OLGU SUNUMU CASE REPORT

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Ocular Cicatricial Pemphigoid Activation After COVID-19 Infection

COVID-19 Enfeksiyonu Sonrası Oküler Sikatrisyel Pemfigoid Aktivasyonu

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ABSTRACT A 58-year-old male patient was admitted with the complaint of burning, watering, stinging, redness and pain in both eyes after he had had coronavirus disease-2019 (COVID-19) infection 3 weeks ago. It was determined from the anamnesis of the patient that he had severe vision loss in the right eye for about 35 years and had been treated with some previous treatments. He had a best spectacle-corrected visual acuity of "hand motion" in the right eye and LogMAR 0.2 in the left eye. The patient was considered ocular cicatricial pemphigoid (OCP) reactivation in the right eye and new diagnosis OCP in the left eye after COVID-19 infection with the slit lamp examination findings. After the relevant consultations, medical treatment was applied to the patient and it was observed that the symptoms regressed in the first month follow-up.

Keywords: COVID-19; ocular cicatricial pemphigoid; cornea

ÖZET 58 yaşında erkek hasta, 3 hafta önce koronavirüs hastalığı-2019 [coronavirus disease-2019 (COVID-19)] enfeksiyonu geçirdikten sonra her iki gözünde yanma, sulanma, batma, kızarıklık ve ağrı şikâyeti ile başvurdu. Hastanın anamnezinden yaklaşık 35 yıldır sağ gözünde ciddi görme kaybı olduğu ve daha önce bazı tedaviler gördüğü belirlendi. Sağ gözde en iyi düzeltmeli görme keskinliği "el hareketi seviyesinde" ve sol gözde LogMAR 0,2 düzeyindeydi. Biyomikroskobik muayene bulguları ile hastanın COVID-19 enfeksiyonu sonrası sağ gözünde oküler sikatrisyel pemfigoid (OSP) reaktivasyonu ve sol gözünde yeni OSP tanısı düşünüldü. İlgili konsültasyonların ardından hastaya medikal tedavi uygulandı ve ilk ay takibinde semptomlarının gerilediği görüldü.

Anahtar Kelimeler: COVID-19; oküler sikatrisyel pemfigoid; kornea

Ocular mucous membrane pemphigoid, also known as ocular cicatricial pemphigoid (OCP), primarily affects the conjunctiva and in lesser frequency oral, nasal, and esophageal mucosae. The clinical course of OCP is characterized by slow progression from chronic conjunctivitis to subepithelial fibrosis, fornix foreshortining, symblepharon, and ankyloblepharon formation with ocular surface keratinization. The disease typically lasts for several years and can ultimately lead to blindness without treatment.[1-5]

It has been reported that coronavirus disease-2019 (COVID-19) infection stimulated the immune system and caused the activation of autoimmune diseases.[6] We aimed to present a patient who had reactivation of OCP in the right eye and new diagnosis of OCP in the left eye, after COVID-19 infection. We would like to emphasize that the immune response caused by COVID-19 can activate OCP, an autoimmune disease.

Written informed consent was obtained from the patient for publication of his case details and for images.

CASE REPORT

A 58-year-old male patient applied to our clinic with the complaint of burning, watering, stinging, redness and pain in both eyes following COVID-19 infection 3 weeks ago.

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It was detected from the anamnesis of the patient that the he was not hospitalized during the COVID-19 disease process. He had only some complaints such as dry cough, mild fever, joint pain and weakness. It was also detected that he used 200 mg favipiravir treatment for a total of 5 days, 2x8 on the 1st day and 2x3 on the other days, and did not receive any treatment other than this treatment.

