• Letter to the Editor •

Corneal lipid degeneration following herpes zoster ophthalmicus keratitis

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Dear Editor,

I am Dr. Asako Kodama, affiliated with the Department of Ophthalmology at Eiju General Hospital in Tokyo, Japan. Varicella-zoster virus (VZV) induces two distinct states: the primary infection (varicella) and secondary endogenous reactivation of latent VZV in herpes zoster form. While herpes zoster lesions typically manifest on the trunk and abdomen, the most frequently involved cranial nerve is the trigeminal nerve. When the ophthalmic branch of the trigeminal nerve is affected, ocular structures may be compromised, resulting in herpes zoster ophthalmicus (HZO), which accounts for 10%–20% of all herpes zoster cases[1-2]. While manifestations of HZO are highly variable, the cornea is the most frequently affected ocular tissue[3], with keratitis occurring in <65% of HZO cases[1]. Epithelial, stromal, and endothelial keratitis all occur in HZO. Generally, HZO stromal keratitis is considered an inflammatory manifestation rather than an active infection, although controversy exists. Remarkable corneal haze, vascularization, and lipid degeneration may develop following any intense preceding forms of HZO keratitis[1]. Reports detailing precise changes in lipid degeneration following HZO stromal keratitis in response to its treatment are rare, with only a few cases documented in the literature[4-5]. Here, we present a case of corneal lipid deposition in a patient with HZO, which occurred as a secondary degeneration of stromal keratitis. There were also fluctuations in the response to treatment with a combination of topical corticosteroids and acyclovir ophthalmic ointment.

Ethical Approval This study was approved by Eiju General Hospital Ethics Committee and adhered to the Declaration of Helsinki. Written informed consent was obtained from the patient for publication of the photographs.

A previously healthy 41-year-old man presented with conjunctival injection of the right eye (OD) since January 2nd, 2020, followed by an abnormal sensation, pain, and vesicular eruptions around the OD and upper right facial skin since January 3rd. At admission to the dermatology department in Eiju General Hospital on January 6th, vesicular eruptions were observed on the upper right side of the face. Clinical examination revealed abnormal sensation and pain along the ophthalmic branch of the trigeminal nerve, with inflammatory changes indicated by a body temperature of 38.4℃ and altered blood test results [the total white blood cell count was 3700 cells/μL (normal, 3300–8600/μL): lymphocytes were 25.5% (normal, 20%–50%) and monocytes were 15.5% (normal, 2%–9%); the C-reactive protein level was 3.627 mg/dL (normal, <0.3 mg/dL)]. Extraction of the VZV antigen using an anti-VZV monoclonal antibody kit (DermaQuick®, Maruho Co. Ltd., Osaka, Japan)[6] was performed on the day of admission. The VZV antigen was detected in fluids from eruptions on the forehead and around the OD.

He visited our ophthalmology division at the dermatology department's request on the next day of admission. At his initial presentation to the ophthalmology division, he complained of pain and swelling of the upper and lower eyelids of the OD. He could not open his OD owing to the severe swelling of his eyelids. He declined the collection of tears to perform a polymerase chain reaction test for VZV deoxyribonucleic acid. A slit-lamp examination showed conjunctival injection and inflammation of the cornea, with stromal opacity and infiltration in the temporal-lower side of the OD (Figure 1A). The corneal epithelium was intact, and there were no pseudodendrites. No sign of inflammation was observed in the anterior chamber or vitreous humor. The fundus was normal. The best-corrected visual acuities, in decimals, were 0.8 in his OD and 1.2 in his left eye (OS); the intraocular pressures were 20 and 20 mm Hg in the OD and OS, respectively.

