

Managing ophthalmic herpes zoster in primary care

Wim Opstelten, Michel J W Zaal

During their professional career, most general practitioners will be consulted by various patients with an acute manifestation of ophthalmic herpes zoster. In addition to the diagnostic dilemma that doctors face in the initial phase of the disease, they may be uncertain about the course and treatment (when is referral indicated, who should be prescribed antiviral medication?). We present an evidence based policy.

Herpes zoster (shingles) is a commonly encountered disorder in general practice. One fifth of the population, mainly elderly people, will present with this neurocutaneous infection during their lifetime. Most immunocompetent patients will experience spontaneous and complete recovery within a few weeks. Some, however, will develop complications such as postherpetic neuralgia and, in cases of ophthalmic herpes zoster, sight threatening eye problems. We outline the main points that general practitioners should keep in mind when faced with a case of ophthalmic herpes zoster.

Methods

In February 2005, we searched the Cochrane Controlled Trial Register (keyword: "herpes zoster"), Embase, and Medline (MESH terms: "herpes zoster" and "therapy") for clinical trials, randomised controlled trials, meta-analyses, practice guidelines, and reviews. We selected only articles written in English and disregarded any studies of immunocompromised patients.

Incidence and pathophysiology of herpes zoster

Herpes zoster is a commonly seen disorder; one fifth of the population will present with the disease during their lifetime. The reported incidence varies from 2.2 per 1000 to 3.4/1000 people per year. Herpes zoster develops mainly in elderly people: its incidence in people aged over 80 is about 10 in 1000/year.^{1,2} It is caused by reactivation of the varicella zoster virus (human herpes virus type 3). In temperate climates, primary infection with this virus usually occurs before the age of 10 and manifests itself clinically as chickenpox (varicella). The virus then becomes latent, nestling in the sensory ganglia. Later it may become active again, spread to the corresponding dermatome by means of a spinal or cerebral nerve (usually the trigeminal nerve), and generate the characteristic unilateral vesicular exanthema. The accompanying

Summary points

One out of every 100 individuals will contract herpes zoster ophthalmicus during his or her lifetime

The risk of ocular complications in ophthalmic herpes zoster is not related to age or severity of the skin rash

Doctors should be alert for sight threatening eye complications if skin lesions are located in the dermatome of the nasociliary nerve. This area includes not only the tip of the nose, but also involves the skin at the inner corner of the eye, and the root and side of the nose (Hutchinson's sign)

All patients with ophthalmic zoster, irrespective of age or severity of symptoms, should be prescribed oral antiviral drugs at the first sign of disease. Moreover, they should be re-examined after at most one week

Hutchinson's sign in the early phase of ophthalmic zoster, visual complaints, or a red eye are indications for referral to an ophthalmologist

Because ophthalmic zoster can cause late complications, the disorder must be included in a patient's medical file

inflammation of the sensory nerve and skin damage are supposedly responsible for the acute pain.³ Reactivation of the virus is linked to a diminished virus specific and cell mediated immunity, which is related to age. Immunocompromised patients also run an increased risk of developing herpes zoster (especially patients with haematological malignancies or those receiving immunosuppressive drugs). In contrast to other herpes infections, recurrence of herpes zoster is relatively rare (6-14%).¹ Since it has not yet been proved that herpes zoster is provoked by any serious underlying pathological condition (for example, a malignancy),⁴ a search for possible risk factors is not warranted in otherwise healthy patients in whom herpes zoster develops.

Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Julius Center for Health Sciences and Primary Care, PO Box 85060, 3500 AB Utrecht, Netherlands
Wim Opstelten
general practitioner

Department of Ophthalmology, VU University Medical Center Amsterdam, Netherlands
Michel J W Zaal
consultant ophthalmologist

Correspondence to: W Opstelten
W.Opstelten@umcutrecht.nl

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Box 1: A 70 year old woman tells her story

Acute skin rash without involvement of the nasociliary

My complaints started as tender skin when I ran my hand through my hair—a stinging feeling as if my scalp were covered with glass splinters. Initially, I thought it was because I had driven with my car window open. In addition, I did not feel that well. I had a slight fever and a headache. After a few days, I noticed some red spots on the left side of my forehead. For this reason I consulted the general practitioner in attendance. Because my forehead hurt, he thought I had sinusitis. I have had that a few times in the past. The doctor diagnosed the red spots as eczema. I was prescribed nose spray and painkillers. The pain was worse the next day. I felt really sick and stayed in bed. I also noticed several blisters on my forehead and my left upper eyelid was swollen. My own doctor came to my house and diagnosed me as having shingles. He prescribed antiviral drugs. A day later, the eyelids of my left eye were so swollen that I could no longer see out of that eye. As a result, my doctor referred me to an ophthalmologist. Fortunately, only my eyelid was affected—there was no eye infection.

