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Orbital Apex Syndrome With Encephalitis: A Rare and Serious Complication of Herpes Zoster Ophthalmicus

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ABSTRACT

Introduction: Herpes zoster reactivation is more common in the elderly population. Although ocular complications are seen in 20-70% of patients with herpes zoster ophthalmicus, orbital apex syndrome is a rare case. Encephalitis is also a rare neurologic complication of HZO.
Purpose: To report a Herpes Zoster Ophthalmicus (HZO)case with rare neurologic complication that ophthalmologist should be aware of.
Case Presentation: A 68-year-old man had a chief complaint of a sudden blurred vision in right eye two days before admission, followed by rash and pain on the right upper eyelid and forehead. Visual acuity was hand movement on the right eye and 0.5 on the left eye. The patient had total ophthalmoplegia and total ptosis on his right eye, reverse relative afferent pupillary defect on his left eye and right peripheral facial nerve palsy. Optic discs were found to be normal on both eyes. The patient was diagnosed as orbital apex syndrome on his right eye associated HZO and right peripheral facial nerve palsy. The patient received oral acyclovir 800 mg five times/day and intravenous methylprednisolone 250 mg four times/day for three days. After four days of admission, the patient had a seizure and loss of his consciousness. The patient was consulted to neurology department and was given anticonvulsant therapy. The spinal tap revealed pleocytosis and increased protein. The patient was diagnosed as herpes zoster encephalitis. After one week, the patient regained full consciousness and his visual acuity was improved to 0.16 on the right eye. Color vision, visual field, and contrast sensitivity were also improved, ophthalmoplegia were partially resolved and peripheral facial nerve palsy was fully resolved.
Conclusion: Herpes Zoster Ophthalmicus affect the central and peripheral nervous system at the same time and can be life-threatening with delayed diagnosis and treatment. It may be necessary to collaborate with the neurology department for every HZO case to minimize the life-threatening complications of HZO.
Keywords: encephalitis, orbital apex syndrome, herpes zoster ophthalmicus

INTRODUCTION

Herpes zoster ophthalmicus (HZO) refers to involvement of the ophthalmic division of the trigeminal nerve from reactivation of latent Varicella-Zoster Virus (VZV) harboured in the trigeminal sensory ganglion. Herpes zoster reactivation is more common in the elderly population, resulting from a decline in cell-mediated immunity. The incidence in those > 65 years of age is thought to be in the range of 3.9–11.8 cases/1000 person-years. Ocular complications are seen in 20-70% of patients with HZO. Ocular motor cranial nerve palsies are reported in 5%-31% of patients.[1-3]

Although there are several case reports of internal or external ophthalmoplegia (partial or total), optic neuropathy in HZO is rare, with orbital apex syndrome (OAS) being reported in about 20 cases. Postherpetic neuralgia is the most common neurologic complications, but other complications, including cranial nerve

palsies, stroke, myelitis, meningoencephalitis, and polyneuropathy, have also been reported. Some of these conditions can be life-threatening with delayed diagnosis and treatment. Here we report a rare case of Herpes Zoster ophthalmicus complicated with orbital apex syndrome and encephalitis.[4-6]

CASE PRESENTATION

A 68-year-old man came to Neuro-Ophthalmology Division, Cicendo National Eye Hospital on June 7th, 2019 with a chief complaint of sudden blurred vision on his right eye two days before admission, following rash and pain on the right upper eyelid and forehead for about six days before. He also complained of headache, stiffness and swelling in his right face. The patient did not encounter either fever, nausea, vomitus, swallowing difficulty, double vision, otalgia, seizure, tinnitus, or limbs weakness. He had no history of using spectacles, trauma, recurrent ocular redness, long-term medication, chicken pox and other systemic diseases before. On general examination, the patient was fully alert, with a blood pressure of 107/62mmHg, heart rate of 77 beats/minute, respiratory of 20 times/minute, and body temperature of 36.7 o C. His body weight was 43 kg.

