Anterior Scleritis Manifesting After Coronavirus Disease 2019: A Report of Two Cases

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Purpose: The purpose of this study was to report 2 patients with anterior scleritis manifesting after coronavirus disease 2019 (COVID-19).

Methods: The patients with confirmed COVID-19 developed anterior scleritis after their systemic symptoms were markedly improved. A thorough systemic workup identified no underlying autoimmune diseases. Ocular characteristics and safety and efficacy of systemic immunosuppressive therapy were evaluated.

Results: Case 1 was a 67-year-old woman who presented with necrotizing anterior scleritis in both eyes 3 weeks after the onset of COVID-19. One-week treatment with topical betamethasone and oral prednisolone (65 mg daily) did not result in improvement, so she was started on intravenous cyclophosphamide and subcutaneous adalimumab in addition to oral prednisolone. Necrotizing scleritis was gradually improved over 3 months. Case 2 was a 33-year-old man who presented with sectoral anterior scleritis in his right eye 2 weeks after the onset of COVID-19. He was started on topical betamethasone and oral prednisolone (85 mg daily). One week later, all signs and symptoms disappeared, and topical and oral corticosteroids were gradually tapered off over 2 weeks. There was no recurrence of respiratory symptoms or active scleritis in any cases after discontinuation of treatment.

Conclusions: These cases suggest that COVID-19 can be associated with anterior scleritis, which responds to immunosuppressive and biologic agents. Ophthalmologists should consider anterior scleritis in patients with COVID-19 who present with ocular pain and redness during the convalescent phase of the illness.

Key Words: COVID-19, SARS-CoV-2, ocular involvement, anterior scleritis

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Since December 2019, coronavirus disease 2019 (COVID-19) has been spreading rapidly worldwide. The pathogen is a beta coronavirus that belongs to the Coronaviridae family [severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)].[1] COVID-19 is a very contagious infectious disease, which can progress to acute respiratory distress syndrome and even death. Other organs could be involved as well, and ocular manifestations have been reported in up to 31.6% of infected patients.[2] Its most common ocular manifestation is conjunctivitis.[3–5] Eyelid dermatitis,[6] keratoconjunctivitis,[7] episcleritis,[8–10] isolated retinal findings,[11–13] and posterior scleritis[14] are among other reported ocular complications of COVID-19. In a span of 4 months since July 2020, we observed 6 cases with anterior scleritis, a rare ocular disease, in our emergency department (2 cases with confirmed COVID-19 and 4 cases with negative laboratory test, but positive COVID-19 family members). Based on this observation, we hypothesized that there is a link between anterior scleritis and COVID-19. Herein, we report the 2 cases who developed anterior scleritis after laboratory confirmed COVID-19. The institutional review board approved this study which followed the tenets of the Declaration of Helsinki in all interventions. A signed informed consent form was achieved from the patients.

CASE REPORTS

Case 1 was a 67-year-old woman with unremarkable medical history except for bilateral cataract and pterygium surgery 3 years before presentation. She first presented to the hospital with fever, headache, myalgia, dry cough, and dyspnea on July 25, 2020. Nasopharyngeal swab was positive for SARS-CoV-2 on real-time reverse transcriptase polymerase chain reaction assays (Abbott Laboratories, Abbott Park, IL), and her chest computed tomography scan exhibited bilateral diffuse ground-glass opacifications in the lower lungs. She probably acquired COVID-19 from her husband who was diagnosed with the infection earlier. She was admitted and started on oral azithromycin 500 mg once daily, acetaminophen 500 mg every 6 hours, vitamin supplements, and supportive measures. Seven days later, symptoms improved, and she was discharged to be isolated at home for 2 weeks. Three weeks after the onset of COVID-19, she presented to our clinic complaining of redness, pain, and photophobia in both eyes. She denied any previous history of similar episodes. Slit-lamp examination disclosed diffuse chemosis and engorgement of superficial and deep episcleral vessels and episcleral and scleral edema in both eyes and peripheral corneal epithelial defects in the left eye (Fig. 1). Intraocular pressure was 10 mm Hg, and dilated fundus examination was unremarkable in both eyes. The patient was diagnosed with anterior scleritis. A thorough laboratory evaluation was performed while topical betamethasone every 6 hours, frequent lubrication, and oral prednisolone

