Herpes zoster ophthalmicus. Part 2: some complications of a common disease

MEDDUMA B. KAPPAGODA
MB BS, DO, FRCS(Ed), FRACS, FRACO, FRCOphth

Part 2 of this article discusses the nature of complications in herpes zoster ophthalmicus, which can be some of the most debilitating aspects of the disease.

The incidence of herpes zoster ophthalmicus in the general population is about 1 in 1000. The typical presentation is a vesicular rash in the dermal distribution of the ophthalmic division of the trigeminal nerve (see Figure 1). Complicated disease occurs in over 50% of cases, with the risk increased in elderly and immunocompromised patients.

Part 2 of this article discusses ocular and neurological complications of herpes zoster ophthalmicus, and complements the discussion about diagnosis and management of uncomplicated disease that was presented last month.

Neurological complications

The best known complication of herpes zoster ophthalmicus is postherpetic neuralgia. However, a range of other problems can be seen.

Postherpetic neuralgia

The most common complication of herpes zoster is postherpetic neuralgia, which is defined as pain lasting for more than three months. Prevalence, severity and duration of postherpetic neuralgia are increased in elderly patients. On account of its chronic nature, patients may develop anorexia, insomnia, mood changes or depression.

Postherpetic neuralgia remains a difficult therapeutic problem. Early treatment of ophthalmic zoster with high dose antiviral therapy is effective in preventing many complications but is unlikely to help prevent postherpetic neuralgia. Low dose amitriptyline (Endep, Tryptanol 25 mg daily) may be useful for preventing and treating postherpetic neuralgia and associated affective disorders.

CNS inflammation and infection

There are indications that subclinical extension of viral inflammation into the central nervous system occurs commonly in ophthalmic zoster. Rarely, infection of the central nervous system may occur, with myelitis or meningoencephalitis resulting.

Cranial nerve palsies

Ocularmotor and facial nerve palsies (of the third, fourth, sixth and seventh cranial nerves) have been reported as late complications of herpes zoster ophthalmicus (see Figures 2a and b). Extraocular motor pareses may occur several days after the onset of the rash. Although the incidence of ocular muscle paresis in herpes zoster ophthalmicus is not insignificant (31%), many patients may not experience diplopia except in the extremes of gaze and therefore they may remain asymptomatic.

Ocularmotor paralysis is most commonly due to third cranial nerve palsy (see Figure 2a). Ocularmotor nerve palsies are often associated with severe rash and the later occurrence of severe neuralgia

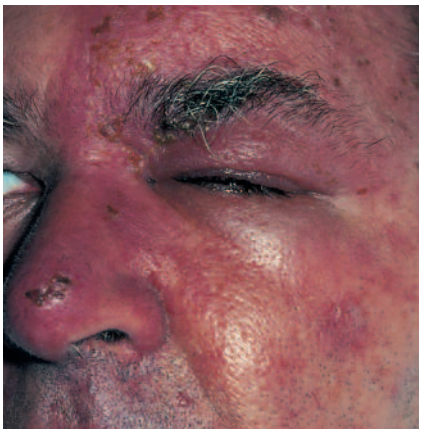
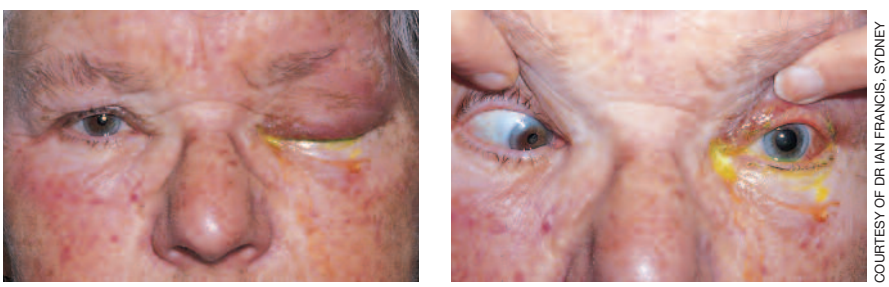


Figure 1. A patient with the typical rash of herpes zoster ophthalmicus. The vesicles on the tip of the nose indicate nasociliary involvement and that ocular complications are likely to occur.



COURTESY OF DR IAN FRANCIS, SYDNEY

Figures 2a and b. A patient with neurological complications following herpes zoster ophthalmicus. a (left). A third cranial nerve palsy prevents the patient from raising the upper lid of the left eye. b (right). When the eyelid is lifted and the patient is asked to look left, the left eye does not move past the midline, indicating a sixth nerve palsy.

