





DOI: 10.14744/eer.2022.29974
Eur Eye Res 2022;2(4):199–202

EUROPEAN
EYE
RESEARCH

CASE REPORT

Bilateral herpes simplex epithelial keratitis in a patient with pemphigus foliaceus

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Abstract

Bilateral herpetic keratitis is a rare event and can occur in atopy, measles, and immunodeficiency. Long-term use of systemic steroids for any autoimmune condition also creates iatrogenic immunodeficiency. A 62-year-old female with Pemphigus Foliaceus who had been on long-term steroids presented with bilateral epithelial herpetic keratitis. She received topical ganciclovir 5 times daily for a total of 10 days and intravenous (iv) acyclovir 5–10 mg/kg for 2 weeks for diffuse periocular skin involvement. In 2 weeks, corneal lesions completely disappeared with intact epithelium and no stromal involvement. Treatment was discontinued as no further ocular signs were observed. Peroral antiviral prophylaxis was not initiated since systemic steroids were also discontinued. Three months after resolution, she underwent bilateral cataract surgeries with pre-operative and post-operative systemic prophylaxis during topical steroid use. Long-term systemic steroid use seems to be a predisposing factor for bilateral herpetic ocular infections.

Keywords: Herpes virus; keratitis; pemphigus.

Herpes simplex virus type 1 keratitis (HSV) is the most common cause of infectious blindness worldwide. Clinically, disease can affect all layers of the cornea from epithelium to endothelium, leading to recurrent epithelial desquamation, ulceration, scarring, and neovascularization of the cornea. A better understanding of the global burden of HSV keratitis has significant implications for the prevention and treatment of the disease. Studies show that the global annual incidence of HSV keratitis is 1.5 million and 40,000 new cases result in severe monocular impairment or blindness.^[1] Bilateral herpetic keratitis is rare and occurs with a frequency of 1–10%. Ocular HSV involvement can be

bilateral in atopy, measles, graft-versus-host disease, immunodeficiency, and in young patients.^[2]

Herein, we present a case with bilateral herpes simplex epithelial keratitis after 2 years of oral and topical steroid treatment due to the Pemphigus Foliaceus.

Case Report

A 62-year-old female patient diagnosed with Pemphigus Foliaceus had been treated with peroral 40 mg methylprednisolone (Prednol tb, Mustafa Nevzat pharmaceuticals, Istanbul, Türkiye), topical clobetasol propionate 0.05%



Cite this article as: Mammadov T, Utine CA. Bilateral herpes simplex epithelial keratitis in a patient with pemphigus foliaceus. Eur Eye Res 2022;2:199–202.

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Submitted Date: 07.08.2022 **Revised Date:** 08.09.2022 **Accepted Date:** 21.09.2022

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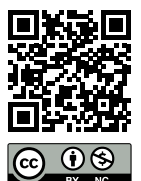




Fig. 1. Periorbital and forehead lesions of the patient.

cream (Dermovate cream, GSK plc, London, England), and 20 mg betamethasone valerate cream (Betnovate cream, GSK plc, London, England) for 2 years. She has been admitted to the dermatology department due to a facial exacerbation of her disease. She received isoconazole nitrate 1% (Travogen, Bayer Turk Kimya San. Trade Ltd. Sti., Istanbul, Türkiye) cream for fissures around the lips, clobetasol propionate 0.05 cream for lesions on the limb, fusidic acid cream (Fucidin cream, Leo Pharma, Ballerup, Denmark) for erythematous lesions on the face bid, and chlorhexidine plus benzamidine mouthwash (Geral gargara, Biofarma, Sancaktepe, Istanbul) for intraoral lesions.

She was referred to ophthalmology department due to the complaints of burning, stinging, and redness in both eyes on her follow-up. Physical examination revealed bilateral periorbital dry lesions (Fig. 1). Visual acuity was 0.6 on the right eye and 0.4 on the left eye, in Snellen lines. The

intraocular pressures with icare tonometer (I-care Finland Oy, Antaa, Finland) were 14 mmHg and 15 mmHg in her right and left eyes, respectively. Biomicroscopy revealed fluorescein dye uptake of dendritic lesions in paracentral 11, 3, and 7 o'clock positions on the right cornea and in paracentral 11 o'clock position on the left cornea, mild hyperemia in the bulbar conjunctiva, and stage 2 nuclear sclerosis in both eyes. There was no evidence of iridocyclitis, bilaterally (Fig. 2a and b). Fundus examination revealed no significant pathologic changes in the optic disc, macula, or vitreous.

