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Case report

Conjunctival geographic ulcer: An overlooked sign of herpes simplex virus infection

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ABSTRACT

Herpes simplex virus (HSV) ocular infection causes significant visual burden worldwide. Despite the fact that dendritic or geographic corneal ulcers are typical findings in HSV epithelial keratitis, conjunctival ulcer as a sign of HSV infection has rarely been reported. Although easily overlooked, this important sign could be enhanced by fluorescein staining. We report two cases of conjunctival geographic ulcers proven to be HSV infection by viral isolation and polymerase chain reaction (PCR). One patient had bilateral disease and blepharitis, and the other had unilateral involvement without skin lesions. With timely diagnosis and proper management, excellent visual outcome can be expected.

1. Why this case is important?

Herpes simplex virus (HSV) ocular infection remains a leading cause of corneal blindness in the world [1]. Dendritic or geographic corneal lesions are classic findings in HSV epithelial keratitis, and the lesions are enhanced by fluorescein staining [2]. HSV replicates in the epithelial cells, and leads to swelling and their eventual destruction [3]. The lesion usually begins with fine elevated vesicular eruptions, and the vesicles rapidly coalesce to form a dendritic or geographically shaped ulcer [4]. However, dendritic or geographic lesions of conjunctiva are rarely studied.

Herein, we report two cases of conjunctival geographic ulcers in otherwise healthy adults proven to be HSV infections. One patient had bilateral disease and typical erosive-ulcerative blepharitis as a primary infection, and the other patient had unilateral involvement without any cutaneous lesions.

The purpose of this report is to emphasize conjunctival geographic ulcers as a physical finding in ocular HSV infections, which has received little attention previously, and to demonstrate that this sign could be very helpful for diagnosis, especially in the absence of other skin lesions.

2. Case description

2.1. Patient 1

A 26-year-old woman with underlying allergic rhinitis, asthma and atopic dermatitis presented with redness and foreign body sensation in her left eye for two days. Epidemic keratoconjunctivitis was suspected, but her symptoms worsened after two-day use of topical 0.1% dexamethasone (Delone, Sinphar, I-Lan Taiwan), with the development of painful eruptions on the left upper and lower lids as well as redness in the right eye.

At presentation, the best corrected visual acuity of the right eye and left eye was 20/25 and 20/20, respectively. Biomicroscopic examination disclosed patches of conjunctival ulcers and edema distributed in geographic pattern over the inferior bulbar conjunctiva in both eyes using fluorescein staining under a cobalt-blue filter. There was no dendritic edge around the lesion (Fig. 1A). The inferior palpebral conjunctival epithelium was loosening along

Abbreviation: HSV, Herpes simplex virus.

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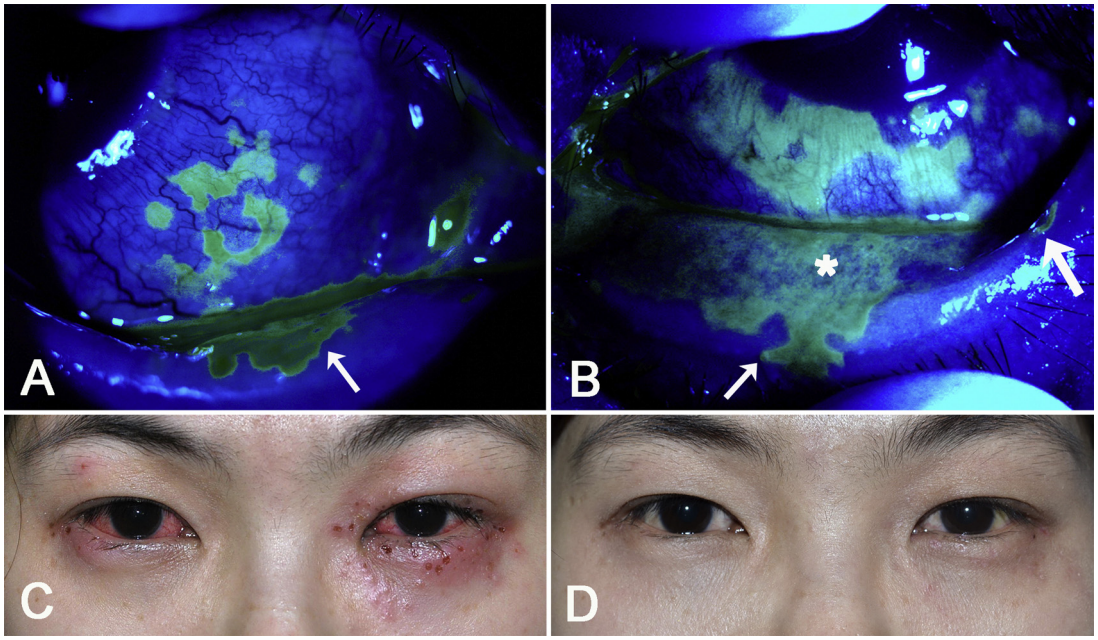

