The Dilated Rarity of Complications with Herpes Zoster Ophthalmicus

Abstract

Herpes zoster, commonly known as Shingles, is a disease caused by the reactivation of varicella-zoster virus, a human herpes virus. After an initial outbreak of chicken pox in the first or second decade of life, the virus lays dormant in sensory ganglia\(^1\). When reactivated, the virus spreads down the related dermatome and manifests with a typical unilateral, painful, vesicular rash\(^1\).

Herpes zoster affects 20-30\% of the population\(^2\). Of these cases, only 10-20\% have subsequent ocular involvement, commonly known as herpes zoster ophthalmicus (HZO), which is a result of viral invasion of the ophthalmic branch of the trigeminal nerve\(^2\).

We present a unique case of herpes zoster ophthalmicus in an elderly patient, which rapidly progressed to oculomotor nerve palsy, a rare sequela of HZO. While the overall incidence of HZO is 2.2-3.4 cases per 1000 persons/year, occurrences are much higher in patients over 80 years old at 10 cases per 1000 persons/year. The higher prevalence requires a heightened awareness, diligent daily examination for signs of ocular complications, and strict adherence to preventive vaccination protocols to increase successful outcomes for these patients\(^1\).
The Dilated Rarity of Complications with Herpes Zoster Ophthalmicus

An 89-year-old Caucasian female presented to the emergency department with a three-day history of a painful rash on the left side of her face and swelling of her left eye along with new-onset generalized weakness. The rash was preceded by eight days of lacerating left head, facial, and eye pain, for which she was seen in the emergency room on two separate occasions. On the first visit, she was given analgesics, and on the second visit, two days after the onset of the rash, she was prescribed acyclovir, which she had not begun.

History of Illness

On this current visit associated symptoms included left eye redness and discharge, and a decreased appetite. The patient denied neck pain or stiffness, ear pain, sore throat, or trouble swallowing. Her past medical history was significant for chicken pox as a child, macular degeneration (AMD), hypertension, and recently diagnosed hypothyroidism, but negative for any history of immune-compromising disease. Past surgical history was positive for bilateral intraocular lens implants for cataracts in 2006. The patient denied any significant family history and her social history was noncontributory with the patient denying current or prior tobacco use, alcohol use, or illicit drug use. She was a retired schoolteacher who lived at home with her husband with low stress levels. Her medications included amlodipine, levothyroxine, and lisinopril, and she had last received intravitreal injections for the AMD 5 weeks prior. The patient agreed to having allergies to ciprofloxacin and sulfa. Her family history and social history were noncontributory. Of note, she admitted that she had not received the herpes zoster vaccination.

On a complete review of symptoms the patient was positive the above mentioned and lacked symptoms of or similar to night sweats, weight loss, photophobia, flashes of light, double
vision, dizziness, loss of consciousness, mental status changes, changes in sleep, runny nose, ringing ears, cough, sore throat, trouble swallowing, nausea, vomiting, diarrhea, constipation, chills, chest pain or tightness, shortness of breath or difficulty breathing, changes in urination or pain while urinating, new rashes noted on other areas, decrease in the range of motion in her upper or lower extremities, calf pain or tenderness, numbness or tingling, changes in gait, or generalized edema.

