

# Herpes Zoster Ophthalmicus: A Case of Reactivated Varicella

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**H**erpes zoster ophthalmicus (HZO) is the clinical manifestation of reactivated varicella zoster virus (VZV) (or chickenpox) in the ophthalmic division of the trigeminal nerve. The symptoms of HZO vary in severity from acute lesions that resolve completely in weeks to chronic complications that last for years and may lead to blindness if left untreated. This case report documents a case of HZO in a 78-year-old woman and discusses disease etiology, pathogenesis, anatomic basis, and treatment.

## CASE PRESENTATION

A 78-year-old woman presents with a 4-week history of vesicular eruption on the left side of her upper forehead and scalp, pain in her left forehead, and a general feeling of malaise.

## Patient History

The patient was undergoing treatment for shingles by her primary care physician and was referred to an ophthalmologist for evaluation of HZO following 3 to 4 days of redness and blurred vision in the left eye. Patient history is significant for chickenpox during childhood.

## Physical Examination

The patient has mild to moderate erythema and scaling of erupted lesions on her upper forehead and scalp on her left side. No active lesions are observed. Cataracts unrelated to HZO are observed in both eyes. In her right eye, vision is 20/30 and the remaining examination is unremarkable. In her left eye, vision is 20/200 and 20/70+ on a left pinhole test. The cornea of the left eye is hazy and edematous and exhibits subepithelial scarring, 4+ keratic precipitates of the corneal endothelium, and active granulomatous iridocyclitis with development of a fibrin membrane on the lens capsule (**Figure 1**). Findings in the left eye are consistent with the diagnosis of HZO.

## Treatment

Antiviral treatment of the affected eye is initiated with oral acyclovir (400 mg four times daily for 14 days) and topical trifluridine (1 drop five times daily). Topical corticosteroid anti-inflammatory drops (prednisolone acetate 1%, every hour) are also prescribed.

## Course and Outcome

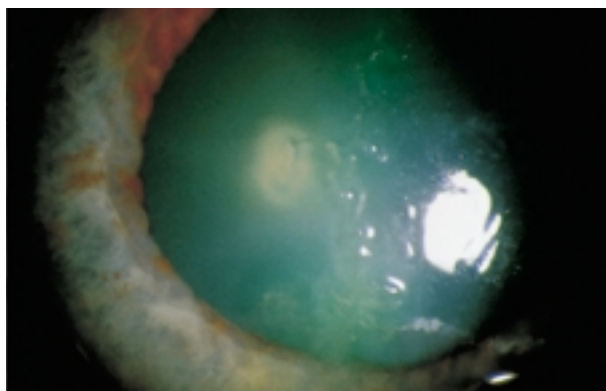
The patient returns 5 days after her initial presentation for a follow-up examination, and she reports improved vision and less forehead pain and overall discomfort. Vision in her right eye remains 20/30, and vision in her left eye has improved to 20/80. Vision on a left pinhole test is 20/50, indicating less refractive blurring than was noted in the initial visit. Fine particles and a halo of haze are observed in the corneal subepithelium of the affected eye. The patient continues her treatment (acyclovir, trifluridine, corticosteroids) at the same doses.

The patient presents 10 days after the first follow-up and reports feeling "okay." Vision is 20/30 in her right eye and 20/60+ in her left eye. A fine haze with 2+ keratic precipitates of the corneal endothelium are present in the region of the original epithelial defect. She continues her treatment (acyclovir, trifluridine, corticosteroids) at the same doses.

The patient presents 13 days after the second follow-up and reports feeling "good." Vision in her right eye is 20/30, and vision in her left eye is 20/70. A small area of haze persists in the region of the original epithelial defect. No cell is observed in the anterior chamber (ie, no lymphocytes were seen floating in the anterior chamber aqueous), indicating a quiet eye and resolution of

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**Figure 1.** Photograph of the left eye of a patient with herpes zoster ophthalmicus. Hazy edematous cornea, subepithelial scarring, and active dendrites with epithelial staining are evident. Photograph courtesy of Robert M. Kershner, MD (Orange Grove Center for Corrective Eye Surgery, Tucson, AZ).

HZO. Her treatment with prednisolone acetate 1% is continued at 5 times daily, tapering to cessation over the next 30 days.

The patient presents again at 30 days after the third follow-up, and her HZO has resolved. The subepithelial haze (scarring) in the affected eye is almost completely healed. A 6-month follow-up visit is scheduled.