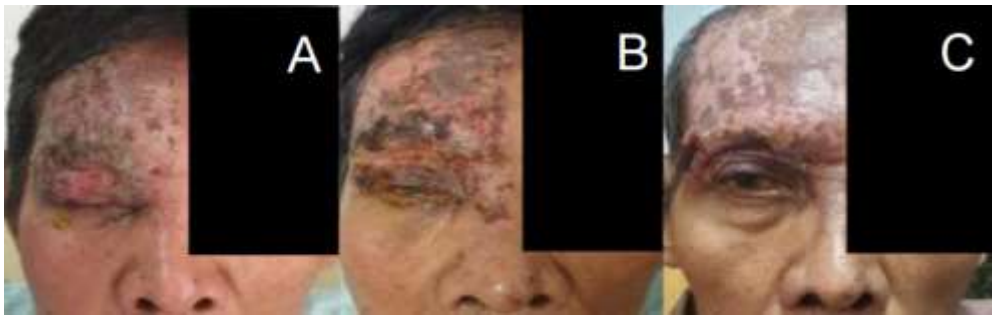

Figure 1. Herpetiform vesicular desquamation on the right upper eyelid and frontal region at first day of admission (A); Desquamation and Hutchinson's sign on the tip of the nose became more prominent after three days of admission(B); and both signs finally improved after one week and the patient was able to open his eye (C).

On ophthalmologic examination, his uncorrected visual acuity (UCVA) was hand movement on the right eye (RE) and 0.5 on the left eye (LE) on the Snellen chart. His primary eye position was orthotropic. Intraocular pressure on both eyes was normal. Ocular movement showed total ophthalmoplegia (-4 on all direction) with total ptosis in RE. Slit-lamp examination on RE revealed mucopurulent discharge, conjunctival chemosis, corneal epithelial defect, corneal edema and dilated pupil but anterior chamber reaction cannot be assessed. His left eye examination showed a reverse relative afferent pupillary defect (RAPD). Fundus examination revealed normal discs and macula on both eyes although on the RE is not too clear. Visual function examinations were tested on the LE with the normal results of Amsler's grid test, Ishihara test, and contrast

sensitivity, but it cannot be assessed for his RE.

In addition, the erythema and herpetiform vesicular desquamation was appeared on the right upper eyelid and frontal region and there was Hutchinson's sign on the tip of the nose. Right peripheral facial nerve and sensory part of trigeminal nerve over the right half of the forehead and right cornea were impaired. Other neurologic examination show normal findings. Initially, the patient was diagnosed with orbital apex syndrome and blepharokeratoconjunctivitis RE caused by Herpes zoster ophthalmicus with right peripheral facial nerve palsy. Patient was hospitalized for administration of intravenous methylprednisolone 250 mg four times/day, intravenous ranitidine 50 mg two times/day, intravenous mecobalamin 500 mcg once/day, oral acyclovir 800mg five times/day, oral calcium hydrogen phosphate 500 mg and cholecalciferol 133 IU three times/day, oral mefenamic acid 500 mg three times/day, levofloxacin eye drop six times/day, and artificial tears six times/day, and mupirocin cream three times/day.

He was planned to undergo magnetic resonance imaging (MRI) brain with contrast. On the second day of admission, after receiving two dosages of intravenous methylprednisolone 250 mg, UCVA increased on RE 0.08 on Snellen chart. Ophthalmoplegia and conjunctival chemosis were partially resolved (-2 on all direction). Visual function examinations on right eyes can be examined with the normal results of Amsler's grid test, demo plate of Ishihara test, and 25% of contrast sensitivity. Anterior and posterior segments findings were still the same as initial examination. Treatments were continued without any systemic side effects. After administration of 10 dosages of intravenous methylprednisolone, VA showed improvement on right eyes 0.1 on the Snellen chart. Ophthalmoplegia (-2 superonasal and superotemporal direction, other -1), conjunctival chemosis, mucopurulent discharge, and ptosis were improved. Visual function examinations on right eyes show no improvement with the normal results of Amsler's grid test, demo plate of Ishihara test, and 25% of contrast sensitivity.

