

Case Report

Bilateral Herpes Simplex Virus-related Peripheral Ulcerative Keratitis Leading to Corneal Perforation in a Patient with Primary Herpes Simplex Virus Infection

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Abstract

Purpose: To present a case of bilateral peripheral ulcerative keratitis (PUK) caused by primary herpes simplex virus-1 (HSV-1) infection resulting in corneal perforation.

Case Report: A 24-year-old man presented at the eye casualty of our clinic, with a 20-day history of severe pain, redness, photophobia, and tearing in both of his eyes. Slit-lamp examination revealed bilateral superior corneal perforation. A laboratory work-up that included immunological testing for infectious and autoimmune factors showed primary HSV infection. Positive PCR analysis of corneal scrapings for HSV confirmed initial end-organ ocular infection. Because the patient showed progressive HSV-1-related PUK resulting in bilateral superior corneal perforation with iris prolapse, he was prescribed both systemic and topical acyclovir and prednisone. He then underwent bilateral surgical intervention, namely eccentric penetrating keratoplasty in one eye and a two step procedure in the other, whereby two corneal patch grafts and an amniotic membrane transplant were initially used, followed 1 month later by a large diameter penetrating keratoplasty.

Conclusion: In cases of PUK, differential diagnosis should include infectious and autoimmune diseases. Primary HSV should also be considered as a potential cause of this form of keratitis, which, if left untreated, can lead to devastating outcomes. To our knowledge, this is the first published case of bilateral PUK caused by primary HSV-1 infection.

Keywords: Bilateral Corneal Perforation; Herpes Simplex Virus-1; Peripheral Ulcerative Keratitis; HSV-1 PUK; Primary HSV Infection

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INTRODUCTION

Herpes simplex virus (HSV) causes a wide variety of ocular diseases, particularly because HSV can infect a

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host and establish an indefinite latent status in ganglionic neurons. Primary HSV infection occurs in nearly 60% of the population by the age of 5 years. However, clinical manifestations occur in only 6% of those infected, typically affecting the perioral region, rather than the eye. Primary clinical HSV infection usually responds to antiviral therapy and is typically not associated with serious complications. Conversely, recurrent infection poses a serious threat to vision. Spontaneous and recurrent reactivation is facilitated by latency, which provides a viral reservoir within the population.^[1-3]

In particular, HSV keratitis is one of the most challenging pathologies encountered by clinicians. The most common ophthalmic manifestation of HSV is unilateral infectious epithelial keratitis, with corneal vesicles and dendritic, geographic, or marginal ulcer.^[4] Bilateral herpetic keratitis usually develops in younger patients^[5] and reportedly occurs in 1-11.76% of patients with ocular HSV.^[6-9]

In the present report, we describe a rare case of primary HSV-1 infection with ocular manifestations that led to bilateral corneal perforation. To our knowledge, there is only one other report of bilateral HSV-related peripheral ulcerative keratitis (PUK), and this is the first report of bilateral primary HSV-1-related PUK presenting as bilateral corneal perforation.

CASE REPORT

A 24-year-old man presented at the eye casualty of our clinic, with a 20-day history of severe pain, redness, photophobia, and tearing in both of his eyes. He had been treated repeatedly with corticosteroids and prophylactic topical antibiotics for bilateral viral conjunctivitis. His medical history revealed only congenital hepatitis B that was well under control. There was no ocular history of trauma, surgery, infection, or allergic/atopic episodes prior to this incidence, although minor trauma caused by eye rubbing remained a possibility.

Upon ophthalmic assessment, the patient's visual acuity was 3/10 in both eyes. Slit-lamp examination revealed acute conjunctival hyperemia and inflammation, bilateral superior corneal perforation, and peripheral subepithelial and stromal neovascularization extending to the margins of the perforation and causing sizable iris prolapse was also noted. Both anterior chambers were shallow [Figures 1 and 2]. The crystalline lenses were clear and fundoscopy was normal bilaterally.

The patient underwent physical examination followed by laboratory work-up, including complete and differential blood cell counts, platelet counts, erythrocyte sedimentation rate, and liver and renal function tests. Because his condition was rather suspicious, immunological testing was ordered, including rheumatoid factor (RF), antinuclear antibodies (ANA), antineutrophil cytoplasmic antibodies, and C-reactive