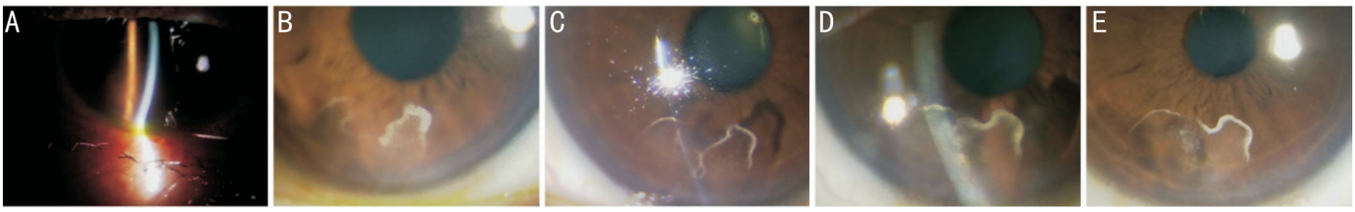

Figure 1 Follow-up slit-lamp examination photographs of the right eye A: At the initial visit, the slit-lamp examination showed conjunctival injection and inflammation of the cornea, with stromal opacity and infiltration in the temporal-lower side; B: Eight months after the last visit, slit-lamp examination revealed a remarkable opacity at 7 o'clock of the corneal stroma that resembled a fine opacity that looked like frosted glass and had a thick linear outline; C: Four weeks after treatment initiation, the fine opacity and width of the linear opacity at 7 o'clock had decreased, while the outline remained; D: Four months later, a recurrence of the corneal opacity at 7 o'clock was observed. Both the density of the fine opacity, which looked like frosted glass, and width of the linear opacity increased again; E: Treatment was resumed with positive outcomes. Despite some remaining outline deposition, the combination of topical steroids and antivirals effectively prevented central corneal involvement.

The detection of the VZV antigen and typical clinical findings confirmed the diagnosis of herpes zoster and stromal keratitis of HZO. Treatment with intravenous acyclovir 750 mg/d for 6d, followed by oral valacyclovir hydrochloride 3000 mg/d for 2d, and topical medications (acyclovir eye ointment, betamethasone sodium phosphate eye drop five times daily, and gatifloxacin hydrate eye drop three times daily) resulted in significant improvement. The eye drops and ointment were slowly tapered (acyclovir eye ointment, betamethasone sodium phosphate eye drop reducing the frequency twice every three weeks, and gatifloxacin hydrate eye drop reducing once a week). Eight weeks later, the conjunctival injection and inflammation of the cornea had completely resolved, prompting a return to the local eye clinic.

However, 8mo after the last visit, the patient reported a corneal opacity at 7 o'clock in the OD, the same place as before, leading to further examinations and subsequent treatments. On November 25th, 2020, a slit-lamp examination in our hospital revealed a remarkable opacity at 7 o'clock of the corneal stroma that resembled a fine opacity that looked like frosted glass and had a thick linear outline (Figure 1B). No signs of infiltration, inflammation, or neovascularization of the cornea were found. The corneal epithelium was intact. No conjunctival injection or inflammation of the anterior chamber was observed. No typical clinical signs of herpes zoster, such as vesicular eruptions, were found. Enzyme immunoassays (EIA) of the serum indicated negative anti-VZV immunoglobulin G (IgG) and immunoglobulin M (IgM). In addition to VZV, other typical causes of stromal keratitis include herpes simplex virus (HSV) and treponema pallidum. Anti-HSV IgG and IgM were negative in the serum EIA. The results were also negative in the rapid plasma regain (RPR), and treponema pallidum hemagglutination (TPHA).

These findings might indicate stromal keratitis, with mild inflammation, that is not related to the current activation of the VZV virus[1]. Topical medications (acyclovir eye ointment, betamethasone sodium phosphate eye drop five times daily, and gatifloxacin hydrate eye drop three times daily) were initiated. Four weeks later, the fine opacity and width of the linear opacity at 7 o'clock of the cornea had decreased, while the outline remained (Figure 1C). The maximum width of the linear opacity decreased from 429 to 169 μm. The treatment with eye drops and ointments was tapered and completed, and the patient returned to the local eye clinic.

Four months later, the corneal opacity at 7 o'clock recurred, leading to a visit to our hospital at the local eye clinic's request on July 12th, 2021. Both the density of the fine opacity, which looked like frosted glass, and width of the linear opacity increased again (Figure 1D). No infiltration or inflammation of the cornea was found. No conjunctival injection or inflammation of the anterior chamber was observed, as before. No typical clinical signs of herpes zoster, such as vesicular eruptions, were found. EIA of the serum revealed negative anti-VZV IgG and IgM. Anti-HSV IgG and IgM in the serum EIA, and the results in the rapid plasma regain, RPR, and TPHA, were all negative. Only neovascularization of the cornea was observed this time (Figure 1D). Treatment was resumed with positive outcomes. Four weeks later, the fine opacity and width of the linear opacity at 7 o'clock of the cornea had decreased, while the outline remained (Figure 1E). The maximum width of the linear opacity decreased from 424 to 190 μm. The neovascularization of the cornea disappeared. The best-corrected visual acuity, in decimals, remained at 1.2 in his OD before and after the treatment without any deterioration. Despite some remaining outline deposition, the combination of topical steroids and antivirals effectively prevented central corneal involvement and reduced visual acuity. He returned to the local eye clinic 4wk after treatment initiation.