**Physical Examination, Pertinent Findings, and Results**

On arrival the patient was moderately distressed, but alert and oriented, with a Glasgow Coma Scale of 14/15. Vital signs were 97.8°F—68—18--189/98 mmHg, with a SpO2 of 96% on room air. The head was normocephalic, with a unilateral, well-defined, erythematous area extending from the left upper eyelid into the left frontal hairline and from the midline frontal bone into the left temporal hairline, with vesicles and superficial crusted lesions (see figure A). All facial bones were intact without any significant sinuous pressure during palpation. Her pupils were equal and reactive to light with extraocular muscles intact bilaterally. There was marked periorbital edema of the left eye, which restricted lid opening, as well as a moderate amount of yellowish discharge and mild conjunctival injection. There were no deformities noted on or around the external ears, canals were clear with pearly gray and translucent tympanic membranes demonstrating a cone of light and no fluid in the middle ear. Examination of the nose revealed nasal patency and the rash showed no involvement of the tip of the nose, constituting a negative Hutchinson’s sign. Nasal and oral mucous membranes were pink and moist, with upper and lower dentures noted, no tonsilar exudates, and adequate oral hygiene. On examination of the neck, no cervical lymphadenopathy was found, the trachea was midline, with no thyromegally. And lastly, cranial nerves 2-12 were found to be grossly intact.
Examination of the patient’s chest showed no obvious deformities and a regular heart rate and rhythm were noted on the cardiac exam. No murmurs, rubs or gallops were found. The patient chest moved symmetrically and on auscultation the lungs were clear with no wheezes, crackles or ronchi. Her abdomen was soft, non-tender, and non-distended with normal tympany and bowel sounds appreciated in all 4 quadrants. With no hepatosplenomegally and no accompanying CVA tenderness the benign abdominal exam was concluded. The patient’s generalized breast exam and external genital exam was found to be within normal limits with no lymphadenopathy palpated. Her skin was warm, dry, and no signs of edema or rash were found. The patient’s extremities demonstrated a full range of motion on active examination with a 3/5 strength and 2/4 reflexes bilaterally on all extremities.

The patient was within normal limits in gross sensory testing and showed no abnormalities with rapid alternating movements or shin-to-heal testing indicating no acute cerebellar defects. Basic labs were drawn and found to be within normal limits. No new images
were taken at the time. An initial working diagnosis of herpes zoster ophthalmicus (HZO) with a possible secondary bacterial infection was made. Due to the national shortage of IV acyclovir, the patient was treated with oral acyclovir 800 mg 5 times daily, as well as erythromycin ointment topically.

**Course of Stay**

On day two of her hospitalization, immediate concern for oculomotor nerve palsy was raised when the left eye examination revealed a mid-dilated, fixed pupil, diminished visual acuity, and decreased extraocular movement due to an obstructing chemosis (see figure B).

**Figure B**

An ophthalmologist and a retinal specialist were emergently consulted their complete findings are noted on Table A.

**Table A**

<table>
<thead>
<tr>
<th>Ophthalmic Exam</th>
<th>Right (OD)</th>
<th>Left (OS)</th>
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<tr>
<th>Visual Acuity Without Correction</th>
<th>20/200</th>
<th>Counting fingers= 4’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pupils</td>
<td>Minimally reactive</td>
<td>Fixed, Dilated</td>
</tr>
<tr>
<td>Extraocular Muscles</td>
<td>Within normal limits</td>
<td>-2 Overall restriction -3 Lateral gaze restriction, due to chemosis</td>
</tr>
<tr>
<td>Lids/Lashes</td>
<td>No lesions/edema</td>
<td>Superficial crusting and yellow discharge</td>
</tr>
<tr>
<td>Conjunctiva/Scleral</td>
<td>No chemosis, No injection</td>
<td>2-3+ Chemosis with injection</td>
</tr>
<tr>
<td>Cornea</td>
<td>Clear</td>
<td>Pseudodendritic changes</td>
</tr>
<tr>
<td>Retinal Exam: Vessels</td>
<td>Normal</td>
<td>Drusen along superior nasal vessel</td>
</tr>
<tr>
<td>Retinal Exam: Periphery</td>
<td>No retinal tears, No detachment</td>
<td>Choroidal effusion versus inferior detachment</td>
</tr>
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</table>

Their ophthalmic exam showed conjunctival and corneal edema, iritis, and a choroidal effusion due to an intraocular pressure of 0 mmHg (normal: 10-12 mmHg), which led to the decision to begin topical prednisolone acetate. In addition, extensive imaging was ordered. MR venogram was negative for evidence of sinus thrombosis, and MRI of the orbits revealed periorbital soft tissue inflammation without abscess and prominent choroidal enhancement with mild buckling, which was consistent with the intraocular pressure on examination. Furthermore,
the retro-orbital fat showed infiltrating enhancement along the left optic nerve, which raised concern for optic nerve involvement (see figure C & D).

