corticosteroids, anti-inflammatory agents, and lubricating eye drops, led to substantial improvement and complete healing within two months.

Conclusion: Systemic immune dysregulation following COVID-19 infection may alter the ocular surface immune microenvironment, thereby predisposing patients to ocular surface complications.

Keywords: post-COVID-19 syndrome, immune-related peripheral keratopathy, dry eye disease, immunology, cornea

Introduction

SARS-CoV-2 not only causes the acute infection known as COVID-19 but also leads to a series of long-term symptoms, collectively referred to as Post-COVID-19 Syndrome, which can profoundly affect patient health.[1,2] Post-COVID-19 ocular manifestations have been reported to include conjunctivitis, anterior uveitis, and vitritis.[3,4]

Post-COVID-19 Syndrome often triggers systemic immune dysregulation, characterized by excessive release of inflammatory mediators and cytokines, as well as abnormal immune cell activation.[5] This dysregulation can lead to the chemotaxis of inflammatory cells and the release of collagenases and proteases, ultimately damaging the peripheral cornea.[6] In this report, we present a case of immune-related peripheral keratopathy combined with pneumonia in a young patient secondary to Post-COVID-19 Syndrome.

Case Presentation

A woman in her 30s presented to the ophthalmology clinic with symptoms of eye redness, dryness, and a foreign body sensation. She had not received any systemic medications and had no significant medical history. Notably, she had a history of mild dry eye disease managed with artificial tears in both eyes. Prior to the onset of her recent symptoms, her corneal assessments were normal.

The patient had been diagnosed with COVID-19 eight weeks before this visit, confirmed by a positive SARS-CoV-2 antigen test from a throat swab specimen. She had previously contracted the virus twice. Two weeks prior to her ophthalmology visit, she experienced fever and a mild cough that worsened and evolved into sore throat, chills, and nasal congestion. She sought treatment at the Respiratory and Critical Care Medicine outpatient clinic, where laboratory

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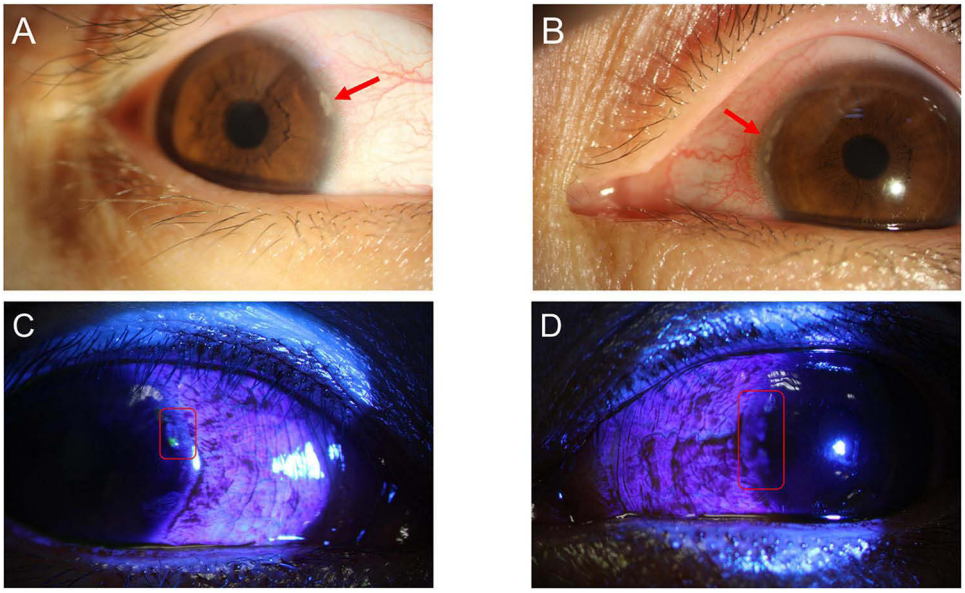

Figure 1 External photographs of the right eye (**A**) and left eye (**B**) at the initial ophthalmology clinic visit. The red arrows indicate the corneal infiltrative lesions. And fluorescein staining photographs of the right eye (**C**) and left eye (**D**) at the initial ophthalmology clinic visit. The red box indicates the corneal ulcerative lesion.

investigations revealed elevated white blood cells, an increased neutrophil ratio, and decreased lymphocytes. Tests were negative for influenza A and B RNA, suggesting a bacterial infection. The patient was diagnosed with bronchiolitis and treated for pneumonia with oral cefradine (0.5 g per dose, twice daily) for two weeks.

