



Orbital Apex Syndrome Secondary to Herpes Zoster Ophthalmicus

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*Dokuz Eylül University Faculty of Medicine, Department of Ophthalmology, İzmir, Turkey

**Dokuz Eylül University Faculty of Medicine, Department of Radiology, İzmir, Turkey

Abstract

Orbital apex syndrome is a rare complication of herpes zoster ophthalmicus. A patient being followed in our clinic for herpes zoster ophthalmicus developed orbital apex syndrome in the second week of treatment. Clinical diagnosis was supported by magnetic resonance imaging. Treatment with systemic steroid and antiviral therapy resulted in total regression of ophthalmoplegia at 2 months. However, optic neuropathy-induced vision loss was permanent. This case report examines orbital apex syndrome secondary to herpes zoster ophthalmicus, which has rarely been documented in the ophthalmic literature.

Keywords: Herpes zoster ophthalmicus, orbital apex syndrome, total ophthalmoplegia

Introduction

Herpes zoster ophthalmicus (HZO) occurs due to reactivation of latent varicella zoster virus (VZV) infection in the trigeminal ganglion, which contains the ophthalmic branch of the trigeminal nerve. Ocular complications are seen in 20-70% of patients with HZO.¹ These complications can include blepharitis, keratoconjunctivitis, iritis, scleritis, and acute retinal necrosis. Neurologic complications are less common compared to ocular complications. Some of the neurological complications reported include ophthalmoplegia, optic neuritis, ptosis, and less frequently orbital apex syndrome (OAS).² OAS can lead to dysfunction of the ophthalmic branch of the trigeminal nerve (cranial nerve V1), oculomotor nerve (cranial nerve III), trochlear nerve (cranial nerve IV), abducens nerve (cranial nerve VI), and optic nerve (cranial nerve II). In this case report, we discuss our treatment and management of complications in a patient with HZO-related OAS.

Case Report

A 67-year-old male patient presented to our clinic with rash and redness on the right upper eyelid and forehead.

He also complained of redness and pain in the right eye. On ophthalmologic examination, his best corrected visual acuity (BCVA) on Snellen chart was 0.2 in the right eye and 0.8 in the left eye. Direct and indirect light reflexes were intact bilaterally and there were no signs of relative afferent pupillary defect. In addition to the erythema and herpetiform vesicular desquamation observed on the right upper eyelid and frontal region, slit-lamp examination revealed corneal epithelial keratitis, 2+ cells in the anterior chamber, and keratic precipitates. The patient's systemic medical history was unremarkable except for diabetes mellitus (controlled with oral antidiabetic therapy for 10 years) and hypertension. The patient was diagnosed with HZO and treatment was initiated with oral valacyclovir (1000 mg 3 times daily), topical ganciclovir (5 times daily), ofloxacin drops (2 times daily), cyclopentolate drops (3 times daily), prednisolone acetate drops (6 times daily), and oral nonsteroid anti-inflammatory tablet (dexketoprofen trometamol, 25 mg, 2 times daily). At 2-week follow-up examination, the patient had no light reflex in his right eye with fixed, dilated pupil. He exhibited anisocoria with right and left pupil diameters of 6 mm and 3 mm, respectively. He also had relative afferent pupillary defect, total ptosis (Figure

Address for Correspondence: Canan Aslı Utine MD, Dokuz Eylül University Faculty of Medicine, Department of Ophthalmology, İzmir, Turkey

Phone: +90 232 412 30 67 E-mail: cananutine@gmail.com **ORCID-ID:** orcid.org/0000-0002-4131-2532

