Case report

A case of tri-segmental cranial nerve V herpes zoster

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A B S T R A C T

Varicella-zoster is the causative virus underlying varicella or “chickenpox” and herpes zoster or “shingles.” Cases of disseminated disease have been widely reported in immunocompromised patients. We describe an interesting case of tri-segmental cranial nerve V herpes zoster here with discussion of the salient clinical features as well as brief discussion about ongoing trials for herpes zoster ophthalmicus prophylaxis. This case also highlights the importance of timely treatment and diagnosis, as the patient presented 6 days prior to hospitalization with a mild vesicular facial rash but was lost to followup without filling a prescription for acyclovir, returning with severe facial involvement.

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Introduction

Varicella-zoster virus (VZV) is a human herpesvirus implicated in varicella (chicken pox) in predominantly children [1]. The virus commonly remains dormant in the sensory ganglion of the host and results in zoster following reactivation, with the highest risk of reactivation in advanced age or with severe stressors, immunosuppression, infection, or medication side effect [2]. Initial infection with V2V typically presents as a self-limited diffuse vesicular and pruritic rash; after the acute illness period, the host develops immunity to VZV. Shingles presents with a prodrome of burning pain, followed by an eruption of a vesicular rash unilaterally in a single dermatomal distribution [3]. In rare cases, particularly in the setting of immunocompromise, primary infection with varicella or reactivation with zoster can develop into disseminated disease, including encephalitis, pneumonia, hepatitis, and can have more extensive skin involvement in several adjacent dermatomes (multi-dermatomal zoster) or non-adjacent dermatomes (zoster duplex unilateralis or bilateralis) [1,4].

Case synopsis

In February 2019, a 63-year-old African American male presented to the emergency department on two occasions with complaint of painful vesicular lesions in a right-sided dermatomal distribution. On initial presentation, the patient complained of right-sided frontal headache, photophobia, rhinorrhea, and three days of right eye erythema and pruritis. His past medical history was notable for small lymphocytic lymphoma status post stem cell transplant, diffuse large B cell lymphoma (DLBCL) in remission status post stem cell transplant, peripheral neuropathy secondary to chemotherapy, sensorineural hearing loss, and tinnitus. Review of the patient’s medical record found no history of chickenpox. He did not receive the shingles vaccine as an adult. The patient’s past surgical history consisted of an uncomplicated hernia repair. Home medications were modafinil 100 mg daily, tramadol as needed for pain, and sildenafil as needed. He had no known drug allergies. Family history was non-contributory. The patient was a retired army veteran who lived with his son. He denied any history of tobacco or illicit drug use and discontinued alcohol several years prior. The initial physical exam was significant for a right-sided vesicular facial rash in a V2 distribution. Neurologic exam was normal and ophthalmologic exam was benign with no signs of zoster ophthalmicus. He was diagnosed with herpes zoster and discharged with hydrocodone/acetaminophen for pain relief, a prescription for a 7-day course of acyclovir 800 mg oral 5 times a day and instructions to return for an ophthalmology appointment scheduled for the following day. The patient did not fill the acyclovir prescription and did not attend the scheduled ophthalmology appointment. The patient’s full clinical course is summarized in Fig. 1.