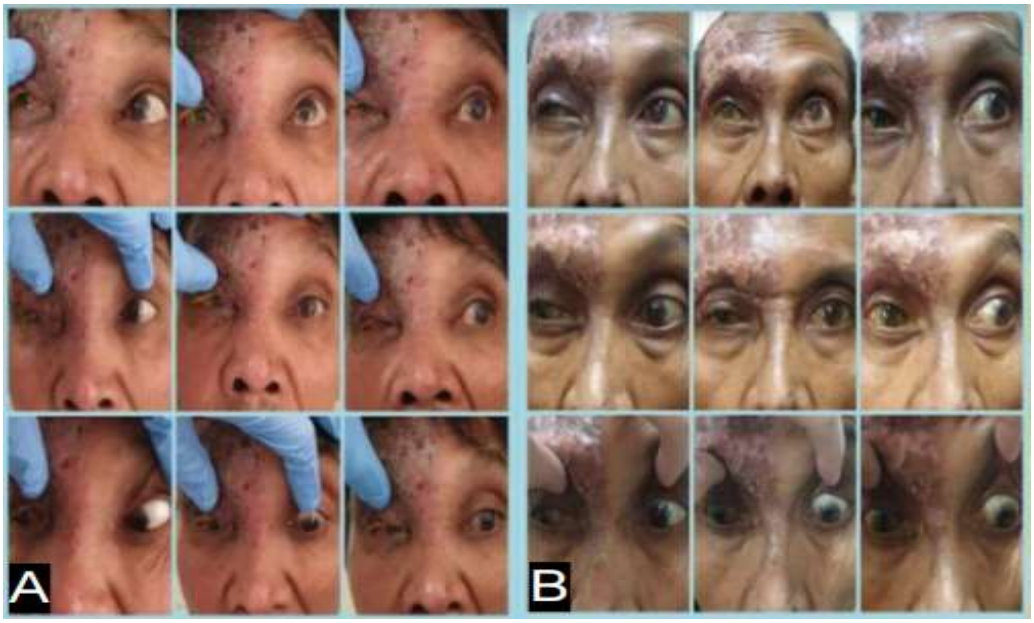

Figure 2. Ophthalmoplegia became -2 on all direction after four days of admission (A); and after one week, ophthalmoplegia were improved to -1 on all direction, except superonasal and superotemporal direction(B)

Patient was planned to be discharged after the twelfth dosage of intravenous methylprednisolone, but the patient had a general seizure for 1 minute and loss of his consciousness on the 4th day of admission. On general examination, the patient was coma with Glasgow coma scale 5 (E1M3V1), with a blood pressure of 150/100mmHg, heart rate of 120 beats/minute, respiratory of 28 times/minute, oxygen saturation 94% on nasal cannula 5 Litre per minutes and body temperature of 36.7 0C. On neurologic examination, tendon reflexes were normal, no pathological reflexes, and absence of meningeal signs. The patient was administered 45 ml/hour of Ringer Lactate, 5 Lpm oxygen by nasal cannula and a single dose of 10 mg diazepam intravenously. The patient was stable and then referred to the neurology department in Hasan Sadikin General Hospital. The patient was given intravenous phenytoin continued by intravenous levetiracetam.