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1), and total ophthalmoplegia (Figure 2) in the right eye. BCVA was 0.2 on the right. Color vision score was 1/21 in the right and 21/21 in the left eye. Slit-lamp examination revealed persistent herpetic keratouveitis in the right eye. Papillary stasis was not observed on fundoscopic examination. However, fundus structures were pale due to choroidal ischemia when compared with the left eye (Figure 3). The macula appeared normal in both eyes on optical coherence tomography. Orbital magnetic resonance imaging (MRI) revealed non-mass enhancement in the right orbital apex (Figure 4a-e). On cranial magnetic resonance venography, venous thrombosis was detected in the left transverse sinus (Figure 5). In light of these findings, the patient was admitted to the Neurology inpatient unit with a diagnosis

of OAS. He received pulse prednisolone treatment (500 mg/day), anticoagulant therapy (warfarin), and fixed combination dorzolamide/timolol (2 times daily) and brimonidine drops (2 times daily) to mitigate the retinal and choroidal hypoperfusion. After 5 days of pulse prednisolone therapy, the patient continued to receive oral prednisolone (100 mg/day) and maintenance dose of valacyclovir (1000 mg/day). Two months after the OAS diagnosis, the patient's BCVA in the right eye improved to 0.4, and the ptosis and extraocular muscle paralysis regressed (Figure 6). Fundoscopic examination at 2 months showed that the pallor persisted in the temporal aspect of the optic disc, but



Figure 1. Total ptosis and ophthalmoplegia of the patient's right eye



Figure 2. Right eye movements were restricted in all 9 positions of gaze

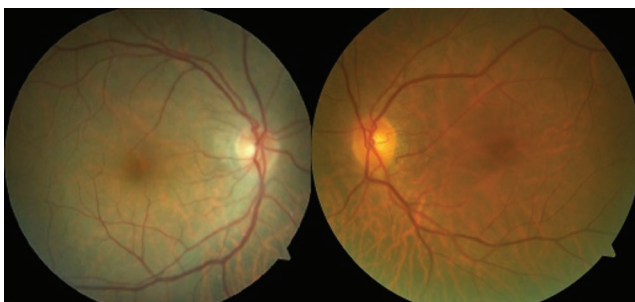


Figure 3. Fundus images of the right and left eyes: retinal pallor was observed in the right eye due to choroidal ischemia

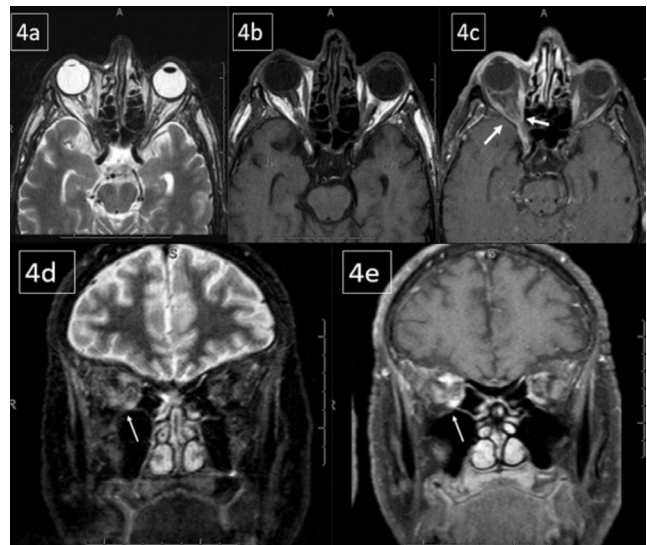


Figure 4. Orbital magnetic resonance imaging: The right orbital apex appeared overcrowded on axial T2-weighted (a), precontrast axial (b) and postcontrast (c) T1-weighted, coronal fat-suppressed T2-weighted (d), and postcontrast coronal fat-suppressed T1-weighted (e) images, and was especially pronounced in the postcontrast fat-suppressed axial and coronal T1-weighted sections (c and e). This appearance was caused by edematous thickening of the optic nerve sheath, contrast enhancement, and streaking in the fatty tissue