With a preliminary diagnosis of bilateral epithelial herpetic keratitis, topical ganciclovir (Virgan, Theapharma, Besiktas, Istanbul) 5 times a day was administered for 10 days. At the same time, (iv) acyclovir (Asirax 250 mg I.V., VEM pharma., Maslak, Istanbul) 5–10 mg/kg was commenced. As the patient was already on intravenous acyclovir treatment due to the wide-spread dissemination of the virus, corneal debridement was not considered. On the 5th day of treatment, the dose was changed to 3×350 mg due to decreased glomerular filtration rate. Systemic antiviral therapy was continued for 2 weeks due to diffuse periorbital skin involvement.

The polymerase chain reaction analysis of conjunctival swab that was obtained at initial examination yielded positive results for HSV type 1 DNA. PCR of conjunctival swabs had been performed to verify our diagnosis, although the antiviral therapy was started empirically before PCR results were available.

After 2 weeks of treatment, corneal lesions disappeared completely, the epithelium was intact with no stromal ulceration, and the treatment was discontinued as no further ocular findings were observed in both eyes (Fig. 3a and b). Three months after treatment, she underwent bilateral cataract surgeries with uneventful phacoemulsifi-

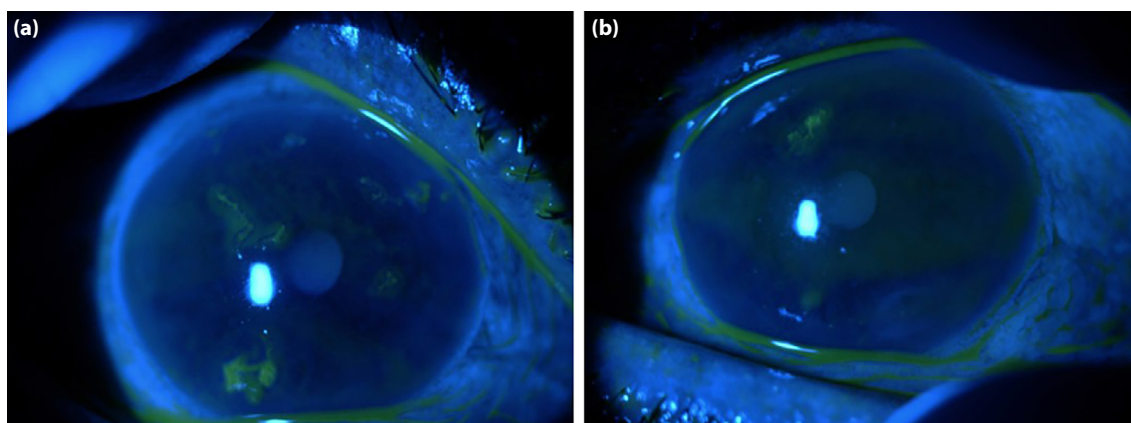


Fig. 2. (a, b) Dendritic epithelial lesions on the right and left corneas.

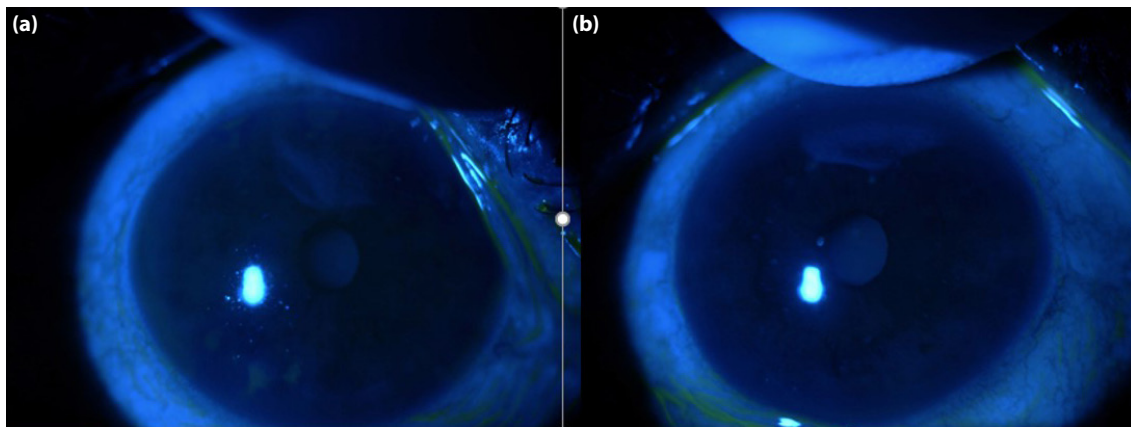


Fig. 3. (a, b) Intact corneal epithelium after treatment on the right and left eyes.

cation under systemic acyclovir prophylaxis (i.e., peroral valacyclovir 500 mg bid) for the whole duration of topical steroid use.