Now, three weeks after my complaints started, I am feeling better. I still have some scabs on my forehead, but I can see again with my left eye. The skin over my forehead, however, is still tender to the touch.

Ophthalmic herpes zoster

Ophthalmic herpes zoster represents 10-20% of all zoster cases.⁵ In other words, one out of every 100 individuals will develop ophthalmic zoster during his or her lifetime. The disease is potentially serious and may result in severe and lasting pain, particularly in elderly patients. Moreover, without antiviral treatment, about half of all patients will develop various eye disorders. Conjunctivitis, for example, is seen in nearly all of ophthalmic zoster patients with ocular involvement. More severe disorders include keratitis, uveitis, and optic neuritis of the affected eye. If these latter disorders are not diagnosed and treated adequately the patient's

sight may become permanently affected. The cornea may lose optical quality because of clouding and surface irregularities. Moreover, a decreased corneal sensitivity combined with inadequate blinking may lead to severe problems with dry eyes with subsequent corneal complications (neurotrophic ulceration and exposure keratopathy, secondary bacterial infection). The risk of corneal ulceration is particularly enhanced in patients with a substantial loss of corneal sensitivity. The risk of ophthalmic complications is not related to age or severity of the skin rash.

Symptoms and signs of ophthalmic zoster

Herpes zoster can present with extraocular and ocular features (table), sometimes simultaneously.

In box 1, a patient shares her experiences with the condition, and in box 2, a close family member, a son, reports how he was affected by his father's illness.

Extraocular features

In the prodromal phase, patients may report malaise, pain, itching photophobia, and low grade fever up to one week before the skin rash appears. The rash usually starts with progressive pain sensations that are accompanied by hypersensitive areas on the forehead.⁶ Then erythematous macules appear that progress to form clusters of papules and clear vesicles in the affected dermatome. In most patients, new skin lesions usually continue to appear for three to five days; the rash then evolves through stages of pustulation and crusting. Patients with deeper involvement of the dermis may develop permanent scars with loss of normal pigmentation. Rash in the dermatome of the nasociliary nerve may indicate ophthalmic complications. Although ophthalmic zoster is usually characterised by this typical rash, a minority of patients have only ophthalmic symptoms.^{7 8} With typical ophthalmic zoster, the skin rash usually precedes the ocular lesions by some days. Several studies have proposed a greater risk of protracted pain in patients with ophthalmic zoster, but this relation has not been found consistently.⁹

Ocular features

A wide range of symptoms affecting the eye may occur during the various phases of ophthalmic zoster.

Eyelids

The skin of the forehead and upper eyelid is commonly affected and may give rise to substantial periorbital oedema in the early phase of the disease. In patients with severe dermal inflammation, late phase contraction scars may lead to incomplete eyelid closure and corneal exposure.

Conjunctiva

Conjunctivitis is a common finding in ophthalmic zoster with involvement of the eye. The conjunctiva appears oedematous and injected, sometimes with petechial haemorrhages. These signs usually resolve within a week.

Episclera, sclera

Episcleritis and scleritis may be diagnosed when a localised redness with dilatation of the deeper vessels

appears. The presence of pain, however, is not helpful in differentiating between these complications, as ocular sensitivity is invariably affected. After the inflammation has resolved completely, patchy scleral atrophy may become apparent.

Cornea

Small corneal epithelial defects may be visible during the acute phase, but those microdendritic lesions will disappear within days. In patients with a red eye, corneal sensitivity is often substantially and irreversibly reduced. Although corneal hyposensitivity is the norm, hypersensitivity can sometimes occur.¹⁰ In prolonged keratitis, regular eye examinations by an ophthalmologist are necessary to evaluate and treat surface problems and deep corneal inflammation and to prevent subsequent neovascularisation. In a minority of patients, topical steroids are indicated on the advice of an ophthalmologist to control inflammation and to maintain corneal transparency.

Anterior chamber

Inflammatory cells may be observed in the anterior chamber when a biomicroscope is used. In most patients, the inflammatory signs will gradually disappear within weeks to months without topical steroid treatment. The release of viral antigens in the iris and ciliary body initiates a mild uveitis often accompanied by temporary elevation of the intraocular pressure. Chronic uveitis, possibly related to an insufficient immune response and prolonged viral activity, is a rare finding in patients who have not been treated with steroids.

