CASE REPORT

# Orbital apex syndrome as an unusual complication of herpes zoster ophthalmicus in HIV-positive young man: a case report

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## Abstract

Herpes zoster ophthalmicus (HZO) is a neurocutaneous disease caused by reactivation of herpes zoster infection from latent phase after varicella infection in elderly population. It affects ophthalmic division of trigeminal nerve. Common ocular presentation includes conjunctivitis, anterior uveitis, and keratitis. Orbital apex syndrome rarely occurs as a complication of herpes zoster ophthalmicus in young human immunodeficiency virus (HIV)-positive men.

A 20-year-old, recently diagnosed HIV-positive man, presented with vesicular skin rashes over right periorbital and forehead area, associated with right eye redness. He was treated as herpetic zoster ophthalmicus with oral antiviral (acyclovir). Three days later, he developed right eye ptosis, reduced visual acuity, anisocoria, and total ophthalmoplegia. An orbit magnetic resonance imaging showed swelling of all rectus muscles of right eye with right optic nerve perineural enhancement. Diagnosis of right eye herpes zoster ophthalmicus with orbital apex syndrome was established, and intravenous acyclovir was initiated. Systemic antiviral acyclovir continued for up to 10 days. Upon discharge, his ocular features improved; however, his visual impairment persisted.

Orbital apex syndrome is a rare complication of herpes zoster ophthalmicus. This irreversible sight-threatening complication can be prevented by early diagnosis of HZO and immediate starting of antiviral treatment.

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**Key words:** herpes zoster ophthalmicus, orbital apex syndrome, varicella zoster infection, HIV.

## Introduction

Herpes zoster (HZ) is typically characterized by painful, blistering, dermatome distributed vesicular rashes. It results from reactivation of varicella-zoster virus (VZV) in sensory ganglia, after a long latency period, following primary infection from varicella. HZ is quite common, as in the United States, approximately 1 million new cases are reported per year, and HZ occurs in 1 in 3 persons [1]. Although, the rate of HZ increases with age, over half of all cases occur under the age of 60 years. In elderly, the pain may continue to persist after the rash heals and develops into postherpetic neuralgia (PHN). Moreover, HZ also causes neurological sequelae, HZ ophthalmicus (HZO) with eye involvement or disseminated disease [2].

Herpes zoster ophthalmicus (HZO) specifically is caused by reactivation of latent varicella infection in the trigeminal gan-

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glion, involving ophthalmic division of trigeminal nerve [3, 4]. Between 20 to 70% of patients with HZO presented with ocular involvement include blepharitis, keratoconjunctivitis, iritis, scleritis, and acute retinal necrosis [3]. In other words, orbital apex syndrome is characterized by dysfunction of ophthalmic division of trigeminal nerve (V), oculomotor nerve (III), trochlear nerve (IV), abducens nerve (VI) as well as optic nerve (II) [4]. Apart from aspergillosis and mucormycosis as common infectious causes for orbital apex syndrome, herpes zoster ophthalmicus also contribute to orbital apex syndrome; however, its occurrence is unusual. The aim of the study was to report a case of orbital apex syndrome as a complication of herpes zoster ophthalmicus in a young human immunodeficiency virus (HIV)-positive man.

## Case report

A newly HIV-diagnosed 20-year-old man presented with vesicular skin rashes over right periorbital region and forehead, associated with right eye redness for the past 1 week. He was seen in a clinic and treated as outpatient herpes zoster ophthalmicus case with keratouveitis and was prescribed with oral and topical acyclovir. He revisited the clinic again 3 days later, with a new onset of right eye ptosis and severe generalized blurring of vision, while his forehead vesicular rashes were drying up and turning into a scar.

On examination, he suffered from right eye almost complete ptosis with scar formation over right periorbital and frontal area, corresponded to the distribution of first and second division of trigeminal nerve (Figure 1). Hutchinson sign was positive. The patient had a right proptosed eye, and a measurement performed on Hertel exophthalmometer at 115 intercanthal distance showed 19 mm for OD and 16 mm for OS. Extraocular muscles movement for all gaze of the right eye were restricted, causing so-called "frozen eye" (Figure 2). Relative afferent pupillary defect (RAPD) was negative for the right eye. His visual acuity parameters were 6/36 (OD) and 6/6 (OS). Right conjunctiva was injected, and the presence of keratic precipitate (KP) over right cornea endothelium was noted. Anterior chamber was deep with cells of 2 plus, and the patient's pupils were unequal with pupillary size of 5 mm (OD) and 3 mm (OS) (Figure 1). Intraocular pressure was 12 mm Hg (OD) and 10 mm Hg (OS). Dilated fundus examination for the right eye revealed slight tortuous vessels, however optic disc had a well-defined margin. No evidence of vasculitis, retinitis, or choroiditis was observed. Examination of the patient's left eye revealed typical anterior and posterior segments. Others optic nerve functions, including light brightness and red saturation were undamaged for both eyes.