Discussion

Epithelial keratitis is the most common form of ocular HSV. Disease accounts for approximately 80% of all cases. Linear lesions with a branching pattern and swollen end structures secondary to infection and erosion-dendritic epithelial keratitis are the typical form of epithelial HSV keratitis and usually occur unilaterally. Reactivation of HSV is seen more common in patients with systemic atopy or altered systemic immunity. In the case, we presented, following long-term systemic and topical steroids for the vesiculobullous autoimmune skin disorder on the body and periorbital area led to clinically bilateral herpes simplex epithelial keratitis, which is suggestive of disseminated HSV infection. Marzano et al.^[3] have reported that HSV infection is not a precipitating factor for pemphigus disease; however, the presence of HSV in pemphigus lesions is a common and early complication of immunosuppression. When skin lesions spread over one or more dermatomes unilaterally, disseminated varicella zoster virus (VZV) infection should also be suspected. Margolis et al.^[4] recommended the use of a systemic antiviral (iv or PO) in addition to topical antivirals for eczema herpeticum. Although topical treatment is sufficient for epithelial herpes keratitis according to HEDS reports, systemic treatment is recommended for bilateral/disseminated disease in immunocompromised patients.^[5] In accordance with these recommendations, our case was treated with topical ganciclovir and acyclovir (iv) for 2 weeks due to bilateral involvement and diffuse periocular skin involvement.

Although there is no strict consensus about the timing of cataract surgery after herpetic keratitis, it is recommended

to have a quiescent period between the active disease and the surgery. The time of quiescence before surgery is known to be significantly associated with post-operative disease recurrence.^[6] Given our patient had poor visual acuity bilaterally, the surgeries were performed at post-operative 3rd month. This period of quiescence is in accordance with the majority of the U.K. corneal specialists who recommend waiting 3 to 6 months before performing cataract surgery on patients with previous HSV keratitis or keratouveitis.^[7]

It has been known that long-term prophylactic antiviral treatment can reduce the incidence of recurrence in HSV keratitis.^[8] Since topical and systemic steroid use was discontinued for skin disorder, systemic antiviral prophylaxis was not commenced and no occurrence has been seen. There is strong evidence that oral prophylaxis should be recommended perioperatively in patients with HSV/VZV infection in patients undergoing penetrating keratoplasty. The American Academy of Ophthalmology also recommends that antiviral prophylaxis be strongly considered for all patients with a history of HSV ocular disease in the immediate perioperative period, especially while being treated with corticosteroids.^[9] There have been no published prospective studies exploring the efficacy of antiviral prophylaxis in cataract surgery alone, but a recent retrospective observational cohort study yielded a significant risk for recurrent inflammation in the 1st year postoperatively.^[6] The UK study revealed that, postoperatively, there was a wide range of treatment duration with antiviral drugs among surgeons, ranging from 7 to 365 days. Regarding post-operative topical corticosteroid therapy, most surgeons (80.9%) would not change their usual regimen from routine cataract surgery.^[7] Surgeons recommended commencing oral antiviral prophylaxis preoperatively and continuing for as long as the patient is on topical corticosteroid therapy.^[7] Based on available evidence, prophylaxis

with oral acyclovir 400 mg 2 times daily or equivalent dose of valacyclovir, starting just before surgery, and sustained until steroids are withdrawn, would be recommended.^[10]

The prophylaxis after surgery could be continued for 1 year for the possibility of any late activation of the herpes virus, particularly if there was a history of stromal keratitis or keratouveitis. However, in this particular patient with first episode of herpetic epithelial keratitis under aggressive antiviral therapy and reduced glomerular filtration rate indicating renal insufficiency, we preferred to cease antiviral treatment simultaneously with topical steroids. As in many cases in medicine, period of quiescence, timing of the surgery and post-operative prophylaxis time can be custom for each patient, under general guidelines and close observation of the patient for any reactivation symptoms.

Conclusion

Long-term systemic steroid use seems to be a predisposing factor for bilateral herpetic ocular infections. This should be kept in mind in patients with any autoimmune skin or rheumatological disorder who need to be long-term immunosuppression with steroid, along with other known complications of corticosteroids.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: T.M., C.A.U.; Design: C.A.U.; Supervision: C.A.U.; Resource: T.M., C.A.U.; Materials: T.M.; Data Collection and/or Processing: T.M.; Analysis and/or Interpretation: T.M., C.A.U.; Literature Search: T.M.; Writing: T.M.; Critical Reviews: C.A.U.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study received no financial support.

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