Cranial Nerve VI Palsy Secondary to Herpes Zoster Ophthalmicus: A Case Report and Literature Review

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ABSTRACT

Introduction: In this report, we describe a rare case of a cranial nerve VI palsy secondary to herpes zoster infection with polyneuropathic involvement.

Case Presentation: An 82-year-old male was seen by ophthalmology for acute onset of double vision. Fourteen days before presenting, he was diagnosed with herpes zoster ophthalmicus. He was suspected to have zoster polyneuropathy also involving cranial nerve IX and X given a sore throat that began prior to the characteristic trigeminal dermatomal rash. He was diagnosed with cranial nerve VI palsy secondary to herpes zoster infection.

Discussion: Ophthalmic complications of herpes zoster ophthalmicus are many; however, extraocular nerve palsies secondary to herpes zoster infection and zoster polyneuropathy are documented infrequently in the literature.

Conclusions: Extraocular muscle palsies are a rare complication of herpes zoster infection. This case reviews the most current literature surrounding this condition and discusses the significance of polyneuropathic involvement in varicella zoster virus reactivation.

INTRODUCTION

Varicella zoster virus (VZV) reactivation is a common disease that mainly affects older adult patients, often due to reduction in the level of T-cell immunity to VZV following initial infection with chicken pox and senescence in ganglion cells.[1] Herpes zoster ophthalmicus (HZO) is a frequent presentation of VZV reactivation and is characterized by a unilateral painful skin rash along the dermatomal distribution of the ophthalmic division of the trigeminal nerve. Complications of HZO include keratitis, uveitis, retinitis, secondary glaucoma, and the involvement of other cranial nerves.[2] The presence of the rash on the nose—known as a positive Hutchinson's sign—increases the risk of ocular complications from HZO.

Extraocular muscle palsies as a result of cranial nerve involvement are a rare complication of HZO, occurring in 7% to 31% of cases.[3] Even more rare is the involvement of cranial nerves IX and X in VZV reactivation, which have been shown to present with odynodysphagia and dysphonia.[4] We describe here a case of an 83-year-old male presenting with HZO complicated by cranial nerve VI palsy and suspected cranial IX and X involvement.

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CASE PRESENTATION

An 82-year-old White man with a past ocular history of keratoconus and bilateral nuclear sclerotic cataracts presented to the ophthalmology clinic with a 3-day history of acute double vision. His past medical history was remarkable for thyroid cancer status post thyroidectomy and radioactive iodine, prostate cancer status post radical retropubic prostatectomy, hyperlipidemia, hypertension, severe asthma, and bronchiectasis, as well as history of pulmonary mycobacterium avium-intracellulare superimposed on pulmonary norcardiosis, for which he was on chronic trimethoprim/sulfamethoxazole and followed closely by infectious disease. Notably, he was HIV negative and with no other underlying immunologic or immunosuppressive conditions. Years prior to his presentation, he had shingles of his left flank. He received the live zoster vaccine in 2011 and the recombinant zoster vaccine in 2018 and 2019. Fourteen days prior to the onset of diplopia, he was seen by infec-

Table. Review of Cranial Nerve Involvement in Varicella Zoster Virus Reactivation

Cranial Nerve	Relative Incidence of Herpes Zoster Cranial Neuropathy	Signs of Herpes Zoster Cranial Neuropathy	Symptoms of Herpes Zoster Cranial Neuropathy	Cranial Nerve Involvement in Case Report
I (olfactory)	Rare	Impaired olfaction	Impaired olfaction	No
II (optic)	Rare	Optic neuritis, decreased visual acuity	Vision loss, eye pain	No
III (oculomotor)	Rare	Abnormal extraocular motility (restricted or absent elevation and adduction of eye)	Double vision	No
IV (trochlear)	Rare	Abnormal extraocular motility (restricted or absent depression of eye)	Double vision	No
V (trigeminal)	Common	Hutchinson's sign, eyelid lesions, conjunctivitis, keratitis including dendritic lesions, uveitis, elevated intraocular pressure	Eye pain, red eye, tearing, photophobia, blurry vision	Yes
VI (abducens)	Rare	Abnormal extraocular motility (restricted or absent abduction of eye)	Double vision	Yes
VII (facial)	Common	Ramsay Hunt syndrome, facial palsy	Facial droop, ear pain	No
VIII (vestibulocochlear)	Moderately common	Cochlear neuritis	Hearing loss, tinnitus	No
IX (glossopharyngeal)	Rare	Mucosal lesions in the laryngopharynx	Odynophagia	Yes
X (vagus)	Rare	Mucosal lesions in the laryngopharynx, vocal fold hypomobility	Dysphonia, dysphagia, odynophagia, aspiration	Yes
XI (spinal accessory)	Rare	Weakness of sternocleidomastoid muscles	Head and face pain	No
XII (hypoglossal)	Rare	Abnormal tongue protrusion	Aphasia, dysphagia	No

The cranial nerves most frequently affected by herpes zoster infection include the trigeminal nerve (57.9%), facial nerve (52.1%), and vestibulocochlear nerve (20.0%).[8] Although the other cranial nerves are rarely affected, there are reports in the literature that all can develop cranial neuropathy from VZV reactivation.[9-11] Of the cranial nerves innervating the extraocular muscles, the oculomotor nerve is most frequently involved.

tious disease for right-sided scalp discoloration and vesicular rash that began approximately 1 week after he had a right-sided sore throat with white, tonsillar exudate. On exam, he had a decreased gag reflex, tenderness to the preauricular and cervical chain lymph nodes, and the right tonsil was enlarged without exudate. A rapid strep test was negative. He had no vision changes, ear pain, ear drainage, headache, anosmia, or nose lesions. He was diagnosed with HZO and treated with a 10-day course of oral valacyclovir. The infectious disease specialist believed the sore throat was related to zoster polyneuropathy of cranial nerve IX and X.

