More than meets the eye: Varicella zoster virus-related orbital apex syndrome

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A 67-year-old male patient with poorly controlled type-2 diabetes mellitus developed an orbital apex syndrome and anterior cavernous syndrome secondary to herpetic zoster ophthalmicus (HZO), despite being on oral acyclovir. Urgent treatment with intravenous acyclovir led to improvement of the orbital and ocular inflammation but had no effect on the complete ophthalmoplegia and profound visual loss. At the 9-month follow-up visit, the patient had complete unilateral ophthalmoplegia and monocular blindness due to optic atrophy.

Key words: Optic neuritis, orbital apex syndrome, varicella zoster virus

Orbital and central nervous system involvement secondary to herpes zoster ophthalmicus (HZO) is a rare event.[1] In a recent review of cases of orbital apex syndrome (OAS) secondary to varicella zoster virus (VZV), the authors found only 15 such cases over 5 decades (1966–2015).[2] We present a case of unilateral OAS and anterior cavernous syndrome (ACS) secondary to VZV leading to complete irreversible blindness.

Case Report

A 67-year-old Chinese man with past medical history of poorly controlled hypertension, type-2 diabetes mellitus, hyperlipidemia and ischemic heart disease presented to the emergency department with a recent history of vesicles over the right side of forehead, tip of the nose and mild congestion of the right eye. Ocular examination was within normal limits other than mild right eye conjunctival congestion. His best-corrected vision was 6/6 in both eyes and the patient had no corneal involvement. He was diagnosed with right HZO associated with Hutchinson sign. He was prescribed topical 3% acyclovir ointment and 800 mg oral acyclovir 5 times/day.

The patient experienced decrease in vision and a droopy right eyelid the next day. He presented again to the emergency department 2 days later. The ophthalmic examination revealed complete ptosis in the right eye and severe visual loss, to "no perception of light" (NPL). Associated with right periorbital edema, chemosis, proptosis (3 mm) and complete limitation of all extraocular movements, including intorsion. The right pupil was dilated (7 mm), unreactive to light and was associated with reverse relative afferent pupillary defect. He also had anterior iritis and increased intraocular pressure (IOP) of 36 mm Hg. Retinal evaluation was normal and optic disc appeared normal. Sensation in the territory of ophthalmic division of right trigeminal nerve was reduced. He was diagnosed with right OAS. Left eye and the remaining neurological examinations were normal.

He was started on intravenous 800 mg acyclovir 8th hourly, 1.2 g co-amoxiclav 8th hourly, oral acetazolamide 250 mg 6th hourly and topical medications including timolol, brimonidine and prednisolone eye drops to control IOP and iritis. Magnetic resonance imaging of the brain and orbits revealed enhancement of the right optic nerve sheath [Fig. 1], fat stranding, mildly swollen recti muscles [Fig. 2], prominent superior ophthalmic vein, crowding at the orbital apex [Fig. 3] and mild enhancement of the ipsilateral cavernous sinus. The left orbit and brain appeared normal. He was diagnosed with OAS and ACS.

Cerebrospinal fluid analysis showed leukocytes >200/µl mostly lymphocytic, high total protein 1.10 g/l (normal <0.4 g/l) and was positive for VZV DNA by polymerase chain reaction. He was noted to have uncontrolled diabetes mellitus with HbA1c 9.8%. Septic work-up was negative.

Periorbital swelling, anterior uveitis and IOP improved over the next few days; however, vision remained unchanged and there was no improvement in ocular motility. The patient was treated with intravenous acyclovir 800 mg 8 hourly for 22 days and amoxicillin/clavulanic acid 1.2 g 8 hourly for 20 days. Subsequently, oral valacyclovir 1 g 8 hourly was prescribed for next 4 weeks. A treatment with systemic steroids was not initiated, due to the increased risk of complications and worsening of the systemic co-morbidities.

At the last follow-up, nine months later IOP was normal and anterior uveitis had subsided. However, the patient continued to have complete total ophthalmoplegia [Fig. 4], and no perception of light due to marked ipsilateral optic atrophy.

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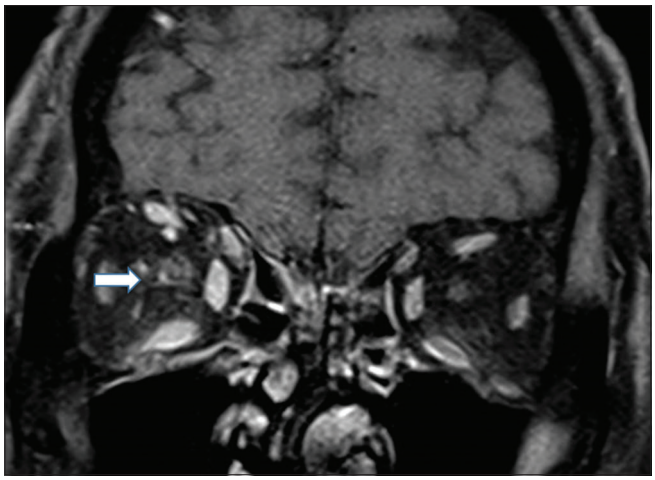

Figure 1: Fat-suppressed and contrast-enhanced magnetic resonance imaging showing right peri-optic nerve sheath enhancement