Significant corneal opacity, vascularization, and lipid degeneration may occur following severe HZO keratitis.

Corneal lipid degeneration has primary and secondary forms. Primary lipid degeneration occurs without corneal vascularization and inflammation, typically with normal serum lipid levels and no history of trauma or infection[4]. True primary lipid degeneration is rare. Secondary lipid degeneration, known as lipid keratopathy, is associated with corneal vascularization[4,7] and commonly follows herpetic infections, trauma, corneal ulceration, and interstitial keratitis[8]. Secondary lipid degeneration is linked to corneal neovascularization, which hinders lipid removal, making improvement challenging[4,9]. Central corneal involvement in lipid degeneration impairs visual acuity. Reports detailing precise changes in lipid degeneration following HZO keratitis are rare[4-5]. This study reports a case of lipid degeneration following HZO stromal keratitis, demonstrating responsiveness to treatment and recurrences.

Although antivirals are used in the acute, infectious stage of VZV, treatment in the later, post-infectious stages is more varied. The potential for chronic and recurrent disease can leave clinicians stumbling along a poorly defined treatment protocol. The most widely used treatment algorithm for HZO combines topical corticosteroids and antivirals[1,10]. Following the literature, we prescribed topical corticosteroids and acyclovir eye ointment to treat recurrences.

When the first recurrence occurred in November, 2020, there were no signs of inflammation or neovascularization in the cornea. Despite treatment, some residual outline deposition persisted. In this case, the corneal findings were considered secondary changes in HZO stromal keratitis. It was presumed that the inflammation of stromal keratitis had already subsided to some extent, with lipid degeneration persisting as a secondary change.

Despite some remaining deposition, the combination of topical steroids and antivirals effectively prevented central corneal involvement, emphasizing the importance of continuously examining patients with HZO.

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REFERENCES

1 Bronner A. Get to know HZO. *Review Education Group* 2021. https://www.revieweducationgroup.com/ce/get-to-know-hzo

2 Liesegang TJ. Herpes zoster ophthalmicus. *Ophthalmol* 2008;115(2):S3-S12.

3 Niederer RL, Meyer JJ, Liu K, Danesh-Meyer HV. Herpes zoster ophthalmicus clinical presentation and risk factors for loss of vision. *Am J Ophthalmol* 2021;226:83-89.

4 Reidy JJ. Corneal and conjunctival degenerations. Mannis MJ, Holland EJ. *Cornea.* Fifth Edition. Netherland: Elsevier; 2022;784.e1-801.

5 Labetoulle M, Boutolleau D, Burrel S, Haigh O, Rousseau A. Herpes simplex virus, varicella-zoster virus and cytomegalovirus keratitis: facts for the clinician. *Ocul Surf* 2023;28:336-350.

6 Watanabe D. Diagnosis of cutaneous varicella-zoster virus infection by immunochromatography. *Jpn J Clin Dermatol* 2019;73(5):82-86.

7 Cogan DC, Kuwabara T. Lipid keratopathy and atheroma. *Trans Am Ophthalmol Soc* 1958;56:109-19;discussion 109-19.

8 Barchiesi BJ, Eckel RH, Ellis PP. The cornea and disorders of lipid metabolism. *Surv Ophthalmol* 1991;36(1):1-22.

9 Kasuya Y, Sano I, Makino S, Kawashima H. Corneal opacity induced by antiglaucoma agents other than brimonidine tartrate. *Case Rep Ophthalmol Med* 2020;2020:4803651.

10 Stephenson M. How to manage ocular herpes. *Review of Ophthalmology* 2020. https://www.reviewofophthalmology.com/article/how-to-manage-ocular-herpes