The patient subsequently presented to the emergency department 6 days after the initial encounter with worsening facial rash and swelling, now with ocular involvement, including the inability to
open his right eye due to pain and swelling, as well as involvement of the contralateral eye including blurry vision. The patient also reported severe burning throat pain. The physical exam was notable for a fever (39.2 °C), blood pressure 103/63 mmHg, heart rate 130. A sharply demarcated vesicular rash was noted in the right trigeminal cranial nerve dermatome, with overlying crusting, erythema, and exudate (Fig. 2). Additional lesions were noted on the right lateral flank and right lateral thigh. The right oropharynx was noted to have multiple 1–4 mm vesicular lesions extending along the soft palate. Otoscopic exam by the primary team revealed no vesicles in the bilateral auditory canals or tympanic membranes. Inner ear evaluation by ENT revealed intact tympanic membrane on the right without obstructive or vesicular lesions. Ophthalmologic slit lamp exam revealed diffuse 3+ conjunctival/scleral injection of the right eye, mild right temporal corneal haziness with no evidence of dendrites. The right iris was irregular and minimally reactive. Left eye exam was normal. The patient was noted to have new deficits in right lateral gaze with extraocular movements intact. There were no other focal neurologic deficits. He showed no evidence of symptoms related to active malignancy or recurrence of his previously treated DLBCL. Laboratory values were significant for lactate 2.5 mmol, bicarbonate 16 mEq/L, 131 mEq/L, and creatinine elevation from 1.7 to 3.7 mg/dL. Blood cultures collected at the time of presentation showed no growth after 5 days of incubation. Imaging of the head on computed tomography (CT) with intravenous contrast showed asymmetric facial edema and enhancement consistent with severe facial zoster in a tri-segmental distribution. On further evaluation by the ophthalmology team, the patient had evidence of endothelitis and iridocyclitis, cranial nerve palsies of the right CN III and CN IV, blepharoconjunctivitis, and likely Adie’s atonic pupil.

Fig. 1. Timeline of patient presentation and hospital course.

Fig. 2. (clockwise). Lateral view of patient’s facial lesions includes severe crusting and oozing in a clearly demarcated dermatomal distribution along the right CN V distribution with associated right facial edema. Right oral mucosal involvement with multiple ulcerated vesicular lesions along the right hard palate not crossing the midline and without associated edema. Patient had bilaterally mobile vocal cords on scope view of oropharynx. Also, with right upper and lower lip edema with crusting and associated trismus secondary to pain. Inner ear evaluation by ENT revealed intact tympanic membrane on the right without obstructive or vesicular lesions. Four vesicular lesions involving the T10 – T11 dermatomes on the right lower anterior abdomen.
The management included initiation of intravenous (IV) acyclovir for antiviral coverage, as well as intravenous vancomycin (later switched to linezolid for renal protection) and cefepime for empiric coverage of possible skin and soft tissue superinfection. Ophthalmic moxifloxacin and topical mupirolcin were also applied to the eyes and affected skin, respectively. Six days into antiviral treatment with IV acyclovir, patient was re-evaluated by ophthalmology and found to have right eye mydriasis mildly reactive to light with new right eye abduction deficit. Recommendation was for an MRI to evaluate for possible stroke and herpes zoster ophthalmicus (HZO). An MRI brain with and without contrast showed asymmetric right-sided periopic nerve linear enhancement, particularly involving the right posterior intraorbital optic nerve, without evidence of an acute intracranial process or temporal FLAIR abnormality, or enhancement to suggest herpes encephalitis, confirming the diagnosis of HZO. The patient was started on a five-day course of IV sulomedrol. The course of acyclovir was extended to fourteen days to limit the risk for acute retinal necrosis. An MRA was also performed to rule out stroke syndromes and results were unremarkable.

In total, the patient received fourteen days of IV acyclovir, one day of IV vancomycin, four days of IV linezolid, four days of IV cefepime, six days of topical ophthalmic moxifloxacin, and fourteen days of topical mupirolcin. He was also treated with a five-day course of IV methylprednisolone for right optic neuritis. Upon discharge, the patient’s facial lesions had crusted, with persistent symptoms of hypoesthesia of right hemiface and right eye abduction gaze palsy.

Twenty-four hours after discharge, the patient returned to the emergency department with complaint of increasing right eye pressure and worsening right eye and face neuralgia. Exam was unchanged except for progressive healing and crusting of the previous cutaneous lesions. The patient was evaluated by ophthalmology and eye exam findings were notable for resolved dendritiform, improved iridocyclitis, right CN III and complete right CN VI involvement, and acute worsening of blepharocconjunctivitis compared to the initial presentation. No evidence of acute retinal necrosis was found. Right ptosis and diffuse extra ocular movement restriction persisted. The ophthalmology team recommended treatment with prednisolone acetate 1% eye drops applied to the right eye three times daily.