Dr Kappagoda is former Head of the Department of Ophthalmology, Concord Hospital, Concord, NSW.

and iris inflammation. Nerve palsies are most likely to be secondary to occlusive vasculitis induced by the virus.

Retrobulbar optic neuritis is discussed in the section 'Complications in immuno - compromised patients' on this page.

Delayed contralateral hemiplegia

Postherpetic hemiparesis syndrome is an unusual but distinct clinical entity caused by arteritis induced by herpes zoster virus, with subsequent cerebral infarction confined to the ipsilateral cerebrum. The stroke syndromes are largely in the territory of the middle and anterior cerebral arteries and may manifest as a transient ischaemic attack, infarction or a stroke in evolution. Subclinical cerebral vasculitis in herpes zoster may be a common occurrence.

Elderly patients are prone to both herpes zoster and stroke, as well as giant cell arteritis. Therefore, cerebral granulomatous arteritis may be underdiagnosed in elderly patients and its pathogenesis may remain obscure.

CNS disease

CSF changes of pleocytosis and elevated proteins have been observed even in immunocompetent patients without clinical symptoms of CNS involvement. Viral spread following herpes zoster ophthalmicus may affect the meninges, brain and spinal cord. CNS disease may take the form of meningoencephalitis or myelitis. Zoster-associated CNS disease appears to occur almost exclusively in patients with AIDS.

Ocular complications

Ocular complications do not become apparent until several days after the initial rash. They may be seen in approximately 50% of patients with ophthalmic zoster and could be more common in patients with involvement of the nasociliary nerve.

Chronic infectious epithelial keratitis, retrobulbar optic neuritis, retinitis and progressive outer retinal necrosis as well as complicating neurological disease are all difficult to manage. Such ocular complications invariably lead to blindness, even with aggressive antiviral treatment.

Eyelid complications

Eyelid vesicles may lead to ulceration and pitting. Any scarring of dermal tissues may result in permanent lid retraction and distortion of lid margins, as well as damage to the roots of eyelashes and the meibomian glands.

Conjunctival complications

Conjunctival involvement is minor in ocular complications of ophthalmic zoster. Vesicles, hyperaemia and follicular reaction may result.

Corneal disease

Corneal manifestations from herpes zoster ophthalmicus are diverse and include vesicles, punctate epithelial keratitis and dendrites. Late corneal complications may result from a dry eye, lack of sensation or lid margin anomalies.

The characteristic corneal lesions are subepithelial nummular opacities that last for a long time. Often epithelial vesicles rupture, leaving shallow areas of ulceration with crenated edges that heal rapidly. Occasionally, ulceration becomes trophic and slow to heal, resulting in neurotropic damage to the cornea.

Central and paracentral corneal ulcers may form which result in perforation, and corneal oedema can lead to stromal vascularisation. These complications may eventually lead to visual loss. Cell mediated immunity plays a key role in stromal keratitis and the delayed uveitis (Figure 3).

The dendritic keratitis lesion of zoster appears during the acute phase of the cutaneous eruption, and it is possible for herpes simplex dendritic keratitis to coexist ('combined zoster simplex'). Zosteric corneal disease fares well with topical corticosteroids; however, therapy enhances replication of the herpes simplex virus. Diagnosis and treatment of dendritic keratitis in herpes zoster ophthalmicus should be judicious.

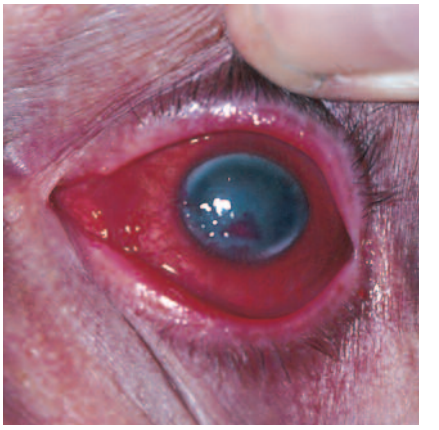


Figure 3. Keratouveitis following herpes zoster ophthalmicus.

Retinal disease

Retinal vascular occlusions and ischaemic optic neuropathy may follow herpes zoster ophthalmicus. Focal and segmental retinal vascular lesions similar to those that occur in meningeal and cerebral vessels following herpes zoster have been described.

Acute retinal necrosis is most often reported in association with herpes zoster. The retina is susceptible to opportunistic infections; acute retinal necrosis is sometimes associated with the other herpetic infections, such as herpes simplex and cytomegalovirus. Acute retinal necrosis demands aggressive treatment with intravenous antiviral drugs but often leads to retinal detachment.