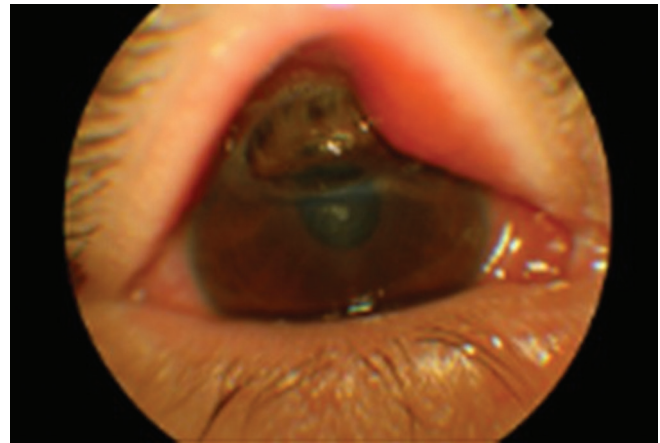


Figure 1. Corneal perforation and iris protrusion in the right eye.

protein (CRP) titers. The patient was also subjected to a fluorescent treponemal antibody absorption test, Mantoux test, chest X-ray, and a complete work-up for sexually transmitted diseases.

The laboratory work-up revealed only lymphocytosis, and this prompted a work-up for systemic HSV infection, whereby paired samples were subjected to serological evaluation with IgG and IgM. A high IgM HSV-1 titer was found, with no IgG HSV-1 titer. Cultures of corneal and conjunctival scrapings were negative for bacteria or fungi, and specimens of corneal scrapings from both eyes were sent for HSV gene detection by polymerase chain reaction (PCR). Intravenous acyclovir treatment (250 mg, twice daily) was commenced, and topical medication was applied, namely acyclovir, prednisone, prophylactic antibiotics, and cyclopentolate.

After 2 weeks of intravenous and topical acyclovir treatment, the patient's clinical status had improved greatly; his symptoms subsided, and little inflammation was noted in either eye. Positive PCR analysis for the HSV genome verified the diagnosis of bilateral HSV-related PUK.

Because the patient's condition was urgent, an aggressive surgical approach was adopted. In his right eye, a corneal and conjunctival resection of 2 clock hours was performed on both sides of the corneal ulcer, removing redundant, protruding, epithelialized iris tissue. Iridoplasty and eccentric penetrating keratoplasty were then performed after two weeks of intravenous and topical acyclovir treatment [Figure 3]. The left eye was managed in two steps. During the first surgical procedure, the same steps were taken as in his right eye, but instead of an eccentric penetrating keratoplasty, two temporary tectonic corneal grafts were used—a nasal and a temporal—and an amniotic membrane was transplanted [Figure 4]. A corneal melt developed 1 month later in the temporal patch graft, so a large diameter penetrating keratoplasty was performed [Figure 5].

Histological analysis of the resected tissue showed a cellular population consisting of lymphocytes,

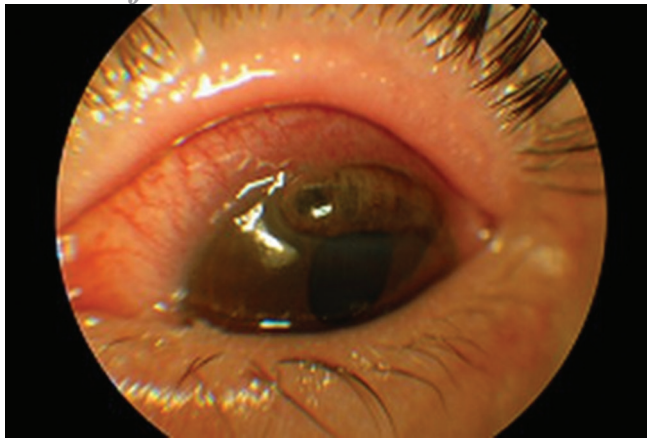


Figure 2. Corneal perforation and iris protrusion in the left eye.

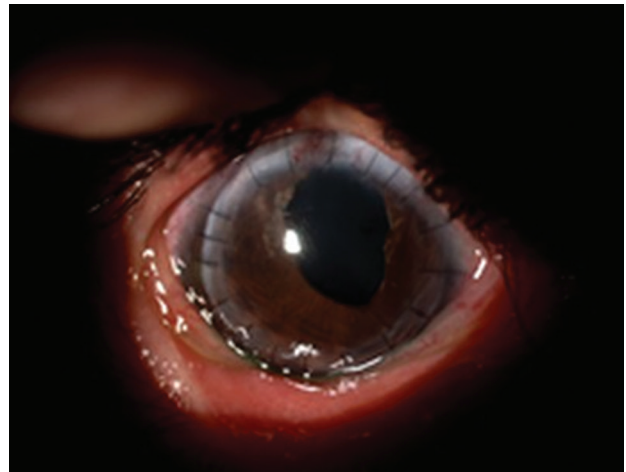


Figure 3. Eccentric penetrating keratoplasty of the right eye.