The patient also had features of post-herpetic neuralgia with pain involving the right eye and surrounding skin. Neurology recommended treatment with titrated doses of gabapentin, morphine, oxycodone, ketorolac, and lidocaine patches. While very sparse data exist regarding secondary prophylaxis in the setting of severe herpes zoster eruption and HZO, the decision was made to initiate valacyclovir 1000 mg daily as secondary prophylaxis. The patient was discharged with plan to continue valacyclovir for a prophylaxis duration of three months.

Discussion

The term “herpes zoster” originates from a combination of the Ancient Greek word herpein meaning “to creep” and zoster meaning a waist-belt or girdle for men, implying the eruption of a rash in a classic belt-like pattern around the waist. The English term shingles has a similar meaning. Herpes zoster is characterized by reactivation of varicella zoster virus, most commonly seen in the setting of advanced age with the relative decline in immune function, immunocompromised state (i.e. HIV/AIDS, impairment of cell-mediated immunity) or immunosuppressive agents (e.g. chemotherapy), physiological stress in excess, chronic illness, and trauma [3,5]. VZV is primarily transmitted by infectious respiratory secretions, replicates initially in lymphatic tissue leading to a primary viremia, followed by a second viral replication in the liver and spleen [6]. This second viremia is the conduit to infectious manifestation in the epidermis causing a blistering, vesicular, unilateral rash, typically in a single dermatome. Following an active infectious period of 1–2 weeks, the infectious cycle transitions to a dormant state via the activity of the cell-mediated immune system, settling into the sensory neurons of the dorsal root ganglion [6]. Reactivation of this latent virus is known as herpes zoster. Immunosuppressed patients are at higher risk for developing disseminated disease, as a significant defect in immunity is necessary for the reactivated virus to spread outside of a single dermatome and involve vital organs [7]. Mechanical trauma has also been reported to increase the risk of zoster at the trauma site [8]. Rarely, dissemination of herpes zoster can occur in immunocompetent hosts [6]. Cutaneous dissemination occurs on average about 7–8 days after appearance of the associated rash, however a range of one to twelve days has been reported.

Varicella zoster is classically a clinical diagnosis based on the pathognomonic vesicular eruption in a single dermatome, although diagnosis can be confirmed via serology and histology, as well as distinguishing between primary infection and reactivation. Primary infection is characterized by elevation in serum anti-VZV IgM, whereas elevation in serum IgG titers is associated with reactivation [9]. The patient in this case did not undergo serologic or histologic confirmatory testing as it was felt it would not change clinical management.

The utility of zoster prophylaxis is now of increasing interest. An initial retrospective study to evaluate this question found that suppressive valacyclovir 500 mg once daily or acyclovir 400 mg twice daily decreased the recurrence of herpes zoster in patients with HSV by 39% and 35%, respectively [10,11]. The study also has looked at long-term complications of ocular herpetic infections, including glaucoma, cataract, and retinal detachment. Due to otherwise limited data in understanding the role of prophylactic treatment to prevent complications of HZO, a multicenter, randomized, placebo-controlled clinical trial called the Zoster Eye Disease Study was initiated and is currently ongoing. Primary end points of the study include delay to first recurrence of dendritiform epithelial keratitis, stromal keratitis, endothelial keratitis, and iritis by 12 months (www.clinicaltrials.gov). The goal is to understand the best approach in treating the ocular manifestations of zoster including tri-segmental distribution, as seen in our patient.

Conclusion

Immunocompromised patients are at a significantly higher risk for severe VZV disease and dissemination. Patients may present typically with a painful, vesicular, singular dermatomal eruption, or with rapid progression with rash involvement of the tri-segmental CN III distribution, including herpes zoster ophthalmicus. Ongoing research is looking into the efficacy of prophylactic treatment with low-dose valacyclovir, which may prove beneficial in certain patient populations in preventing or limiting recurrence.

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Consent

The patient gave full consent to the publication of the report and associated images.

Declaration of Competing Interest

The authors have no conflicts of interest to disclose.
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