The patient stated that similar complaints started 35 years ago in his right eye and he lost his vision over time. He had a best spectacle-corrected visual acuity of "hand motion" in the right eye and LogMAR 0.2 in the left eye. Slit-lamp examination revealed 360º limbal stem cell deficiency in the right eye and secondary corneal neovascularization and opacification, as well as symblepharon in the lower eyelid. The conjunctiva was inflamed and hyperemic. Details of the anterior chamber could not be selected (Figure 1). The cornea of the left eye was clear, limbal insufficiency of about 60º between 11 and 1 o'clock and secondary corneal neovascularization was observed from this region. Anterior chamber structures were normal, and conjunctiva was hyperemic and inflamed. On the lower eyelid, conjunctival blister formation was observed at 6 o'clock with symblepharon (Figure 2, Figure 3). Intraocular pressures were normal in both eyes. In fundus examination, the left eye was normal, however the right eye could not be evaluated due to opaque cornea. The patient was hospitalized with a pre-diagnosis of OCP reactivation in the right eye, and new diagnosis OCP in the left eye. The patient was consulted with dermatology and rheumatology clinics. P-ANCA, C-ANCA, dsDNA, ANA, Anti-Sm, ENA SM-RNP, Anti Centromer B tests were negative. In the thrombophilia panel, MTHFR A1298C and PAI-1 were heterozygous for 4G/5G. The patient had leukocytosis and pathergy test was negative. No rheumatological disease was detected with the current examination and laboratory findings. Conjunctival biopsy was not performed due to the absence of involvement in the extraocular organs and the risk that biopsy from the eye could aggravate the disease. The patient was started on preservative-free artificial teargel, topical cyclosporine 4x1, topical loteprednol 4x1 and 1 mg/kg oral steroid treatment. After 1 week, the steroid dose was started to be reduced and at the same time, mycophenolate mofetil 2x500 mg treatment was started. In the follow-up after 1 month, the patient's complaints decreased in both eyes. There was no decrease in visual acuity scores. Bilateral con-

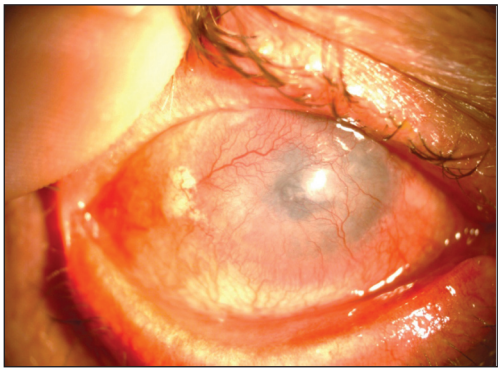

FIGURE 1: 360 degree limbal stem cell insufficiency and secondary corneal neovascularization and opacification in the right eye, symblepharon on the lower lid.

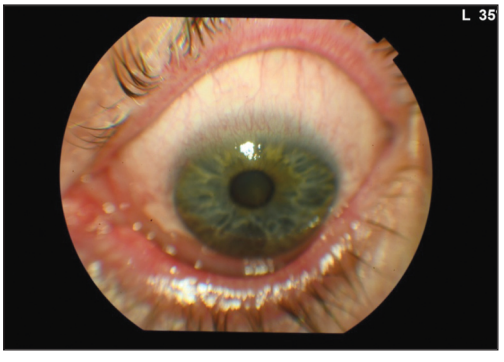

FIGURE 2: Limbal cell insufficiency of approximately 60º between 11 and 1 o'clock and secondary corneal neovascularization in this region in the left eye.

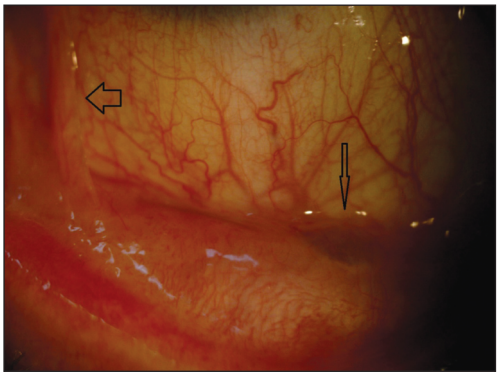

FIGURE 3: Conjunctival bulla formation (thin arrow) at 6 o'clock position with symblepharon (thick arrow) on the lower eyelid of the left eye.

junctival hyperemia and inflammatory findings were found to be regressed in slit lamp examination.