Figure 3. Right peripheral facial nerve palsy at first day of admission (A); and fully resolved after one week (B)

Laboratory examination, chest radiography, head Computed Tomography (CT) scan with and without contrast, electroencephalography (EEG) and lumbar puncture were performed. White blood cell count was elevated

(14.110 cells/uL), which consisted of 3% lymphocytes, 93% neutrophils, and 4% monocytes. Lumbar tap showed a yellow Cerebrospinal fluid (CSF). CSF analysis revealed 128 white blood cells per microliter with 86% mononuclear cells, cerebrospinal fluid glucose was 86 mg/dL (reference range, 45-60 mg/dL), and protein was elevated at 141.2 mg/dL (reference range, 15-45 mg/dL). Acquired immunodeficiency syndrome virus test was negative. Chest radiography and brain CT scan with contrast show normal findings. EEG shows cortical disfunction and slow conduction in frontotemporal lobes suggestive encephalitis. After four days of admission, the patient regained his full consciousness and then fully discharged the next two day. His visual acuity was improved to 0.16 on his RE. Color vision, visual field, and contrast sensitivity were also improved, ophthalmoplegia were partially resolved and peripheral facial nerve palsy was fully resolved as we can see in figure 3.

DISCUSSION

Herpes zoster is a result of reactivation of Varicella-Zoster virus (VZV) infection, commonly called shingles. After primary VZV infection, the virus becomes latent in ganglia along the entire neuroaxis. Reactivation of VZV can be triggered by aging, an immunocompromised host, trauma, surgery, iatrogenic immunosuppression, tuberculosis, syphilis, and radiation therapy. Borkar et al said that the incidence and severity of the disease increase especially in those older than 65 years as we saw in this patient. In this patient we considered that VZV reactivation was triggered by his age due to a negative result of tuberculosis and human immunodeficiency virus. One of the most recognized consequences of aging is a decline in immune function.[1-3,7]

Herpes zoster infection affects the sensory nerves of the thoracic dermatomes most often, followed by the cranial nerves. It is characterized by an acute dermatomal eruption that evolves through papular, vesiculobullous, pustular, and crusting stages over days to 3 weeks. HZO refers to involvement of the ophthalmic division of the trigeminal nerve from reactivation of latent VZV harboured in the trigeminal sensory ganglion. Ocular complications are seen in 20-70% of patients with HZO. The most common ocular manifestations of HZO include blepharoconjunctivitis, keratitis, and uveitis. Ocular motor cranial nerve palsies are reported in 5%-31% of patients. The most frequently involved cranial nerve is the oculomotor nerve, followed by the abducens nerve. Although there are several case reports of neurological complications such as internal or external ophthalmoplegia (partial or total), optic neuropathy in HZO is rare and known to respond to antiviral or steroid treatment with orbital apex syndrome being reported in about 20 cases.[8-10]

Orbital apex syndrome (OAS) is an uncommon clinical presentation consisting of complete ophthalmoplegia with vision loss, involving optic nerve (cranial nerve II), oculomotor nerve (cranial nerve III),

trochlear nerve (cranial nerve IV), abducens nerve (cranial nerve VI) and ophthalmic branch of the trigeminal nerve (cranial nerve V1). The diagnosis of orbital apex syndrome was made by clinical presentation shown in this patient which consist of total ophthalmoplegia, total ptosis, and positive RAPD. The head CT scan with and without contrast shows no signs of trauma or space occupying lesion. The lack of this case is there was no orbital magnetic resonance imaging (MRI) examination to confirm the etiology of OAS. Yeh S and Foroozan R said that neuroimaging examination such as MRI or CT scan should be performed in patient with findings consistent with an OAS so we can rule out traumatic, neoplastic, and vascular lesion as etiologies of OAS. OAS may result from neoplastic, inflammatory, infectious, iatrogenic/traumatic, and vascular conditions. It is important to know the etiology of OAS to determine treatment options and prognosis of the patient. Reactivation of latent VZV infection is an uncommon cause of OAS. Young patients presenting with HZO and associated complications should raise suspicion of the human immunodeficiency virus (HIV)/AIDS and should be tested accordingly.[11-14]