Rare complications

Acute ophthalmic zoster may be complicated by involvement of another cranial nerve—for example, the oculomotor nerve. This is probably related to secondary vasculitis within the orbital apex (orbital apex syndrome)¹¹ and may give rise to transient eye motility disorders with diplopia.¹² Delayed contralateral hemiparesis may develop as a late complication.¹³ Acute optic neuritis is a major form of morbidity, because it may lead to a permanent loss of vision.¹⁴ Problems with perfusion of the retina and virus induced necrosis of the retina as a result of ophthalmic herpes zoster have been reported, but these complications are rare in immunocompetent patients.¹⁵

Examination by the general practitioner

In ophthalmic zoster, diagnostics in general practice is restricted to history taking and a physical examination. The diagnostic possibilities during the prodromal phase are manifold until the typical skin signs become manifest. Doctors should always be on the alert for involvement of the eye. The appearance of skin lesions along the side of the nose, which represents the dermatome of the nasociliary nerve, is a useful prognostic factor for subsequent ocular inflammation in patients with acute ophthalmic zoster (Hutchinson's sign).¹⁶ General practitioners are often advised to focus their attention only on the tip of the nose—the dermatome of the external branch. The nasociliary dermatome, however, is more extensive and also affects

Ocular complications in immunocompetent patients with ophthalmic zoster

Part of eye affected	Acute phase	Late phase
Eyelids	Swelling, vesicular rash	Ptosis, eyelid retraction
Conjunctiva	Conjunctivitis	Self limiting
Episclera or sclera	Episcleritis	Self limiting
	Scleritis	Focal scleral atrophy
Cornea	Epithelial keratitis	Neurotrophic or exposure keratopathy
	Stromal keratitis	Corneal neovascularisation, deposition
Anterior chamber	Uveitis	Focal iris atrophy
	Ocular hypertension	Usually self limiting
Rare complications	Extraocular muscle palsies	Self limiting
	Optic neuritis	Optic atrophy
	Retinal vasculitis, retinitis	Retinal atrophy

the skin at the inner corner of the eye and the root and side of the nose (figure next page).¹⁷

In the acute phase, profound swelling of the eyelids may hinder examination of the eye. Although often difficult to detect (even with the aid of a slit lamp), small corneal epithelial lesions may be visible when the ocular surface is stained with fluorescein. Corneal sensation of the inflamed eye is often

Box 2: A 70 year old man, talking about his late father



Severe acute skin rash with haemorrhagic ulcerative lesions



Permanent depigmented scars on the forehead

These are two photographs of my late father, one taken during the acute phase of shingles and the other several months later. I can still vividly remember the horrible skin rash and the agony of his pain when his shingles started. He was 70 years old at that time and already had pulmonary emphysema. I do not know to what extent the pain or itching sensations influenced his daily life or night's sleep, because my father didn't complain about his health problems. The disease, however, affected his appearance permanently, and he sometimes couldn't stop rubbing the eye because of severe itching. His inability to sleep—he slept only a few hours a night—may also be related to his shingles.

Since the onset of shingles, my father had regular check ups for dry eye disease. Until his death at age 84, his right eye was treated with a lubricating eye gel during the day (three times daily) and an ophthalmic ointment before sleep. An ophthalmologist had prescribed this treatment because eyelid closure remained insufficient despite corrective surgery.

During the last years of his life, my father's vision gradually deteriorated because of macular degeneration. His inability to read, even with the aid of a low vision device, was dramatic for him personally. Fortunately, he could still recognise his close relatives with his poorly functioning, herpes zoster affected right eye.



Visual representation of the nasociliary dermatome

affected, and corneal sensitivity of both eyes should be tested with a cotton wool fibre to assess the risk of future ocular complications. A painful response to light combined with blurred vision may be a symptom of uveitis.

Antiviral therapy

Early treatment with aciclovir (within 72 hours after rash onset) reduces the percentage of eye disorders in ophthalmic zoster patients from 50% to 20-30%.¹⁸ This early treatment also lessens acute pain.¹⁹ Valaciclovir and famciclovir seem to be as effective as aciclovir in reducing pain associated with zoster,^{20 21} but their efficacy in reducing eye disorders associated with zoster has not been studied. In clinical practice, however, these second generation antiviral agents may be more effective than aciclovir because patients are more likely to comply with the treatment regimen (three, rather than five, daily doses). Since the course of disease is unpredictable, all patients with ophthalmic zoster, irrespective of their age and the severity of symptoms, should be prescribed oral antiviral drugs at the first signs of infection. Moreover, they should be re-examined after one week at the most. The efficacy of antiviral medication more than 72 hours after the onset of skin rash has never been confirmed. Nevertheless, prescription of these drugs after this timespan should be considered in elderly patients with ophthalmic zoster, because their immune response is usually delayed and, consequently, viral shedding may last longer.²² Although the additional effectiveness of aciclovir eye ointments has never been established, topical aciclovir can be considered in cases of severe eye infection since much higher concentrations of the drug in the anterior eye segment will be effected by this route. Monotherapy with antiviral eye ointment is, however, insufficient and should be adjuvant to oral treatment.²³