T1-weighted brain/orbit magnetic resonance imaging (MRI) showed an enhancement on the rectus muscles of right eye, with optic nerve perineural enhancement (Figure 3). MRI of the brain indicated no evidence of cavernous sinus thrombosis.

A provisional diagnosis of right herpes zoster ophthalmicus with orbital apex syndrome was established and patient was started on treatment with intravenous acyclovir 500 mg, three times per day, for 5 days, followed by oral acyclovir for 3 months. He also started with topical (ointment) acyclovir 5 times per day for his dermatome lesion. Systemic corticosteroid, oral prednisolone 0.5 mg per kg/daily started after 48 hours of intravenous acyclovir initiation and it was tapered. Additionally, eye drops with dexamethasone was applied for the patient's keratouveitis every 2 hours. Apart for his eye problem, he was also co-managed by infectious disease team for his retroviral issue to initiate a combination of antiretroviral therapy.

Upon discharge, the patient's right eye ptosis as well as extraocular muscles movement improved. He regained his vision back to 6/24. Anterior segment was quiet and posterior segment remained typical. He was discharged with oral acyclovir 800 mg, five times per day.

## Discussion

HZO refer to neurocutaneous disease caused by herpes zoster infection with ophthalmic division of trigeminal nerve involvement. It accounts for 10 to 20% of herpes zos-

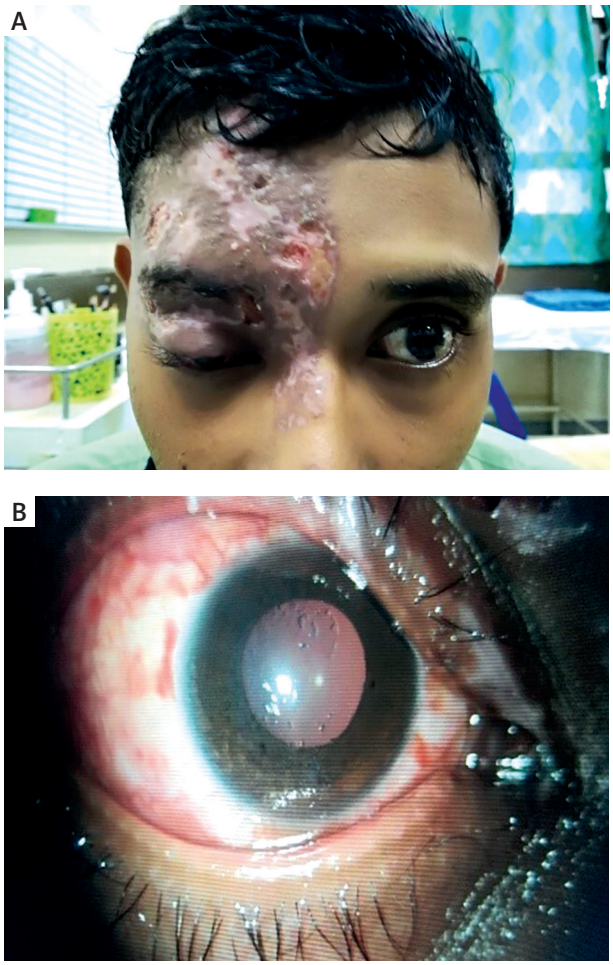


**Figure 1. A)** Right eye ptosis, dried and damaged right periorbital and forehead skin lesion (left). **B)** Mid-dilated pupil with conjunctival injection (right)