At the end of her pneumonia treatment, the patient presented to the ophthalmology clinic with persistent eye redness, dryness, and a foreign body sensation. Her best-corrected visual acuity (BCVA) was 20/20 in both eyes. Intraocular pressure was 16 mmHg (right eye) and 15 mmHg (left eye). No relative afferent pupillary defect was noted. Slit-lamp examination revealed bilateral conjunctival hyperemia. The Schirmer test measured 6 mm in the right eye and 7 mm in the left eye. Elongated spindle-shaped grayish-white lesions were observed at the corneal limbus, with a rough and dry surface and no secretions. In the right eye, two contiguous infiltrates were observed at the 2:30 position, each approximately 0.8 mm in diameter. In the left eye, five contiguous infiltrates were noted from the 8:00 to 10:00 positions, each approximately 0.6 mm in diameter. Significant ciliary injection was also noted, suggesting a possible inflammatory response or ocular infection (Figure 1A and B). Fluorescein corneal staining revealed that the corneal ulcer lesions were smaller than the infiltrates, with each ulcer measuring about 0.5 mm in diameter in the right eye and about 0.2 mm in diameter in the left eye, with the same number of lesions as the infiltrates (Figure 1C and D). The anterior chamber was deep with no inflammation in both eyes, and the posterior segment examination was unremarkable. In summary, the ophthalmic diagnosis was peripheral keratopathy combined with dry eye disease.

The patient was treated with topical tobramycin and dexamethasone eye drops (1–2 drops, four times daily), pranoprofen eye drops (1–2 drops, four times daily), recombinant bovine basic fibroblast growth factor eye drops (twice daily), and artificial tears (1–2 drops, four times daily, mainly contained hydroxypropyl methylcellulose, dextran, and glycerin), with close follow-up.

At the 3-week follow-up, the treatment was effective, with a significant improvement in ciliary injection. In the right eye, the infiltrates had regressed to a single lesion measuring approximately 0.5 mm in diameter, while in the left eye, three residual infiltrates were observed, each with a diameter of approximately 0.3 mm (Figure 2). At the 6-week follow-up, the patient's symptoms continued to improve, with increased but not complete corneal clarity and no signs of recurrence. At that point, she continued treatment only with tobramycin and dexamethasone eye drops. By the 9-week follow-up, the corneal ulcer had nearly healed, and the patient fully recovered and discontinued medication, with no complications observed. Throughout the treatment, her BCVA remained stable.

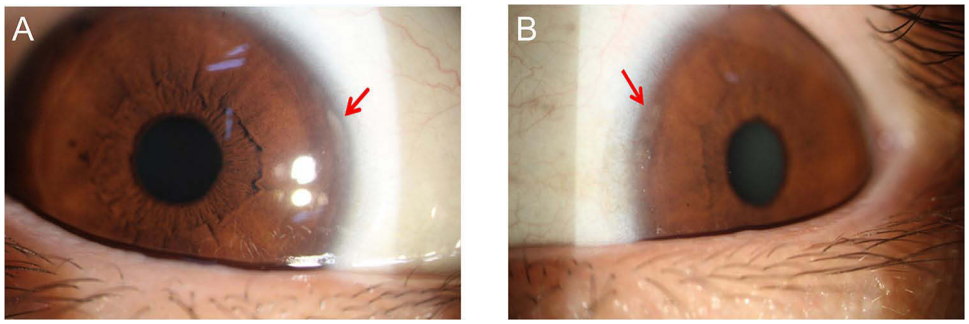

Figure 2 External photographs of the right eye (**A**) and left eye (**B**) after the 3-week follow-up. The red arrows indicate the corneal infiltrative lesions.