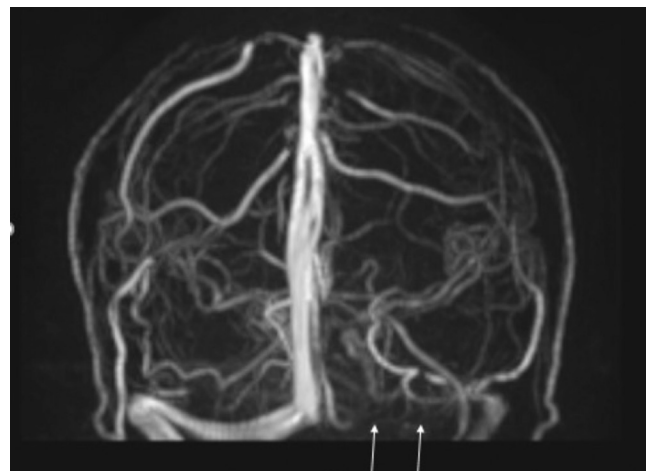


Figure 5. Brain magnetic resonance venography: no flow was observed in left transverse sinus (arrows)

had diminished in the retinal tissue (Figure 7). The patient's right eye regained light reflex, although mild mydriasis was observed. The right eye still showed relative afferent pupillary defect. BCVA remained at 0.4, likely due to optic neuropathy. Follow-up MRI at 3 months demonstrated recanalization of the left transverse sinus and regression of the right orbital apex



Figure 6. Ptosis regressed and extraocular muscle paralysis fully resolved after 2 months

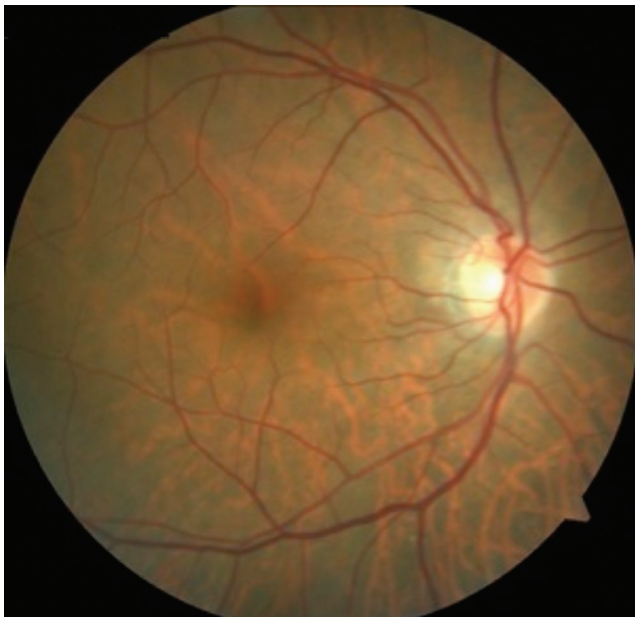


Figure 7. Fundus image of the patient at 2 months: retinal pallor was improved but persisted in the temporal aspect of the optic disc

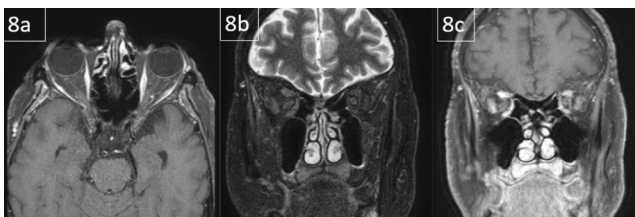


Figure 8. Magnetic resonance imaging at 3-month follow-up: Inflammation in the right orbital apex was attenuated in the axial fat-suppressed poststrate T1-weighted (a), coronal fat-suppressed T2-weighted (b), and postcontrast coronal fat-suppressed T2-weighted sections (c). The overcrowded appearance was resolved and the optic nerve and surrounding structures could be clearly distinguished

inflammation. The optic nerve and surrounding structures were clearly discernible (Figures 8a-c). Anticoagulant therapy was discontinued at 3 months and oral steroid therapy was tapered and discontinued at 4 months.

Discussion

Herpes zoster infection affects the sensory nerves of the thoracic dermatomes most often, followed by the cranial nerves.^{3,4,5} The incidence and severity of the disease increase substantially after age 60.^{6,7} HZO is seen in 10-15% of herpes zoster infections. The most common ocular complications of HZO include blepharoconjunctivitis, keratitis, and uveitis. Neurological complications such as ophthalmoplegia or optic neuritis are rare and known to respond to antiviral or steroid treatment. The prevalence of ophthalmoplegia was reported as 3.5-10.1% in the two large HZO case series in the literature.^{8,9} The most frequently involved cranial nerve is the oculomotor nerve, followed by abducens nerve.^{10,11}

