CASE REPORT

Orbital apex syndrome as a complication of herpes zoster ophthalmicus

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SUMMARY

Orbital apex syndrome is a rare neuro-ophthalmic manifestation of herpes zoster virus infection. We report one such case with favourable outcome in an immunocompetent patient. A 60-year-old woman presented with rash in the dermatome of the left ophthalmic nerve (V1), followed by sudden loss of vision with complete left-sided external and internal ophthalmoplegia. MRI of brain and orbits with contrast revealed optic perineuritis and myositis without intracranial involvement confirming the diagnosis of orbital apex syndrome. Functional visual recovery was achieved after a course of intravenous and oral steroids under antiviral cover over a follow-up period of 3 months.

BACKGROUND

Ocular manifestations are observed in 20–70% of patients with herpes zoster ophthalmicus (HZO), with involvement of any ocular structure.¹ The neuro-ophthalmic complications include involvement of other cranial nerves such as the optic nerve, nerves of ocular motility or facial nerve, and these may occur in combination. Nerve palsies are reported in 5–31% of HZO cases although complete ophthalmoplegia is rare.^{2–3}

Optic neuritis can present as papillitis, retrobulbar neuritis or optic nerve infarcts.⁴ Orbital apex syndrome in HZO is a known but rare entity and is reported in only a handful of cases worldwide.^{5–8} Orbital apex syndrome refers to

involvement of the oculomotor nerve, ophthalmic branch of trigeminal nerve, abducens nerve, trochlear nerve along with optic nerve dysfunction. It is sight threatening if not detected and treated in the early stages. Various treatment modalities have been described; however, there is no standardised regimen although most cases respond to a combination of systemic steroids and antiviral medications.

CASE PRESENTATION

A 60-year-old woman presented with a 2-week history of painful rash involving the left side of face and forehead, and a 1-day history of suddenly reduced vision in the left eye with complete left ptosis and limited eye movements. She was on regular medication for diabetes mellitus and hypertension since 6 years. She had no history of underlying malignancies, usage of immunosuppressive medication or recent trauma.

Her visual acuity was 20/25, 6/6 in the right eye and hand movements in the left eye. The colour vision was normal in the right eye. Clinical examination revealed multiple crusted and few pustular lesions distributed in the left V1 dermatome with impaired facial sensation and positive Hutchinson's sign (rash involving the tip of her nose). There was complete ptosis and complete limitation of all ocular movements including intorsion with mild proptosis of left eye (figure 1). The left corneal sensations were reduced and a clinical picture of keratouveitis was seen (figure 2). The left pupil was

Figure 1 At presentation, the nine gaze photograph shows complete ophthalmoplegia of the left eye.

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Figure 2 Clinical picture of left eye showing keratouveitis with crusted lesions at the lid margin and medial canthus.

fixed and dilated with a left relative afferent pupillary defect. During the course of the disease the intraocular pressure fluctuated from normal to low in the left eye due to the coexistent uveitis. The posterior segment could not be visualised due to corneal epitheliopathy and anterior chamber reaction. Ultrasound B scan in the left eye was normal. The right eye was unremarkable.

INVESTIGATIONS

MRI of brain and orbits with gadolinium contrast revealed enhancement of the optic nerve and perineural sheath, extraocular muscles and soft tissues causing crowding at the orbital apex with sparing of the cavernous sinus and meninges suggestive of optic perineuritis and myositis (figures 3 and 4). Systemic investigations including complete blood picture, erythrocyte sedimentation rate, blood sugar, HIV, Mantoux test and chest X-ray were within normal limits and thus ruled out any immunosuppression. Cerebrospinal fluid analysis was normal except for mild lymphocytosis.

DIFFERENTIAL DIAGNOSIS

1. Orbital apex syndrome due to fungal pathology could be ruled out as there was no associated paranasal sinus pathology which acts as the primary source of inflammation especially in diabetic patients.

Figure 3 T1-weighted MRI brain and orbits with gadolinium contrast, axial sections showing enhancement of the left optic nerve and perineural sheath, extraocular muscles and soft tissues causing crowding at the orbital apex.

Figure 4 T1-weighted MRI orbits with gadolinium contrast, coronal sections showing significant increase in size of the left eye extraocular muscles along with enhancement.