**Figure C**

![Image](image1)

**Figure D**

![Image](image2)

**Diagnosis, Treatment and Resolution**

The studies confirmed the patient had herpes zoster ophthalmicus with complete oculomotor nerve palsy, a rare complication of herpes zoster ophthalmicus. Despite the extensive ophthalmic complications, over the course of a few days, the patient showed marked improvement in ocular function. She was discharged to complete drug treatment at home and continue follow-up with her ophthalmologist.
Discussion

Herpes zoster ophthalmicus (HZO) is a progressive disease with prodromal symptoms of fever or fatigue, which manifest as early as one week prior to visible cues of the disease. The effected dermatome develops searing pain with hypersensitive areas prior to the eruption of a vesicular rash. Within days, the overlying skin rapidly demonstrates vesicles, which erupt to release a serous fluid, followed by yellowish crusts. Typically, the skin manifestations precede any ocular changes by a few days.

HZO manifests as conjunctival inflammation and keratitis in 90% of cases, but can progress to a neuro-ophthalmic emergency, involving other cranial nerves and resulting in serious and severe ocular and extraocular damage. The extent of damage can range from partial single-nerve involvement to complete multi-nerve palsies. While rare, the most common cranial nerve affected is the third cranial nerve, followed closely by the sixth and fourth cranial nerves, respectively. Any cranial nerve involvement requires an immediate ophthalmologist’s evaluation.

The third cranial nerve, when affected, manifests as pupillary dilation, ptosis, and a down-and-out gaze or variations of the three, depending on partial or complete involvement. On day 2 of this case, our patient’s new-onset fixed, mid-dilated pupil was a warning sign of this complication, and led to the prompt consultation and imaging studies to rule out aneurysm, the most dangerous on a list of differential diagnoses. Clinically, another hallmark of concern is a rash noted on the external nasal nerve distribution ranging anywhere from the medial edge of the eye to the bridge, sides, or tip of the nose. This is commonly known as a Hutchinson’s sign, which reflects involvement of the nasociliary nerve. Studies have shown this is a powerful prognostic sign that precedes ocular complications at a rate of 76.2%; however, its absence does
not preclude the presence of ocular involvement\textsuperscript{5,6}. In fact, in 1/3 of HZO cases, the Hutchinson’s sign is absent, as it was in our patient, despite her extensive ocular involvement\textsuperscript{5,6,7}.

The mainstay of treatment for herpes zoster is antiviral therapy, with one of three drugs: acyclovir, valacyclovir, or famciclovir. Our patient received an outpatient prescription for acyclovir, but failed to fill it. In patients with treatment initiated within 72 hours of onset of the rash, the percentage of HZO was reduced by 20-30\%\textsuperscript{1}. Without treatment however, ocular complications were seen in greater than 50\% of those with herpes zoster, demonstrating the importance of early recognition and treatment\textsuperscript{1}. In this case, once hospitalized and diagnosed with HZO, the most appropriate therapy would have been intravenous acyclovir, which was unavailable due to a national shortage\textsuperscript{8}. These factors may have led to her more severe ocular complications.

In HZO cases, if rapid and efficient diagnostic and therapeutic milestones are achieved, most patients recover with minimal long-term ocular deficits. Post herpetic neuralgia (PHN) however, is a common aftermath, present in a great majority of herpes zoster cases\textsuperscript{6}.

**Conclusion**

Recognition of HZO as a complication of herpes zoster is imperative, due to the potential for cranial nerve involvement and irreversible visual deficits that ensue if the diagnosis is missed. Symptoms of oculomotor palsy and other rare complications are easily diagnosed with a simple ophthalmic exam at the bedside and can start a chain of therapeutic measures, which can save vision in the effected eye. Another common clinical pearl is to associate Hutchinson’s sign with concern for ophthalmic involvement; however, it is important to note that this sign may be absent in 1/3 of HZO cases\textsuperscript{5,6,7}. With the prompt use of therapeutic drugs of choice, such as
acyclovir, ophthalmic complications are significantly reduced and a complete recovery is seen in the majority of cases\textsuperscript{1,11}. The current shortages of acyclovir present challenges in treating these patients and call attention to the need for more aggressive focus on preventative measures\textsuperscript{8}. This case serves as a reminder of the importance of vaccination against herpes zoster. Primary healthcare providers should encourage their elderly patients to boost cell-mediated immunity with the vaccination, which has been shown to be safe and effective in preventing herpes zoster infections by 50\%\textsuperscript{2,9}. 
References