## DISCUSSION

### Pathogenesis of Varicella

Varicella is a highly contagious viral disease caused by primary infection with VZV, also known as *human herpesvirus 3*.<sup>1</sup> This virus possesses DNA, an icosahedral nucleocapsid, and a glycoprotein-containing outer membrane typical of members of the herpesvirus family.<sup>1</sup> VZV is usually transmitted from an exogenous source to the host via direct contact with active vesicular lesions or by exposure to air droplets from nasopharyngeal secretions. After gaining entry into a host, the virus spreads locally to a site of augmentation and primary viremia. After several days, a second viremia conveys the replicated virus to the basal and deep malpighian layers of the epidermal endothelium, which results in subsequent cellular degeneration and edema in the formation of vesicular eruptions, seen clinically as chicken pox.<sup>2</sup> **Figure 2** provides a symptom topography of varicella and HZO.

### Reactivation of Varicella and Expression of Herpes Zoster

Individuals that have recovered from VZV retain a latent form of the virus in a small fraction of their sensory ganglia or perineuronal cells. In fact, the trigeminal

ganglia of cadavers demonstrate VZV DNA and RNA at a rate of 1/1000 neurons.<sup>1,2</sup> This latent form of the virus reactivates under the influence of poorly understood trigger factors that likely include waning immunity associated with advanced age, trauma, or alteration of neural metabolism secondary to other conditions such as HIV, colds, influenza, and pneumonia. Additional factors mitigating reactivation may include viral load, proliferative potential, and position of insertion of the viral genome within the host cell nucleus.<sup>1-5</sup> As the latent virus replicates and migrates peripherally along sensory nerves, the virus often causes painful inflammation of the connective tissue sheath surrounding each nerve fascicle and varying amounts of neuronal hemorrhaging and necrosis.<sup>1,2</sup> When the active virus reaches the dermis, probably after several subclinical reactivation events, it is expressed as herpes zoster.<sup>1,4</sup> Herpes zoster, also called *shingles*, is the clinical syndrome of cutaneous vesicular eruption and pain associated with the reactivation of latent VZV in a sensory ganglion. Symptoms are usually ipsilateral to the affected ganglion and restricted to a single thoracolumbar, cranial, cervical, or lumbar dermatome.<sup>2</sup> Men and women are equally affected.