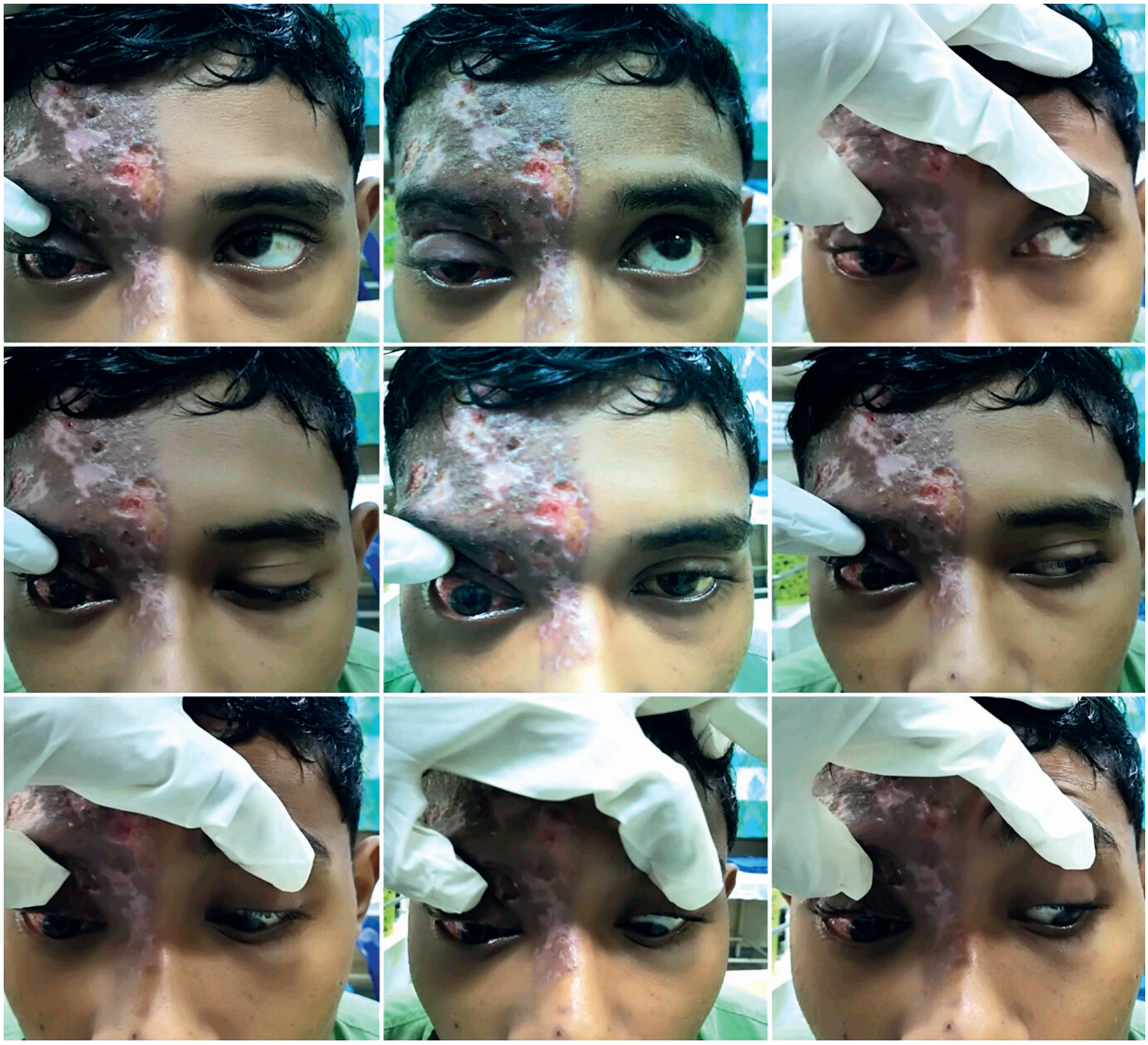

**Figure 2.** Limitation of extraocular muscles movement for all gaze of the right eye

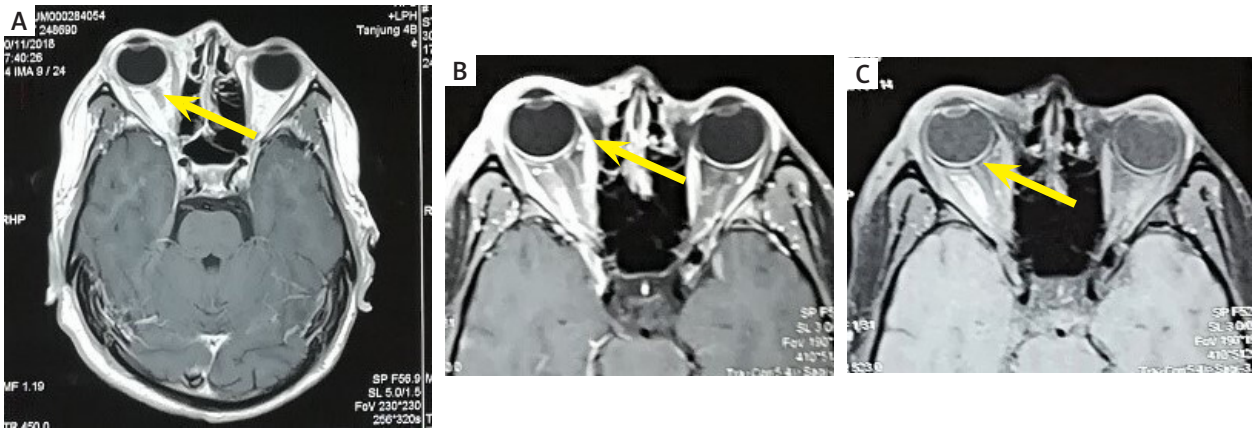


**Figure 3. A-B)** T1-weighted axial brain/ orbit MRI showing an enhancement on the rectus muscle of right eye (arrow). **C)** T1-weighted orbit MRI revealing right perineural enhancement (arrow)

ter infections [4]. Concomitant involvement of dermatome supply by maxillary nerve in HZO is also possible (5.4%) [5]. 65.6% of patients with HZO present ocular manifestations with conjunctivitis as the most common presentation, followed by anterior uveitis and keratitis, whereas optic neuritis, cranial nerve palsy, and acute retinal necrosis cases are rarely reported [5]. The presence of Hutchinson sign is significantly associated with ocular involvement [5]. Ocular involvement can be acute, recurrent, or chronic. Mild to moderate visual loss are reported in 10% of patient with HZO caused by keratitis [5]. Furthermore, more than half of patients who are untreated for dermatomal HZ develop ocular complications, such as chronic debilitating, visual impairment, or eventually irreversible blindness [7]. Schaftenaar *et al*. in their study on ocular HZO complications in rural parts of South Africa revealed that these ocular complications are more common among HIV-infected individuals, and clinical presentation is more severe as compared to non-HIV individuals [7].

Orbital apex syndrome (OAS) is defined as variable degree of involvement of oculomotor, trochlear, abducens, ophthalmic division of trigeminal cranial and optic nerves. It is a rare and devastating ocular complication of HZO, as it might cause permanent reduced vision because of inflammation and compression of optic nerve. Temnogord *et al*. reported a case of orbital apex syndrome in a 47-year-old HIV-positive patient, with CD4 count of 400, who initially completed treatment for HZO at 1 month prior to presentation [8]. Also, other reviewed studies reported cases on middle age to elderly patients with various background history for risk factors, who presented with ophthalmoplegia with reduced vision after episodes of dermatomal vesicular rashes [8-14].