DISCUSSION

Many complications of OCP including corneal epithelial defect, corneal stromal ulcers, corneal perforation, severe dry eye, trichiasis, distichiasis, entropion, lagophthalmos, symblepharon, and glaucoma have been described. An extensive list of causes of chronic cicatrizing conjunctivitis including Stevens-Johnson syndrome, graft-versus-host disease, systemic lupus erythematosus, Sjogren's syndrome, toxic epidermal necrolysis, trachoma, dry eye syndrome, adenoviral conjunctivitis, chemical burn, drug toxicity, atopic keratoconjunctivitis, and radiation exposure should be considered in the differential diagnosis. The distinctive clinical charcteristic of OCP is a progressive symblepharon.[7] Our patient also had symblepharon signs in both eyes. Although it has been reported that OCP causes erosions, bullae and stenosis by affecting the mucous membranes of other organs, our case applied to our clinic with only ocular involvement.

OCP has been classically described as an autoimmune disease with a genetic predisposition and probably a "second hit" environmental requirement to trigger the onset or activation of the disease. The second-hit environmental trigger that stimulates the genetically suspectible individual to devolop or reactivate OCP may be microbial, as is suspected for idiopathic OCP, or may be chemical, as in the case of so-called drug-induced OCP or pseudo-OCP, which develops in some individuals exposed to practolol or to a limited variety of ocular medications.[8] When we examined our patient, it was detected that he did not have any medication or chemical exposure other than favipiravir. When the side effects of favipravir were investigated, no literature information on the activation of autoimmune diseases such as OCP was observed. Studies demonstrated a lower proportion of Grade 1-4 adverse drug events and a better overall safety profile of favipiravir than placebo. Therefore, we think that the OCP activation in our patient is related to the COVID-19 infection.

The chronic stage of the disease largely has lymphocytic infiltration. Fibroblast activation causes subepithelial fibrosis, which appears as fine white lines in the early stage of the disease. Advancing conjunctival scarring may lead to occlusion of the main and accessory lacrimal gland ducts, creating a deficiency in the aqueous component of the tear film. Although the resulting xerosis is severe, it is associated with limbal stem cell damage and progressive subepithelial fibrosis leading to ocular keratinization.[3] Our patient had severe dry eye in both eyes. While there was 360º limbal insufficiency and secondary total corneal neovascularization in his right eye, there was limbal insufficiency in the 60º area in his left eye and corneal neovascularization in the area corresponding to this region.

According to Foster staging, the disease shows findings such as chronic conjunctivitis characterized by subepithelial fibrosis, shortening of the inferior fornix, formation of symblepharon, ocular surface keratinization, complete destruction of the lower fornix, and formation of corneal neovascularization.[8] Subepithelial fibrosis is the last common pathway to explain the signs of the disease. The change that occurs in the conjunctiva affects the eyelids and causes many changes such as trichiasis, distichiasis, entropion, and lagophthalmus. When the deterioration in tears is added, conjunctival inflammation, which enters a vicious circle, is observed.[9,10] Our patient had signs of conjunctival inflammation such as hyperemia and pain in both eyes. There were signs of all stages of OCP such as conjunctivitis, symblepharon, dry eye, limbal insufficiency, and corneal neovascularization, in particular in the right eye.

No cases of OCP activated after COVID-19 infection have been reported before. In our case report, it was observed that the disease, which remained silent for years, suddenly aggravated. It should be kept in mind that silent autoimmune diseases can be reactivated after COVID-19.

Source of Finance

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Cem Çankaya;* ***Design:*** *Cem Çankaya;* ***Control/Supervision:*** *Cem Çankaya;* ***Data Collection and/or Processing:*** *Yakup Yıldızlı;* ***Analysis and/or Interpretation:*** *Cem Çankaya;* ***Literature Review:*** *Yakup Yıldızlı;* ***Writing the Article:*** *Cem Çankaya;* ***Critical Review:*** *Cem Çankaya;* ***References and Fundings:*** *Yakup Yıldızlı;* ***Materials:*** *Yakup Yıldızlı.*

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