2. Granulomatous inflammation due to tuberculosis which is endemic in our country could be ruled out from the classical clinical presentation of zoster infection and negative systemic investigations

TREATMENT

The patient was administered six doses of intravenous methyl prednisolone (IVMP), 500 mg twice daily for 3 days under the supervision of an intensivist followed by tapering doses of oral prednisolone for a period of 4 weeks, along with oral acyclovir 800 mg five times/day, calcium supplements and antacids. Anterior segment inflammation was treated with prednisolone 1% eye drops initiated four hourly and tapered over 3 months, based on the response. Topical homatropine 2% eye drops were given for 6 weeks. Lubricants were used throughout the course of treatment as the patient had signs of punctate keratopathy. She also received oral pregabalin to relieve symptoms of post-herpetic neuralgia for 1 month duration.

OUTCOME AND FOLLOW-UP

Left eye visual acuity recovered from counting fingers after IVMP to 6/12 at 3 months. At 3 months the rash had resolved with minimal scarring. There was mild residual ptosis, ocular motility showed marked recovery with residual –1 limitation of adduction, elevation and depression (figure 5). Keratouveitis resolved with few dispersed pigments over the endothelium and anterior lens surface, sectoral iris atrophy and few posterior synechiae. There was optic disc pallor and RAPD. The Humphrey visual field (30–2 SITA standard) test was normal in the right eye and showed generalised depression in the left eye.

DISCUSSION

Neuro-ophthalmic complications of HZO usually manifest in the initial 2 weeks following the onset of rash.⁷ Various pathological mechanisms have been described for the neurological complications. Varicella-zoster virus reactivation in the trigeminal ganglion causes the virus to spread along the ophthalmic branch of the trigeminal nerve to the orbit via the cavernous sinus, superior orbital fissure areas. Virus replication on the surrounding tissues can lead to direct injury or immune

complex mediated response causing perineuritis, demyelination, contiguous orbital inflammation and cerebral vasculitis.^{9 10} Lymphocytic infiltration occurs along the posterior ciliary vessels and nerves causing occlusive vasculitis and ischaemic injury.¹¹ An alternative mechanism of injury can be caused by

Figure 5 At 3-month review, left eye ocular motility showing marked recovery with residual –1 limitation of adduction, elevation, depression and mild residual ptosis.

lymphocytic infiltration of the orbital nerves via sensory offshoots of trigeminal nerve to the motor cranial nerves.¹² Orbital soft tissue oedema can also contribute to direct compressive effects on the surrounding cranial nerves.¹³ Age and diabetes are possible triggers for reactivation of herpes virus in our case. Aseptic meningitis has been reported in 88% of cases.⁵ However, there were no meningeal signs in our patient.

Although no standard guidelines exist for the treatment of orbital apex syndrome due to zoster infection, combination regimens of systemic antiviral medication with oral or intravenous steroids with good response have been reported by various authors.^{5–8} Options for antivirals in immunocompetent patients include acyclovir, valacyclovir and famciclovir. Antivirals reduce viral shedding, halt new vesicle formation and prevents long-term recurrence of HZO and work best when administered within 72 hours of onset of rash.¹⁴ Acyclovir in an oral dose of 800 mg five times per day for 2 weeks or intravenous dose of 10 mg/kg administered eight hourly has been the drug of choice.¹⁵ Intravenous acyclovir is recommended in cases with retinitis, meningoencephalitis and myelitis.¹⁴ Systemic steroids in the form of intravenous methyl prednisolone or oral steroids to counter the orbital inflammation are concomitantly used. Immune status of the patient and systemic contraindications should be considered before starting systemic steroids. Oral steroids for management of orbital apex inflammation was recommended by Dworkin *et al.*¹⁴ However, our patient was immunocompetent and had significant optic nerve dysfunction at presentation with prominent orbital apex crowding causing additional compressive effect without meningeal signs. We chose to treat the patient initially with intravenous methyl prednisolone followed by oral steroids under oral antiviral cover to achieve a more rapid recovery of the optic nerve and orbital inflammation.

Sanjay *et al.*⁸ reported an average time to visual recovery of 4 months with 75% recovery in ophthalmoplegia and optic neuritis. Thus a prompt diagnosis and early intervention results in good outcome in these cases.

Learning points

- ▶ Orbital apex syndrome is a rare neuro-ophthalmic manifestation of herpes zoster ophthalmicus.
- ▶ Comprehensive ocular evaluation for any signs of ophthalmoplegia and optic neuritis in early phase of the disease helps identify this presentation.
- ▶ Contrast-enhanced MRI identifies the areas of inflammation in the form of perineuritis, myositis and soft tissue enhancement, also identifies cavernous and meningeal involvement and aids in differential diagnosis.
- ▶ A good clinical history and systemic workup to rule out underlying immunocompromised status and secondary neurological complications is mandatory and helps decide the appropriate treatment regimen.
- ▶ Good functional visual recovery can be achieved by timely intervention with systemic steroids and antiviral medications.

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Competing interests None declared.

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