Discussion

Guo et al reported a COVID-19 patient who developed conjunctivitis 10 days after symptom onset, with a tenfold increase in IL-6 levels and SARS-CoV-2 detected in the conjunctiva.[7] Symptoms improved following treatment with fluorometholone. Additionally, a 67-year-old male developed secondary immune-related peripheral keratopathy after COVID-19 vaccination, which resolved with a combination of steroids, azathioprine, topical cyclosporine, and local dexamethasone treatment.[8] Previous reports suggest that COVID-19 infection can activate innate and adaptive immune responses, leading to the release of inflammatory mediators such as tumor necrosis factor (TNF), interleukin-1 (IL-1), interleukin-6 (IL-6), and interferon (IFN).[1,2,9] Elevated concentrations of IL-6 and IL-1β in the eye could recruit T cells that release cytokines and induce cytotoxicity, which may affect corneal tissue and other ocular structures. In our patient, while we cannot establish a direct mechanistic link, these findings provide a background for considering how post-COVID immune dysregulation could potentially affect the ocular surface.

Although corneal ulcers following bacterial pneumonia are generally rare, in these cases, the immune dysregulation associated with Post-COVID-19 Syndrome may have compromised the ocular surface defense and reduced corneal resistance, thereby increasing the risk of ulceration.[10] Moreover, post-COVID Syndrome can resemble an aberrant immune response similar to autoimmune conditions, leading to persistent inflammation and various ocular complications such as peripheral keratopathy, dry eye disease, and conjunctivitis.[11] Residual viral components, including protein molecules, may further disrupt physiological functions and exacerbate such conditions.[11]

Additionally, this patient's pre-existing dry eye disease was exacerbated by the recent infection, compromising the integrity of the corneal epithelium by reducing tear film stability. This facilitates pathogen penetration, increasing the risk of infections like peripheral keratopathy.[12] Furthermore, dry eye disease increases the levels of inflammatory cells and cytokines such as MMP9 and IL10 in the tear film, disrupting the ocular immune microenvironment and weakening corneal defenses, thus contributing to corneal ulcer formation.[13,14]

Potential treatment strategies for managing ocular complications in post-COVID-19 patients may include local and systemic anti-inflammatory therapies and corneal repair. Corticosteroids might help reduce ocular inflammation. More complex cases, such as severe corneal ulcers, may benefit from systemic immunosuppressants (eg, azathioprine) combined with local treatments (eg, cyclosporine eye drops). In addition, recombinant bovine basic fibroblast growth factor eye drops promote corneal ulcer healing by enhancing corneal epithelial regeneration, angiogenesis and matrix repair, while reducing scar formation.[15–17] They also reduce inflammatory factors in tears and alleviate dry eye disease symptoms.[18] Managing dry eye disease is also important, as artificial tears and anti-inflammatory agents could help restore tear film stability and lower infection risk.

This case has several limitations, including the absence of corneal scraping, PCR, culture/sensitivity, and imaging (AS-OCT) to assess lesion depth, as well as lack of correlation with systemic inflammatory markers.

This case underscores the need for more extensive research to further investigate the possible link between post-COVID-19 Syndrome and ocular complications, guiding better management strategies.

Conclusion

Systemic immune dysregulation following COVID-19 infection may alter the ocular surface immune microenvironment, thereby predisposing patients to ocular surface complications.

Ethics and Consent

Informed Consent: Written consent was obtained from the patient for the publication of this case report, including authorization to use any accompanying images. At The Sixth Affiliated Hospital, Sun Yat-sen University, ethical approval from the Institutional Review Board was not required for case reports.

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Disclosure

The authors report no conflicts of interest in this work.

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