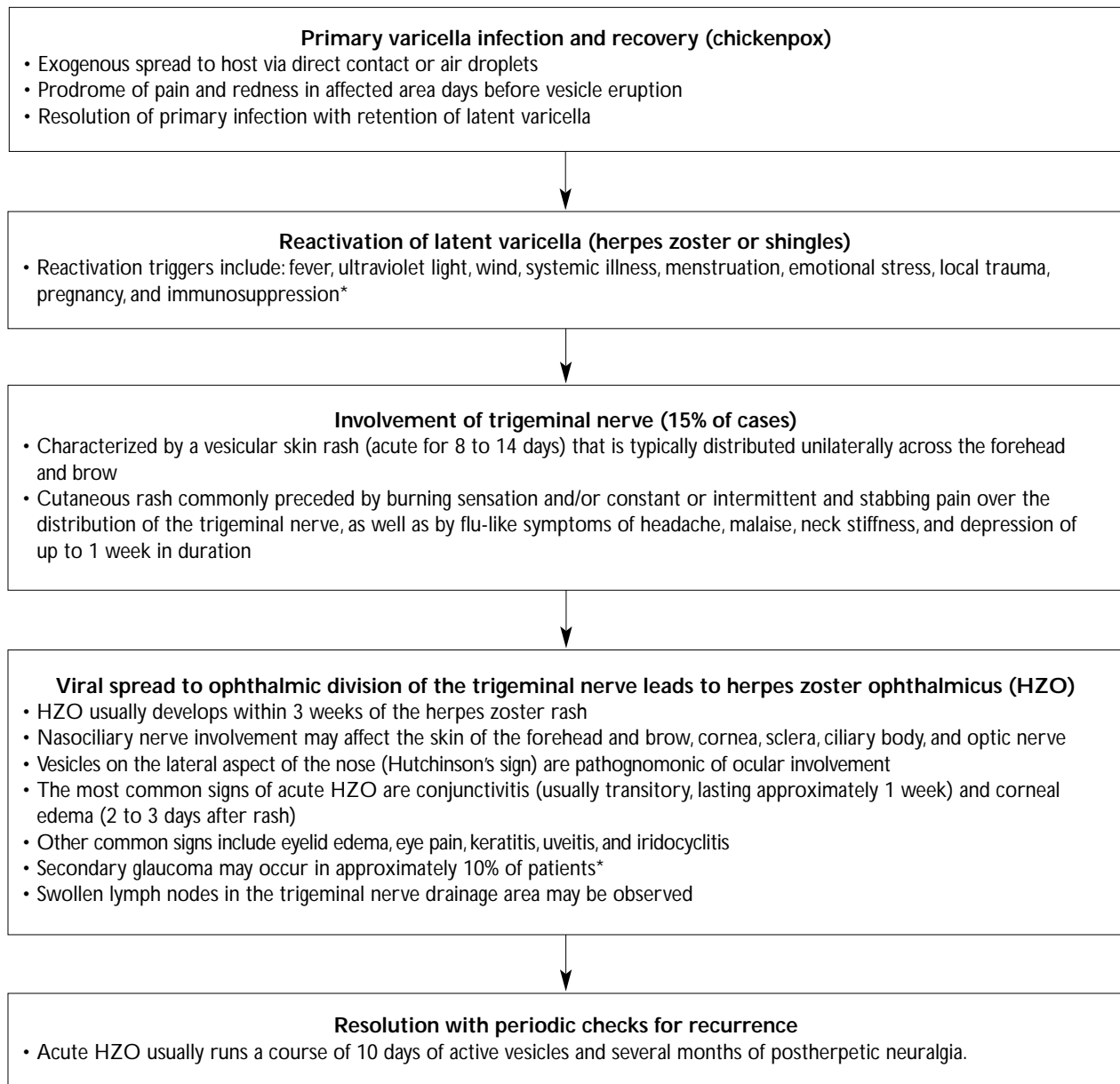
### Herpes Zoster Ophthalmicus

When VZV recurrence involves the ophthalmic division of the trigeminal nerve, this recurrence is termed *herpes zoster ophthalmicus*.<sup>6</sup> Approximately 15% of all cases of herpes zoster are trigeminal.<sup>3</sup> Infection of this nerve division can lead to inflammation of the skin of the forehead as well as the cornea, sclera, ciliary body, and optic nerve.

**Trigeminal nerve distribution.** The HZO disease pattern is best understood by an examination of trigeminal nerve distribution. The trigeminal nerve passes through the lateral wall of the cavernous sinus and branches into the lacrimal, frontal, and nasociliary nerves. The latter nerve sends sensory branches to the ciliary ganglion and nerves, which innervate the cornea, iris, and ciliary body. The terminal branches of the nasociliary nerve are the anterior ethmoid and the inferior trochlear nerves, which innervate the side of the tip of the nose and the medial aspect of the lid and conjunctiva, respectively.<sup>5</sup> Involvement of the nasociliary nerve with vesicles in the lateral aspect of the nose is termed *Hutchinson's sign* and is pathognomonic of ocular involvement.

**Ocular complications.** The ocular complications of HZO are categorized in three groups:<sup>1</sup>

- 1) Inflammatory changes—dendritic, nummular, and disciform keratitis; vasculitis in episcleritis/scleritis, iritis, ischemic papillitis; and orbital vasculitis



\*Hejkal TW: Herpes eye infections. In *Griffith's Five Minute Clinical Consult*. Griffith JA, Dambro MR, eds. Baltimore: Lippincott, Williams & Wilkins, 1998:476-477.

**Figure 2.** Symptom topography of varicella and herpes zoster ophthalmicus.

- 2) Nerve damage—neuroparalytic keratitis, neuralgia, and, rarely, some ocular motor palsies
- 3) Secondary problems associated with tissue scarring—eyelid deformities, neuralgia, and lipid keratopathy

**Clinical course.** The course of HZO is grouped into three phases: acute, chronic, and relapsing. Acute HZO is exemplified by the patient in this case report, and

acute HZO usually develops within 3 weeks of the herpes zoster rash. The cutaneous rash commonly associated with HZO is preceded by influenza-like symptoms of up to 1 week in duration that are often accompanied by headache, malaise, depression, and neck stiffness. The elderly patient in particular may describe feeling unwell, and may appear toxic.<sup>7</sup> Shortly before or after the rash appears, the patient experiences localized

“background” pain or burning sensation, accompanied by sharper intermittent stabbing pains across the distribution of the trigeminal nerve.<sup>1</sup> Swollen lymph nodes in the trigeminal nerve drainage area often accompany HZO.<sup>1</sup>

**Clinical manifestations.** Common clinical manifestations of HZO include conjunctivitis, iridocyclitis, and iritis, as well as corneal involvement.