Complications in immunocompromised patients

In immunocompromised patients, the risks for dissemination, visceral complications and postherpetic neuralgia are higher. Patients with HIV infection who have ophthalmic zoster are more likely to develop painful, sight-threatening complications – bacterial superinfection, ocular complications and postherpetic

neuralgia are all more likely.

In HIV-seropositive individuals, ophthalmic zoster is a common manifestation of varicella zoster virus reactivation, with increased incidence and a younger age of onset. HIV infection changes the nature and severity of herpes zoster disease – a different clinical pattern may be seen, with risk of dissemination. The ocular complications are also changed – in AIDS, retrobulbar optic neuritis may develop with sudden blindness several weeks after the cutaneous rash of zoster. Retrobulbar neuritis after an episode of cutaneous herpes zoster eruption may herald acute retinal necrosis.

Progressive outer retinal necrosis syndrome is a distinct form of necrotising herpetic retinopathy which is seen in the patient with HIV and is rapidly progressive. The most common presenting symptom is sudden loss of vision in one eye; headache and periocular pain often precede the visual loss. Ophthalmoscopic features distinguish it from the other necrotising herpetic retinopathies – the retinal lesions consist of multifocal deep opacities scattered through the periphery and the lesions progress to confluence. Treatment does not alter the final poor visual outcome.

Treatment

Antiviral therapy

If given at the very onset of the disease, aciclovir (Acihexal, Acyclo-V, Lovir, Zovirax Tablets) reduces the incidence and severity of secondary ocular inflammatory disease; valaciclovir (Valtrex), a prodrug that is converted to aciclovir in vivo, and famciclovir (Famvir), are also available. In particular, severe long term complications are significantly reduced. Treatment prevents delayed secondary vasculitis as well as the direct and delayed effects of the virus on nerve tissue. The most significant effect is achieved when treatment is given within 72 hours of the onset of the symptoms. However, antiviral therapy is unlikely to help prevent postherpetic neuralgia.

Treatment with intravenous aciclovir (Aciclovir Intravenous Infusion, Acihexal Intravenous Infusion, Zovirax Infusion) in hospital is necessary for patients with disseminated disease, visceral complications, systemic complications or acute retinal necrosis syndrome. In immunosuppressed patients, the risks of visceral complications, disseminated disease, and postherpetic neuralgia are higher – hospitalisation is necessary for these patients.

Corticosteroids

Systemic steroid therapy (which was discussed in Part 1 of this article) has no

effect on the incidence or severity of postherpetic neuralgia and does not modify the pain in the acute phase. The risk of systemic steroids in the zoster patient is now well recognised, and such therapy for herpes zoster ophthalmicus has therefore been abandoned. However, topical corticosteroids may be used later to treat delayed immunological and inflammatory epiphenomena.

Ophthalmological referral

All patients with ocular complications from ophthalmic zoster need referral to an ophthalmologist. Patients who have symptoms of ocular pain or visual loss demand urgent attention. Early recognition and treatment of surface ocular disease may prevent the serious sequelae of corneal ulceration and opacification or secondary glaucoma from uveitis. Vesicles on the side and tip of the nose indicate that the nasociliary branch of the ophthalmic nerve is involved and that ocular complications are likely to occur.

Untreated intraocular inflammation invariably leads to sight threatening sequelae. Underlying disease may be signified by adjacent zoster rash in the maxillary or mandibular distribution of the trigeminal nerve, a severe necrotic rash (particularly in a young patient) or recurrent ophthalmic zoster – further investigation is then necessary.

Summary

- Pain is a prominent symptom in the acute phase of herpes zoster ophthalmicus. The patient may also experience debilitating postherpetic neuralgia.
- Ocular complications may occur in the acute phase or be delayed. Sudden loss of vision, particularly in a young patient, may be due to retrobulbar neuritis or necrotising retinitis and signify underlying disease. Similarly, severe necrotic multidermatomal disease needs investigation.
- Neurological disease accompanying ophthalmic zoster, progressive outer retinal necrosis syndrome as well as chronic infectious pseudodendritic keratitis are all difficult to manage. Early treatment with high dose aciclovir reduces the duration and modifies the pain of the acute phase and is effective in preventing many complications of ophthalmic zoster. MT

Last month, Part 1 of this article revisited the presentations, investigations and treatment of uncomplicated herpes zoster ophthalmicus.