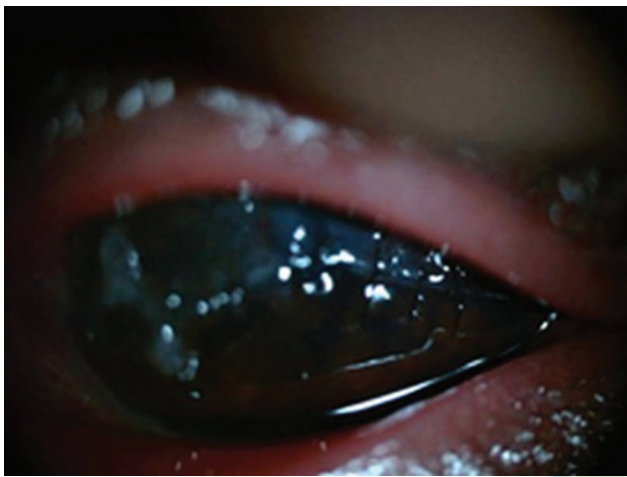


Figure 4. Corneal patch grafts and amniotic membrane transplant of the left eye.

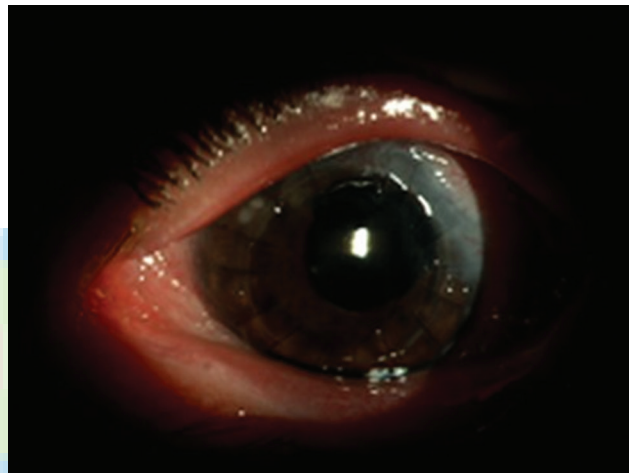


Figure 5. Large diameter penetrating keratoplasty of the left eye.

macrophages, fibroblasts, and mast cells. Neovascular capillaries were also observed.

Twelve months after surgery, the HSV keratitis had not recurred.

DISCUSSION

Primary HSV infection with initial end-organ manifestation involving both eyes is rare in immunocompetent patients. In the present case, identification of lymphocytosis prompted serological evaluation, and the high HSV IgM titers and initial absence of HSV IgG titers confirmed primary HSV infection. Antibody titers can fluctuate independently of clinical recurrence and therefore are only useful in the diagnosis of primary infection. In this regard, IgM antibodies can be detected in early primary infection, whereas seroconversion with IgG usually occurs within 2 to 4 weeks of primary infection.^[10] In the present case, physical examination and laboratory work-up (renal and liver function) excluded the involvement of any other organ, while the ocular involvement was verified by HSV antigen PCR analysis of corneal scrapings.

To our knowledge, only two other articles have associated PUK with HSV, and all three patients in these articles had rheumatoid arthritis. Diagnosis was confirmed by HSV antigen PCR analysis in two cases and by transmission electron microscopy in one case.^[11,12] PUK caused by systemic autoimmune diseases (such as rheumatoid arthritis, Wegener's granulomatosis, polyarteritis nodosa, relapsing polychondritis, and systemic lupus erythematosus) has a pathophysiological mechanism resembling that of herpetic ulcerative keratitis that can lead to severe inflammation of the peripheral cornea and possible perforation.^[12] The patient in the present case showed a similar presentation, so he was subjected to thorough immunology testing that excluded autoimmune diseases as the causal factor.

Histological analysis of corneal and conjunctival scrapings showed a cellular population characteristic of inflammation, namely lymphocytes, macrophages, fibroblasts, mast cells, and neovascular capillaries. These findings were similar to a histopathological analysis reported by Zaher et al, which described the findings of two patients with herpes simplex keratitis who had been

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misdiagnosed as having rheumatoid arthritis-related PUK.^[11]

Misdiagnosis of HSV-1-related PUK and misuse of extensive topical steroid treatment in our patient had led to bilateral corneal perforation. The severity of our patient's condition mandated surgical intervention, as well as topical and systemic pharmacological management.

In the present report, we have described a rare case of bilateral HSV-1-related PUK presenting as bilateral corneal perforation in a patient with primary HSV infection. In cases of PUK, differential diagnosis should include infectious and autoimmune diseases. Primary HSV should also be considered as a potential cause of this form of keratitis, which, if left untreated, can lead to devastating outcomes.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of Interest

There are no conflicts of interest.

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