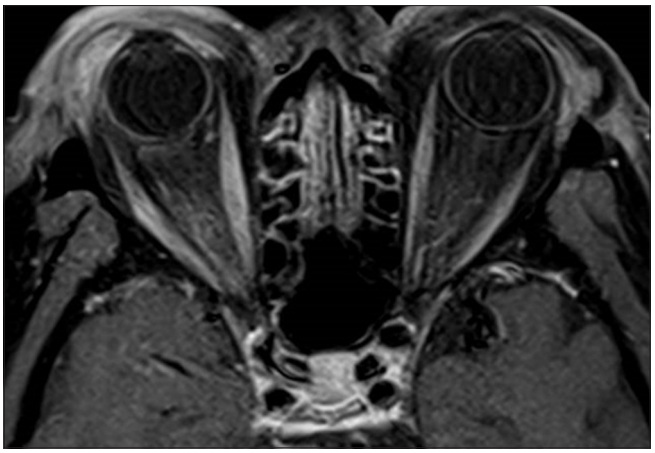

Figure 2: Orbital magnetic resonance imaging, T1-weighted axial sequences with fat-suppression showing enlarged enhancing extraocular muscles on the right side

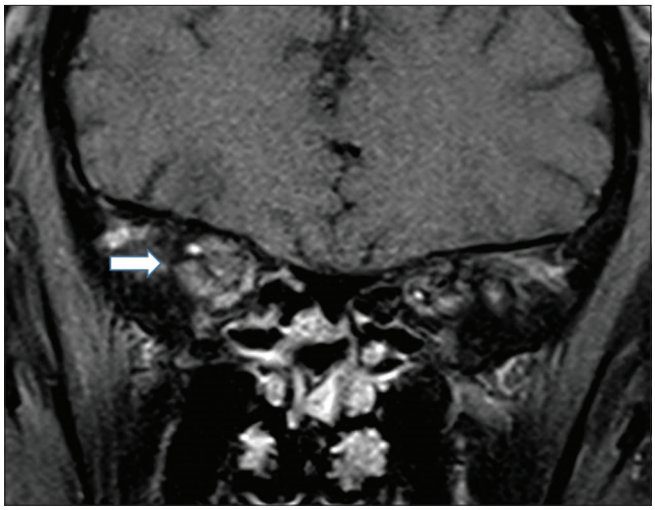

Figure 3: Magnetic resonance imaging, disclosing a crowded right orbital apex

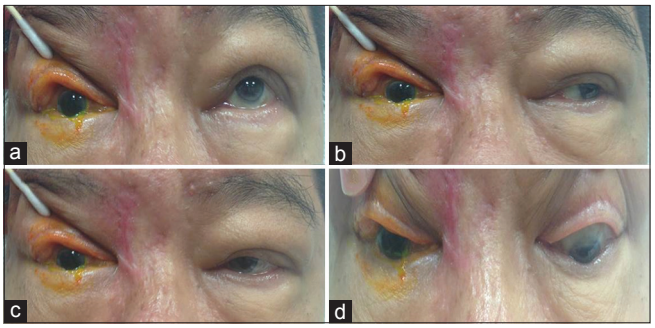

Figure 4: Ophthalmoplegia affecting the right eye, 3 months after the initial presentation. Pupillary dilation and poor reactivity to light in the right eye was associated with limitation of (a) elevation (b) adduction (c) abduction and (d) infraduction

Discussion

Neurologic manifestations are present in 5%–10% of HZO patients.[2] The most common neurologic manifestations include cerebellar ataxia, meningoencephalitis, post-herpetic neuralgia, cranial nerve palsies.[2] OAS secondary to HZO is very rare and only a handful of reports are present in the English literature.[3] OAS, defined as variable degree of involvement of oculomotor, trochlear, abducens, ophthalmic division of trigeminal cranial nerves and of the optic nerve is a rare HZV complication. In a recent review of cases of OAS secondary to HZO, authors found only 15 such cases over 5 decades (1966–2015). Among those, only three patients developed OAS after instituting oral acyclovir, as seen in our case.[2]

Many pathogenic mechanisms have been incriminated in the causation of VZV-related OAS. These include direct viral cytopathic effect,[4] reactive immune-related response,[4] microinfarction secondary to vascular inflammation[5] or direct compression due to the soft tissue swelling and inflammation at the orbital apex.[6] Multiple concurrent pathologic mechanisms including ischemia leading to microinfarction might have been responsible for such manifestations with almost no recovery like in our case. Interestingly, almost 90% of the patients with VZV-related ophthalmoplegia disclose evidence of aseptic meningitis, as seen with our patient.[1]

The role of systemic steroids remains undetermined in VZV-related OAS. There are conflicting reports, ranging from near complete recovery to almost no recovery in patients receiving systemic steroids.[3] On the other hand, there are also reports of spontaneous OAS remission without using systemic steroids.[7] Our multidisciplinary approach took into consideration the combined lack of evidence for the use of steroids in this setting and the specific risks related to co-morbidities in this patient, opting for no such treatment.

HZO is known to occur more frequently in patients with immunosuppression.[8] Despite a few anecdotal reports,[1,3,6,9] it has not been proven conclusively that OAS secondary to HZO occurs more commonly in immune deficient patients. It has been suggested that early treatment with antivirals has a better outcome.[9] Our patient presented 2 days after experiencing visual loss and ptosis. Earlier institution of intravenous acyclovir might have improved the prognosis.

Conclusion

The concurrent occurrence of OAS and ACS syndrome secondary to HZO is rare event, but potentially leading to complete ophthalmoplegia and blindness.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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