Fig. 1. Features of bilateral conjunctival geographic ulcers in Patient 1. (A) Right eye. Biomicroscopic examination disclosed a geographic pattern of ulcers in the nasal inferior bulbar conjunctiva outlined by fluorescein staining under a cobalt-blue filter. Intermarginal erosions are indicated with the arrow. (B) Left eye. Biomicroscopic examination showed a geographic pattern of ulcers involving the inferior perilimbal bulbar conjunctiva highlighted by fluorescein staining under a cobalt-blue filter. Note a pseudomembrane formation in the inferior palpebral conjunctiva (asterisk) continuous with intermarginal erosions (arrow), and another intermarginal erosion (thick arrow) seen at the lateral angle of the lower eyelid. (C) Before treatment, there was erythematous lid swelling, with multiple tiny, punched-out skin ulcers adjacent to the lid margins without clear vesicular lesions. (D) All of the lesions healed without scar about two weeks after treatment.

with the formation of pseudomembrane (Fig. 1B). Punctate epithelial keratitis was also noticed in both eyes. Fundus examination was unremarkable. There were erosions of the intermarginal portion of the lids as well as multiple punched-out skin ulcers adjacent to the lid margins (Fig. 1A–C). Other finding included bilateral preauricular lymphadenopathy. The tentative diagnosis was bilateral herpetic blepharokeratoconjunctivitis. She was treated with topical 3% acyclovir ophthalmic ointment (Devirus; Winston, Tainan, Taiwan) four times a day in both eyes, and intravenous acyclovir (Zovirax; GlaxoSmithKline S.P.A., San Polo di Torrile (PR), Italy) 250 mg every eight hours for three days. The corneal lesions resolved one day after the initiation of treatment. After discontinuation of the intravenous acyclovir, oral valacyclovir (Valtrex; Glaxo Wellcome, Aranda de Duero, Spain) 500 mg three times a day was administered for six days. All of the lesions healed completely about two weeks after the first visit (Fig. 1D).

HSV type 1 (HSV-1) infection was diagnosed by viral isolation and immunofluorescent staining of HSV-1 antigen. In addition, PCR of conjunctival scrapings confirmed the presence of HSV nucleic acid. No adenoviruses or enteroviruses were identified. A biopsy was performed from the eroded area of the conjunctiva, and histologic examination of the conjunctival biopsy revealed widespread destruction of the epithelium, diffuse infiltration of lymphocytes and neutrophils, and rare multinucleated giant cells were visible. Serologic test was negative for anti-HSV-1/2 IgG at the acute phase by using enzyme-linked immunosorbent assay (Euroimmun AG, Luebeck, Germany). Positive seroconversion was documented with the convalescent serum, indicating that this episode was a primary infection.

2.2. Patient 2

A 31-year-old woman presented with foreign body sensation, accompanied with redness and increased watery discharge in the right eye for four days. Epidemic keratoconjunctivitis was suspected initially, but her symptoms aggravated after topical administration of 0.1% dexamethasone (Desalone; Aseptic Innovative Medicine, Taoyuan, Taiwan) four times a day. She denied previous herpes infection history.

The best corrected visual acuity of the right eye and left eye was 20/20 and 20/20, respectively. Intraocular pressure was normal in both eyes. Biomicroscopic examination showed that the bulbar conjunctiva of the right eye appeared edematous and erythematous, and the adjacent tarsal conjunctiva displayed follicular conjunctivitis without pseudomembrane. Fluorescein staining revealed geographic conjunctival ulcers without dendritic edges in the temporal, inferior and nasal perilimbal bulbar conjunctiva (Fig. 2A), which were rendered more visible under a cobalt-blue filter (Fig. 2B). Punctate epithelial keratitis was also noted (Fig. 2B, arrows). The remainder of the anterior segment and fundus examination was normal. In addition, the ipsilateral preauricular and submandibular lymph nodes were swollen and tender. A tentative diagnosis of herpetic keratoconjunctivitis was made. HSV-1 infection was verified by viral isolation and PCR. No adenoviruses or enteroviruses were isolated. Topical 3% acyclovir ophthalmic ointment (Devirus; Winston, Tainan, Taiwan) was then administered every four hours and was gradually tapered. Her eye symptoms recovered completely after two weeks of treatment.

2.3. Viral Isolation and PCR

Conjunctival scrapings on the fluorescein stained area with a No. 15 blade were performed on both patients. To confirm the HSV-1 infection, viral isolation and PCR were carried out. The virological methods have been described previously [5]. In brief, specimens were inoculated into A549 cells, and typical cytopathic effect of cell rounding was observed after four days of incubation. The infected cells were then fixed and HSV-1 antigen was confirmed by direct fluorescent antibody stain using Imagen HSV immunofluorescence kit (Oxoid Ltd., Basingstoke, Hampshire, UK) in both patients' specimens. For PCR, DNA was extracted and amplified using primers 5′-TACATCGGCGTCATCTGCGGGG-3′