**Common manifestations.** Conjunctivitis is one of the most common acute manifestations of HZO. Conjunctivitis is generally transitory, lasts approximately 1 week, and rarely becomes chronic.<sup>1</sup> Another common finding is iridocyclitis, which is an acute inflammation of the iris, ciliary body, and anterior chamber. Iridocyclitis is characterized by pain, tearing, blurred vision, light sensitivity, a constricted pupil, and a congested eye without purulent discharge.<sup>5</sup> A third common finding in HZO is iritis with fine keratic precipitates underlying a swollen stroma.

**Corneal involvement.** In HZO, corneal involvement may be superficial or interstitial. Corneal edema commonly develops 2 to 3 days following the appearance of the herpes zoster rash. Keratic precipitates are inflamed lymphocytes and cells from the iris and ciliary body that enter the aqueous and adhere to the endothelial surface of the cornea. The magnitude of keratic precipitate clusters are quantified on a scale of 0 to 4 (higher numbers indicate larger clusters); the clusters are termed *granulomatous* if large and *punctate* if small.

The most common annular lesion is nummular keratitis, which is characterized by multiple, fine granular deposits in the stroma that are just beneath Bowman's membrane and are surrounded by halos of stromal haze,<sup>1</sup> also known as a *Wesley ring*. These deposits typically appear 10 days after the onset of the disease; they first appear white and then fade to brown. Disciform keratitis may appear about 3 to 4 weeks after disease onset and may develop from the preceding nummular keratitis. In disciform keratitis, new infiltrates appear in the stroma underlying the corneal granules and may be surrounded by infiltrates in the shape of one or more immune rings.<sup>1</sup>

The Wesley ring observed in the patient in this case report is an immune response phenomenon that marks the interface among invading leukocytes and immunoglobulins and the normal corneal subepithelium. Loss of corneal sensation is common in HZO, and may persist for months after the disappearance of lesions.<sup>5</sup>

#### Treatment

Currently, physicians can only minimize the damage caused by a herpes zoster recurrence, which affects 300,000 people annually.<sup>1,7</sup> HZO management involves

limiting viral replication and reducing both the severity and duration of skin and eye inflammation. Early treatment is essential and typically includes supportive care and the use of some combination of steroidal anti-inflammatory drugs, nonsteroidal anti-inflammatory drugs, antiviral agents, analgesics, and antibiotics. Varicella vaccines may also safeguard against herpes zoster complications,<sup>1</sup> but this option is unproved and may only confer protection to immunocompetent patients.

**Supportive care.** Barrier nursing — a treatment regimen in which the patient is isolated and an antiseptic barrier is established by use of gowns, masks, and gloves — is recommended during the vesicular stage until vesicles are resolved and the patient is no longer infective.<sup>1</sup> Dermal scarring may be reduced through energetic massage of the skin.<sup>1</sup> Physicians should expect some patients to become worried or possibly depressed during the course of the disease. If depression occurs, physicians should remind their patients that herpes zoster is self-limiting, and that rapid recovery without recurrence is expected. Patients who are particularly depressed may benefit from support groups or treatment with tricyclic antidepressants or selective serotonin reuptake inhibitors (eg, fluoxetine).

**Steroidal anti-inflammatory agents.** Early use of corticosteroids minimizes skin scarring and neuralgia, diplopia, scleritis, sclerokeratitis, iritis, optic atrophy, and hemiplegia. The patient should apply topical dexamethasone 0.1% (every 2 hours initially) and then dilate the pupil with atropine 1% or cyclopentolate 0.5% to 1% (1 drop 3 times daily).<sup>8</sup> Severe postherpetic neuralgia may be avoided in patients older than age 60 years by using pulse high-dose corticosteroids (eg, a 7-day course of prednisone at 60 mg/day, followed by another 7-day course at 30 mg/day).<sup>8</sup> Topical corticosteroids may increase intraocular pressure and are contraindicated in patients with active corneal epithelial disease.<sup>9</sup> Steroid use may also increase the chance of systemic spread of herpes zoster in immunocompromised patients.<sup>1</sup>

**Antiviral agents.** Acyclovir is the most widely used antiviral for treatment of herpes zoster. The effectiveness of acyclovir in the treatment of HZO is contingent on early administration.<sup>10,11</sup> Typical recommendations involve oral acyclovir (800 mg, 5 times daily for 10 days).<sup>8,9,11</sup> Acyclovir used in conjunction with steroids minimizes rebound inflammation commonly associated with withdrawal of steroids.<sup>1</sup> Acyclovir has also proven effective in reducing the duration of rash and the spread of lesions as well as decreasing neuralgia in immunosuppressed patients.<sup>1,10</sup> Immunocompromised

patients with herpes zoster may be treated with intravenous acyclovir (500 mg/m<sup>2</sup> or 10 mg/kg every 8 hours in 1 hour infusions for 7 days) or vidarabine (continuous 12-hour infusions of 10 mg/kg/day).<sup>11</sup>