Additional therapy

When the natural blinking reflex and eyelid function are affected, long term application of a lubricating eye ointment or eye gel is indicated to prevent corneal epithelial damage. Anaesthesia based interventions, such as stellate ganglion block, may produce short term pain relief²⁴ but are not done on a regular basis. In addition, no evidence exists for their effectiveness in reducing the risk of protracted pain.²⁵

When should patients be referred to an ophthalmologist?

Hutchinson's sign in the early phase of ophthalmic zoster, visual complaints, or an unexplained red eye are indications for referral to an ophthalmologist. Immediate consultation, however, is usually not required, since vision threatening ophthalmic complications that require specific treatment usually do not develop during the first week after onset of skin rash. Importantly, the patient should start taking antiviral medication as soon as possible, independent of the ophthalmic condition.

Long term prognosis

Once an eye has been affected by herpes zoster it will always remain vulnerable. Complications can develop even months or years after the acute phase. The cornea, for example, may be damaged because epithelial regeneration is delayed, particularly in eyes with corneal anaesthesia. Doctors should, therefore, remain alert when the natural defensive mechanisms of the

Additional educational resources

Review papers

Guidelines for the management of shingles. Report of a working group of the British Society for the Study of Infection (BSSI). *J Infect* 1995;30:193-200.

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Websites

International Herpes Management Forum (IHMF), www.ihmf.org

Varicella Zoster Virus Research Foundation (VZVRF), www.vzvrfoundation.org

Both websites offer information to both healthcare professionals and the public

Information for patients

www.familydoctor.org—website from the American Academy of Family Physicians offering health information for patients

eyes of patients with “cured” ophthalmic zoster are affected, as in the state of decreased consciousness and after ophthalmic surgery. Accordingly, we recommend that a past infection with ophthalmic zoster should be registered in the patient’s medical file.

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One hundred years ago

The medical student of to-day

A WRITER in the *St. James’s Gazette* bewails the “passing” of the medical student. He explains that, although there are still young men who devote themselves to the study of medicine, “all that made the medical student distinctive—the gay, irresponsible, irrepressible youth of our imaginations and of our literature—has faded into the light of common day, and the difference between the medical student of these years of grace and the theological student, for example, is that one is studying the Thirty-nine Articles and the other the metacarpal articulations.” The modern student, we gather, is bored by the lectures he has to attend, and a genuine interest in his work, or a real scientific curiosity, is rare. Nevertheless, having the fear of the examiner before his eyes, he reads hard, but the whole system of examinations is “soul-killing, destroying originality, destroying continuity, and bestowing the prize on the man who patiently ‘swots’ up his subjects and mechanically gives forth the answers he has been told to give.” That lectures often cause boredom is true enough, but that is not altogether the fault of the student. That the passing of examinations is to a considerable extent a mechanical art cannot be denied, but that is mainly the fault not of the system, but of the way in which it is too often applied. As long as mere book knowledge is accepted as a passport by those

who guard the portals of medicine, so long will cramming continue. But for keen interest in his work the medical student compares favourably with any other class. This is a frequent subject of remark at the older universities, where he is marked out among his fellows by the eagerness with which he strives after knowledge. He has to work much harder than other students, and that necessarily leaves him less time for frolicking. No one, however, better knows how to put in practice the maxim *Dulce est desipere in loco*. Fortunately, drinking and other undesirable manifestations of the “flamboyancy and sparkle” which are said to be wanting in the medical student of to-day are now generally looked upon as “bad form.” The “chronic,” who was the prototype of the medical student as painted by Dickens, Albert Smith, and Thackeray, has disappeared under the stress of the modern curriculum. He is as much out of place in a modern school as Sawyer, late Nockemorrff, would be in modern practice. If the medical student has lost in “flamboyancy,” he has gained vastly in true manliness of character, as well as in scientific spirit and range of mental outlook—a result of a change in thought and feeling with which the profession and still more the public have every reason to be satisfied. (*BMJ* 1905;ii:971)