OAS is characterized by paralysis of cranial nerves II, III, IV, and VI and the ophthalmic branch of the cranial nerve V, caused by inflammatory, infectious, neoplastic, traumatic, vascular, and sometimes iatrogenic causes along the ophthalmic canal.¹² The most common infectious causes of OAS are mucormycosis and aspergillosis. These should be considered in patients with predisposing conditions such as diabetes mellitus, alcoholism, hematological malignancy and immunosuppression. Primary infection occurs in the paranasal sinuses with invasion of the orbital space.¹³ The diagnosis of these infections is relatively straightforward due to the clinical findings, host factors, and radiological findings. Reactivation of latent VZV infection is an uncommon cause of OAS. There are a total of about 20 case reports describing the development of OAS due to HZO in the ophthalmic literature.^{7,14,15,16,17}

As in our case, the patients in previously reported HZO-related OAS cases were usually over 60 years of age.^{7,18,19,20,21} The youngest documented patient was a 29-year-old woman who had severe, undiagnosed acquired immunodeficiency syndrome (AIDS).¹⁴ Young patients presenting with HZO and associated complications should raise suspicion of human immunodeficiency virus (HIV)/AIDS and should be tested accordingly.

In addition to the peripheral nervous system, HZO can also manifest with central nervous system involvement. Xiao et al.²² observed lesions in the occipital lobe, cerebellum, and dura mater on MRI examination in a case of HZO-related OAS and meningoencephalitis. An interesting aspect of our case was the presence of thrombosis in the cranial venous system, which has not been previously described in association with OAS. MRI performed due to clinical suspicion allowed us to establish a diagnosis before the development of papillary stasis and to initiate anticoagulation therapy early.

The treatment regimen for OAS secondary to herpes zoster includes 4000 mg/day acyclovir (800 mg, 5 times daily) or 3000

mg/day valacyclovir (1000 mg, 3 times daily) and systemic steroids.^{2,23} The clinical course of the disease depends on how rapidly treatment is initiated. Beginning treatment within the first 72 hours is recommended.²⁴

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. Rates of complete recovery from ophthalmoplegia and optic neuropathy have been reported as 76.5% and 75%, respectively.² In our case, ophthalmoplegia resolved in 2 months without sequelae. However, visual acuity remained at 0.4 due to optic neuropathy.

The pathological mechanisms of ophthalmoplegia in cases of HZO have not been clearly determined. Histopathological studies have shown perivascular and perineural inflammation in various ocular tissues, including the optic nerve, cavernous sinus, superior orbital fissure, and retina.²⁵ Extraocular muscle involvement may be caused by the cytopathic effect of the virus in neural tissues, occlusive vasculitis occurring as a direct result of inflammation, or host immune response to the viral infection.²⁶ Using cadaver eyes affected by HZO, Naumann et al.²⁷ demonstrated that infiltrative cells reached the orbital apex along the long posterior ciliary vessels and nerves, and that neuropathy was caused by vascular occlusion. In our case, thrombosis of the left transverse sinus is believed to have resulted from virus-related vasculitis.

AS is a rare but serious complication of HZO. Therefore, patients with a history of HZO should be evaluated for optic nerve, extraocular muscle, and eyelid function at every follow-up examination. MRI and MR venography are useful imaging techniques for the characterization of occlusive vasculitic lesions.

Ethics

Informed Consent: It was taken.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Canan Aslı Utine, **Concept:** Gamze Kocaoğlu, Canan Aslı Utine, Aylin Yaman, Süleyman Men, **Design:** Gamze Kocaoğlu, Canan Aslı Utine, Aylin Yaman, Süleyman Men, **Data Collection or Processing:** Gamze Kocaoğlu, Canan Aslı Utine, Aylin Yaman, Süleyman Men, **Analysis or Interpretation:** Gamze Kocaoğlu, Canan Aslı Utine, Aylin Yaman, Süleyman Men, **Literature Search:** Gamze Kocaoğlu, Canan Aslı Utine, **Writing:** Gamze Kocaoğlu, Canan Aslı Utine, Aylin Yaman, Süleyman Men.

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