Oral valacyclovir (1000 mg 3 times daily for 7 days) and famciclovir (500 mg 3 times daily for 7 days) may also be used to treat herpes zoster.<sup>11</sup> Antiviral agents such as trifluridine, which were originally developed for treating herpes simplex, are available topically. Older treatments, including idoxuridine and adenine arabinoside, are less effective and more toxic than acyclovir.<sup>1</sup> Transplant patients, patients with AIDS, or other patients developing acyclovir-resistant varicella zoster may be treated with foscarnet (40 mg/kg intravenously every 8 hours) for 10 days or until the cutaneous rash resolves.<sup>11</sup>

**Other pharmacologic agents.** Analgesics administered in the first 2 weeks of the infection may help mediate mild pain and limit neural pathway damage, but severe pain is less easily treated.<sup>1</sup> Applications of topical antibiotics (eg, tetracycline) are effective at minimizing the danger of secondary staphylococcal infections of eyelid margins following keratoconjunctivitis.<sup>1</sup> Nonsteroidal anti-inflammatory drugs (eg, oral flurbiprofen) used in conjunction with topical steroids may be helpful in the treatment of episcleritis, scleritis, and sclerokeratitis.<sup>1</sup> Capsaicin cream applications can be used to treat postherpetic neuralgia.<sup>11</sup> Severe HZO that is unresponsive to traditional regimens may be treated with sympathetic blocks with 0.25% bupivacaine and rhizotomy.<sup>11</sup>

#### CONCLUSION

The presence of VZV antibodies in the adult population is approximately 95%, indicating that almost everyone comes in contact with this virus regardless of whether the condition manifests clinically.<sup>1,7</sup> Acute lesions may resolve completely in a few weeks, but the disease can also progress to a chronic stage that may last for years if left untreated.<sup>1</sup> The severity of HZO varies with the immune status of the patient: young individuals with robust immune responses usually

experience relatively benign HZO, whereas older adults with somewhat attenuated immune responses (especially persons older than age 60 years) may contract blinding forms of the condition.<sup>1,5</sup>

HZO should always be suspected in an older adult patient presenting with vague symptoms of unilateral pain of the forehead and brow, with or without erythema or vesicular eruptions. Eye pain, redness, or light sensitivity, or lesions on the lateral aspect of the nose should always alert the physician to the possibility of HZO. Prompt referral to an ophthalmologist is indicated. Resolved cases of HZO must be checked periodically because the disease is prone to reoccur as late as 10 years after the initial presentation.<sup>1</sup> **HP**

#### REFERENCES

1. Marsh RJ, Cooper M: Ophthalmic herpes zoster. *Eye* 1993;7:350-370.
2. Zaia JA, Grose C: Varicella and herpes zoster. In *Infectious Diseases*, 2nd ed. Gorbach SL, Bartlett JG, Blacklow NR, eds. Philadelphia: Saunders, 1998.
3. Donaldson DD: *Atlas of External Diseases of the Eye*, 2nd ed. St. Louis: Mosby, 1980.
4. Hyman RW, ed: *Natural History of Varicella-Zoster Virus*. Boca Raton, FL: CRC Press, 1987.
5. Vaughan D, Asbury T, Riordan-Eva P: *General Ophthalmology*, 14th ed. Norwalk, CT: Appleton and Lange, 1995.
6. Schwab IR: Herpes zoster sine herpette. A potential cause of iridoplegic granulomatous iridocyclitis. *Ophthalmology* 1997;104:1421-1425.
7. Grist NR, Ho-Yen D, Walker E, Will GR: *Diseases of Infection*. New York: Oxford University Press, 1993.
8. Berkow R, Beers MH, Fletcher AJ, eds: Ophthalmic herpes zoster. In *The Merck Manual of Medical Information*, 16th ed. Rahway, NJ: Merck and Co, 1992:2377.
9. Hejkal TW: Herpes eye infections. In *Griffith's Five Minute Clinical Consult*. Griffith JA, Dambro MR, eds. Baltimore: Lippincott, Williams & Wilkins, 1999: 476-477.
10. Liesegang TJ: Diagnosis and therapy of herpes zoster ophthalmicus. *Ophthalmology* 1991;98:1216-1229.
11. Ferri FF: Herpes zoster. In *Ferri's Clinical Advisor: Instant Diagnosis and Treatment*. Ferri FF, ed. St. Louis: Mosby-Year Book, 1999.