The pathological mechanism for ophthalmoplegia in cases of herpes zoster ophthalmicus has not been determined. Earlier histological studies on autopsy specimens have suggested two possible pathological mechanisms, ie, reactivation of Varicella-Zoster Virus in the trigeminal ganglion, which then invades the cavernous sinus and superior orbital fissure, and a second mechanism might be lymphocytic infiltration of the affected nerves by sensory offshoots of the trigeminal nerves to all the motor nerves of the eye. Kocaoğlu G et al showed that inflammatory cells infiltrated the orbital apex along the long posterior ciliary vessels and nerves in 21 enucleated eyes affected by herpes zoster ophthalmicus, indicating that the neuropathy arises from an occlusive vasculitis. Thus, the ophthalmoplegia and optic neuritis are suggested to be due to direct invasion by Varicella-Zoster Virus or by an inflammatory reaction and occlusive vasculitis after virus invasion.[1,4,11,15]

In addition to the peripheral nervous system, HZO can also have a central nervous system involvement. Encephalitis is a rare complication of HZO occurring in less than 0.1%. Other neurologic complications including post-herpetic neuralgia, vasculopathy, cerebritis, and myelitis. Herpes Zoster associated encephalitis is most often reported in immunosuppressed patients and is very rare in the immunocompetent host. The clinical presentation varies from mild self-limiting monosegmental cutaneous affection to severe encephalitis with a mortality up to 12-15%.[16-18]

The ophthalmic branch of the trigeminal nerve supplies the cornea, the skin of the forehead, eyelid, and nose, and it gives off branches to the tentorium cerebelli, dura mater and the posterior area of the falx cerebri, possibly explaining a way for the virus to reach the brain causing encephalitis and meningitis. Another theory said

that VZV is known to replicate in arteries resulting in vasculopathy. Ellul M and Solomon T said that the key to establishing evidence of CNS inflammation is the analysis CSF and brain imaging either CT scan or ideally MRI. There is typically a CSF pleocytosis, normal to moderately raised protein and normal glucose in viral encephalitis. In this patient, the CSF analysis show that viral is suspected as an etiology for encephalitis while for the diagnosis of Herpes Zoster associated encephalitis cannot be confirmed as it needed a PCR examination.[17-19]

The treatment regimen for OAS and encephalitis secondary to herpes zoster includes 4000 mg/day acyclovir (800 mg, 5 times daily) or 3000mg/day valacyclovir (1000 mg, 3 times daily) and systemic steroids. The use of a systemic steroid may be effective to prevent occlusive vasculitis. The clinical course of the disease depends on how rapid is the treatment initiated. The treatment started within the first 72 hours is recommended. In this case, the patient came to the hospital on the sixth day of onset, it may increase the risk of complications, such as encephalitis. The recovery time for HZO-related ophthalmoplegia is reported to be 4.4 months on average, with a range of 2 weeks to 1.5 years. The rates of complete recovery from ophthalmoplegia and optic neuropathy have been reported as 76.5% and 75%, respectively. The prognosis of this patient is ad bonam for quo ad vitam, dubia for quo ad functionam, and dubia ad bonam for quo ad sanationam. Central nervous system (CNS) lesion on this patient had complete recovery but the peripheral nervous system (PNS) showed a slower recovery. Xiao et al suggested Herpes Zoster could affect central nervous system and peripheral nervous system at the same time. Meanwhile, it seems that the lesion of CNS is more reversible than the PNS lesion.[1,3,16,17]

CONCLUSION

Herpes zoster ophthalmicus is a relatively common disease in clinical ophthalmological practice but is rarely accompanied by neurological complications. HZO could affect CNS and PNS at the same time and can be life-threatening with delayed diagnosis and treatment. Orbital apex syndrome and encephalitis are rare and become serious complications of herpes zoster infection. Therefore, ophthalmologists should be careful not to miss the risk of neurological complications, and be especially vigilant during 14 days after the onset of herpes zoster ophthalmicus. It may be necessary to collaborate with the neurology department for every HZO case to minimize the life-threatening complications of HZO.

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