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65 mg daily were started. The requested laboratory tests included complete blood count, erythrocyte sedimentation rate, C-reactive protein levels, and comprehensive metabolic panel such as serum uric acid. Extensive blood tests for detecting autoimmune conditions including antinuclear antibodies, antidouble-stranded DNA antibodies, antineutrophil cytoplasmic antibody, antiphospholipid antibodies, cyclic citrullinated peptide antibodies, complement antibodies, thyroid antibodies, rheumatoid factor, human leukocyte antigen (HLA)-B5, HLA-B27, HLA-B51, and serum levels of angiotensin-converting enzyme were also performed. In addition, serology for infectious diseases that might lead to scleritis such as hepatitis B and C viruses, varicella zoster virus, HIV, and syphilis was requested. Other ancillary tests included urinalysis and tuberculosis skin test. The systemic workup revealed no underlying systemic infectious, autoimmune, or collagen-vascular disease. Despite treatment with oral prednisolone, 1 week later, she developed areas of scleral necrosis, measuring 1.5 × 1.0 and 3.5 × 2.0 mm in the right and left eyes, respectively (Fig. 1). After discussion with the patient, it was decided to start 750 mg pulsed intravenous cyclophosphamide (3 injections 1 month apart) and subcutaneous adalimumab (5 injections 2 weeks apart) in addition to oral prednisolone. Necrotizing scleritis was gradually improved over 3 months, and there was no recurrence of respiratory symptoms or active scleritis 4 months after discontinuation of treatment.

Case 2 was a 33-year-old man with a history of trabeculectomy and Ahmed glaucoma valve implantation for advanced primary congenital glaucoma in his both eyes. He had no underlying systemic disease. Medication history was positive for topical glaucoma eye drops (timolol-dorzolamide fixed combination OU, brimonidine tartrate 0.2% OS, and latanoprost 0.005% OS). On October 16, 2020, he was diagnosed with COVID-19 after a positive nasopharyngeal real-time reverse transcriptase-polymerase chain reaction test (Abbott Laboratories) for fever, myalgia, anosmia, ageusia, dry cough, and dyspnea. On chest computed tomography scan, he had a mild involvement of the upper lobe of the right lung with an oxygen saturation of 98%; therefore, he was closely followed with famotidine 40 mg every 12 hours, acetaminophen 500 mg every 6 hours, and vitamin supplements and instructed to isolate at home for 2 weeks. Oral prednisolone 50 mg daily was started 3 days later and continued for 1 week until his symptoms significantly resolved. Two weeks after the onset of his systemic symptoms, the patient presented to us with red eye, foreign-body sensation, epiphora, and photophobia in his right eye that was not associated with blurred vision. He denied any history of similar episodes in the past. Slit-lamp examination revealed a sectoral superotemporal injection of superficial and deep episcleral vessels and edema of the episclera and sclera in the right eye that persisted despite using topical phenylephrine hydrochloride 10%. The cornea was clear, and the shunt tube was well-positioned in the anterior chamber of both eyes. Intraocular pressure was 10 mm Hg OD and 14 mm Hg OS with antiglaucoma topical medications. The dilated fundus examination disclosed advanced glaucomatous optic neuropathy in both eyes. The patient was diagnosed with sectoral anterior scleritis in his right eye and was started on topical betamethasone every 6 hours and oral prednisolone 85 mg daily. A comprehensive systemic workup, as described in case 1, was performed. This workup was negative for any underlying infectious or autoimmune diseases. One week after treatment, scleritis improved completely and topical and oral corticosteroids were gradually tapered off over 2 weeks. There was no recurrence of respiratory symptoms or scleritis within 5 months of follow-up.

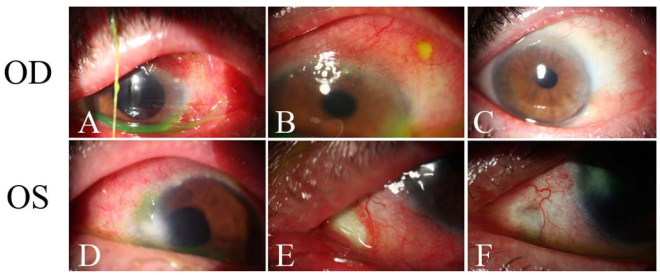

FIGURE 1. Slit-lamp views demonstrate the course of anterior scleritis associated with COVID-19 in case 1. A and D, diffuse chemosis and engorgement of superficial and deep episcleral vessels as well as episcleral and scleral edema in both eyes and peripheral corneal epithelial defects in the left eye at the time of presentation. B and E, necrotic areas 1 week after treatment with topical and systemic corticosteroids. C and F, improved scleritis 3 months after treatment with systemic immunosuppressive and biologic agents. (The full color version of this figure is available at www.corneajrnl.com.)