When presenting to the ophthalmology clinic, the patient described his double vision as constant, binocular, and horizontal. He stated that it became worse when looking right, and he experienced notable improvement when looking left. His visual acuity was 20/50 in each eye, and both pupils were equal and reactive without an afferent pupillary defect. Confrontation visual fields were full in both eyes. Extraocular movements were notable for limited abduction of the right eye. Extraocular movements were normal and full in the left eye. Slit lamp exam was negative for eyelid vesicular lesions, conjunctivitis, keratitis including dendritic lesions, and uveitis. He was diagnosed with a cranial nerve VI palsy of the right eye secondary to herpes zoster infection. Since he already completed a course of antiviral therapy, it was decided to forego any further treatment, especially given evidence of disease regression with the healing of the dermatomal rash. Oral steroids were not prescribed. Close observation and follow-up were recommended. Return precautions, including worsening double vision, decreasing vision, eye pain, light sensitivity, and eye redness, were reviewed with the patient. At his follow-up, he reported the double vision resolved spontaneously approximately 3 to 4 weeks after the onset of the symptoms.

DISCUSSION

Cranial nerve VI palsies have a broad differential, including most commonly microvascular ischemic injury to nerve in the setting of atherosclerotic risk factors, such as older age, diabetes mellitus, hypertension, and hyperlipidemia. Other etiologies include intracranial neoplasm, aneurysm, inflammation, infection, and brain stem infarction.[5] Extraocular nerve palsies in the setting of VZV reactivation are extremely rare, with only 1.1% to 2.9% of all reactivation attacks resulting in ophthalmoplegia.[6] When HZO is diagnosed, the incidence of ophthalmoplegia increases to about 13%.[6] Of these incidences, cranial nerve III is most commonly involved at 47% of the time, followed by cranial nerve VI at 23% of the time, and then cranial nerve IV, which occurs 10% of the time.[6] On average, HZO-associated ophthalmoplegia occurs about 9.5 days after the onset of the HZO rash, with a range from 2 to 42 days.[7] Our patient's experience was consistent with this range, as his double vision began about 11 days after he was seen initially by infectious disease for HZO. Although he also had hypertension and hyperlipidemia, given the rapid improvement of his double vision and the close timing of HZO rash and the double vision, we believe his cranial nerve IV palsy is secondary to VZV reactivation and not a microvascular ischemic injury, which typically takes longer to resolve.

VZV reactivation has been reported to affect all 12 cranial nerves (Table). Isolated involvement of the trigeminal nerve or facial nerve is the most common presentation. VZV polyneuropa-

thy is unusual but has been reported. The polyneuropathy in our patient's presentation includes cranial nerves V, VI, IX, and X. Involvement of cranial nerves IX and X in the setting of VZV reactivation are very rare and poorly characterized in literature.[4] However, a previous study showcased that in 54 cases of VZV reactivation, odynodysphagia and dysphonia reflected underlying hemipharyngolaryngeal palsy.[4] Interestingly in this case, our patient initially presented to infectious disease with a sore throat prior to the onset of the HZO dermatomal rash and eventual diplopia. Strep cultures taken at the time of this visit were negative, and the sore throat was deemed a result of viral infection, presumably zoster polyneuropathy given the constellation of symptoms.

The pathogenesis of extraocular muscle palsies as a result of damage to the nervous tissue is controversial, with several mechanisms being postulated.[3] One suggested mechanism involves direct cytopathic effect of the virus itself on surrounding neural tissue. Another mechanism proposes an immune response of the central nervous system (CNS) is induced as a response to the virus.[3] The third mechanism attributes the ophthalmoplegia to an occlusive vasculitis induced by the virus.[3] The last postulated mechanism suggests that the zoster virus activates a different latent neuropathic virus within the brain.[3]

Another debated topic of discussion is how the virus reaches the nerves that become involved. One commonly referenced mechanism is the retrograde spread of the virus from the trigeminal ganglion to the nucleus of cranial nerve V.[8] From here, it is believed that the virus reaches other cranial nerve nuclei either by axonal spread along interconnections or through random spread.[12] Another suggested mechanism states the virus may reach the brain through basal meningoencephalitis.[12] Considering the involvement of multiple cranial nerves in this patient presentation, our case may offer support to the mechanism of axonal spread through various interconnections between the cranial nerves. Furthermore, given the involvement of specific cranial nerves, it is less likely that the pathogenesis of the palsies in our patient arose from a systemic cause, such as a generalized immune response of the CNS or vasculitis, again suggesting that the cause is more likely related to a direct cytopathic effect.

A topic that is less commonly addressed is the recommended treatment of extraocular palsies secondary to herpes zoster infection. Given the rarity of such cases, no specific treatment protocol exists. As these palsies tend to resolve spontaneously, the effects of a specific treatment are unclear. It is generally understood that in cases of HZO – regardless of complications – the therapeutic goal is to limit the severity of pain and reduce the chances of dissemination by treating with antiviral medication within the first 72 hours of rash onset.[13] Additionally, oral steroids can be considered to decrease neural inflammation, although they were not used in this case.

Given the sequela that can result from VZV reactivation, including cranial nerve palsies, it is important to encourage patients 50 years and older to receive zoster vaccination to help prevent such complications. Vaccination is important even after VZV reactivation. Clinicians, including ophthalmologists, can educate patients that zoster vaccination is safe, effective, and readily available.

CONCLUSIONS

Cranial nerve VI palsy in the setting of herpes zoster ophthalmicus is a rare complication of the VZV reactivation. Although zoster polyneuropathy is uncommon, it is important to appropriately screen and examine patients for this presentation to fully understand and manage their disease.

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