Early diagnosis of HZO and fast initiation of therapy will reduce the duration of symptoms and prevent ocular complications. Ideally, the initiation of systemic antiviral therapy should take place within 72 hours from the onset of symptoms, in order to reduce late stage ocular complications [7, 8]. Standard treatment for HZO include valacyclovir 1,000 mg three times per day, famciclovir 500 mg three times per day, or acyclovir 800 mg 5 times per day for 1 week, which need to be started within 72 hours from the onset of rashes [1]. This recommended therapy reduces the risk of ocular involvement from 50% to 30% at 6 months, and such an antiviral regime can benefit the patients with increased risk of complications, i.e. in older and immunocompromised cases [1]. Apart from a systemic treatment, topical ganciclovir is also considered in patients with dendriform keratitis.

In HZO complicated by OAS, current standard empirical treatment involves systemic acyclovir and steroids. Few studies reported that intravenous acyclovir can be more beneficial than oral acyclovir in optic nerve involvement [4, 5, 8]. The usage of oral acyclovir in immunocompromised patients might carry a risk of insufficient efficacy. However, whenever the intravenous acyclovir is not available, oral therapy should be implemented as soon as possible, rather than waiting until intravenous administration will be possible [15]. In the present study, despite starting oral acyclovir for our patient, the disease was still progressing, and OAS has developed. The patient's immunocompromised status should be considered earlier, where prompt imaging of orbit and brain could help in early diagnosis of OAS. In addition, earlier commencement of intravenous acyclovir might have served a better option of treatment for our patient, considering his retroviral status.

## Conclusions

Herpes zoster ophthalmicus is a common disease, but orbital apex syndrome as a complication is unusual. Early identification and diagnosis of herpes zoster with systemic antiviral therapy helps to reduce the incidence of complication as well as irreversible ocular difficulties.

## Ethical issue

Informed consent was obtained from the patient for publication of this case report and all related images.

## Conflict of interest

The authors declare no conflict of interest with respect to the research, authorship, and/or publication of this article.

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