DISCUSSION

Ocular manifestations are uncommon but well-established complications of COVID-19; however, the pathophysiology of the ocular involvement is not clear yet. SARS-CoV-2 enters host cells through endocytosis of its specific functional receptor, angiotensin-converting enzyme 2 (ACE2).[15] ACE2 is the most representative bioactive in the renin–angiotensin system and exerts antiinflammatory effects on specific tissues.[15] Several studies showed the expression of ACE2 in various ocular tissues including cornea, conjunctiva, retina, retinal pigment epithelium, and choroid.[16,17]

The most frequently reported ocular manifestation of COVID-19 is conjunctivitis.[3–5] Other nonsight-threatening complications include eyelid dermatitis,[6] keratoconjunctivitis,[7] episcleritis,[8–10] and isolated retinal findings.[11–13] There has been 1 report on bilateral posterior scleritis in a COVID-19 patient with multisystemic involvement including renal insufficiency, bilateral pulmonary embolism, mesenteric ischemia, and encephalitis.[14] Ophthalmic examination was remarkable for bilateral posterior scleritis, retinal vascular sheathing, and vitreous condensations.[14] There is no report on anterior scleritis associated with COVID-19 partly because the diagnosis of anterior scleritis could be confounded by systemic comorbidities of acute COVID-19 and difficulties with bedside ophthalmology examination. Moreover, any late-onset ocular complication could be underreported in hospital-based case series on acute COVID-19 cases.

Scleritis is a destructive and vision-threatening ocular disorder that involves deep episclera and sclera. It is mostly an autoimmune disorder, which in half of the cases is associated with an underlying systemic immune-mediated disease, including systemic lupus erythematosus, Wegener granulomatosis, and rheumatoid arthritis.[18] Scleritis has also been reported as an ocular manifestation of viral diseases. Although the members of Herpesviridae family, such as herpes simplex virus type-1 and varicella zoster virus, are more commonly reported to be associated with scleritis,[19] cytomegalovirus,[20] Epstein–Barr virus,[21] and dengue fever virus[22] have also been implicated. Our cases illustrate anterior

scleritis as a possible late ocular manifestation of COVID-19. Although ocular involvement is mostly reported in severe COVID-19 cases,[2,9] our patients had a moderate acute infection. SARS-CoV-2–induced pathology is believed to be caused by a compromised initial adaptive immune response in early viral replication, followed by an unleashed innate immune response.[23,24] This biphasic nature of the inflammatory response to COVID-19 was demonstrated in a coronavirus retinopathy model.[24] This model showed a direct cytopathic effect of the virus at the beginning of the infection that was followed by a vigorous inflammatory response within 10 to 14 days, resulting in a disproportionate release of inflammatory mediators and cytokines such as interleukin (IL)-1β, IL-2, IL-6, IL-8, IL-17, tumor necrosis factor, interferon gamma–induced protein-10, granulocyte colony–stimulating factor, granulocyte macrophage colony–stimulating factor, monocyte chemoattractant protein-1, and macrophage inflammatory protein-1α.[23,24] The relatively late-onset scleritis in our cases is more consistent with a postinfectious immune-mediated response rather than a direct viral infection. However, we cannot exclude the possibility of local ocular infection because conjunctival sampling for viral nucleic acid was not performed in these cases. There has been a report on bilateral conjunctivitis with positive conjunctival swabs for SARS-CoV-2 13 days after confirmed COVID-19, which raises the possibility of local infection in our cases.[3]

The main treatment for anterior scleritis is systemic immunosuppression.[18] One of our patients was successfully treated with oral prednisolone; however, systemic cyclophosphamide and subcutaneous adalimumab were needed for the management of scleritis for the other case. Although we were concerned about using immunosuppression therapy in the recovery phase of COVID-19, our patients remained asymptomatic during the course of treatment and follow-up. This experience offers some degree of confidence that treatment with immunosuppressive agents is largely safe in COVID-19 patients with ocular conditions such as scleritis once they recover from the acute stage of the infection.

In conclusion, ophthalmologists should consider anterior scleritis in patients with COVID-19 who present with ocular pain and redness during the convalescent phase of the illness. Immunosuppressive and biologic agents can be safely and effectively administered for the management of COVID-19–associated scleritis when there are clear signs of recovery from the infection. Further studies with longer follow-up are warranted to determine the true incidence of anterior scleritis in patients with COVID-19.

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