Herpes Zoster Ophthalmicus

the royal victorian eye and ear hospital

Disclaimer

SEE ALSO: Herpetic Corneal Infections, Acute anterior uveitis (AAU)

DESCRIPTION

Herpes Zoster Ophthalmicus (HZO) is a reactivation of the varicella-zoster virus (chickenpox virus) in the ophthalmic division of the trigeminal nerve (CN V1) (i.e. shingles affecting CN V1). Acute HZO usually manifests as a periorbital vesicular rash and can be associated with inflammatory complications involving all ocular structures. Chronic HZO can result in prolonged/recurrent corneal disease and uveitis.

Please note that this CPG is a guideline only. Evidence is lacking for some treatment options for ocular disease, and clinical judgment remains important.

HOW TO ASSESS

Red Flags:

- Ocular involvement in HZO is significantly increased if rash involves the end of the nose (Hutchinson's sign).
- Beware: early presentation with pain prior to onset of rash is not uncommon.
- Beware: delayed ocular involvement in HZO can occur up to 3 weeks following rash onset.
- Isolate patient in a single room when diagnosis first considered (may be from triage).
- Infectious precautions needed until skin lesions healed as can transmit chickenpox. Avoid exposure to non-immunised and previously unexposed (to chickenpox) patients and pregnant women.
- In patients < 40 years old: consider evaluation for immunodeficiency.
- Note: disseminated zoster can occur in immunodeficiency, malignancy, and can rarely cause meningoencephalitis.

Background:

Incidence and severity of HZO increases with advancing age, especially in those >60 years

Without the use of antiviral therapy approximately 50% of patients with HZO will develop ocular involvement.

It is rare to get herpes zoster if previously vaccinated for chickenpox, but not impossible.

On History:

- Systemic: prodromal symptoms (headache, fever, malaise), skin rash, dermatomal

pain, paraesthesias, discomfort.

- Ocular: pain, redness, watering, photophobia, blurred/decreased vision.

On Examination:

Complete ophthalmic examination including intraocular pressure (IOP), check for iris atrophy, perform dilated fundus and cranial nerve exam.

Ocular complications occur at different times following HZO rash (typical time to onset in parenthesis below).

Skin

- Acute vesicular dermatomal skin rash in V1 distribution, unilateral, respects the midline.
- Nasociliary involvement increases the risk of ocular involvement (Hutchinson's sign).

Eyelid/conjunctiva (onset 1-2 weeks)

- Vesicles on skin, lid margin or bulbar conjunctiva
- Blepharitis
- Unilateral conjunctivitis, often with petechial haemorrhages
- Periorbital oedema
- Lid malposition, scarring, trichiasis (late)

Episclera/sclera (onset 1 week)

- Episcleritis
- Scleritis

Cornea

Epithelial disease

- Superficial punctate keratitis (SPK) (2-7days). Can progress to pseudodendrites.
- Pseudodendrite (4-6 days): elevated 'stuck on' plaques, branching pattern with tapered ends. Distinct from HSV dendrites, which have terminal bulbs and stromal ulceration.

Stromal disease

- Anterior stromal keratitis (1-2 weeks)
  - Multiple fine granular infiltrates often directly beneath pre-existing dendrites or SPK
  - Nummular (coin-shaped) lesions
- Deep stromal keratitis (1 month –years)
  - Stromal inflammation/infiltrates, corneal oedema, associated uveitis
- Neurotrophic keratopathy, reduced corneal sensation (1 month –years)
  - Exposure epitheliopathy
  - Corneal thinning with risk of perforation
  - Risk of secondary bacterial infection

Anterior chamber

Anterior uveitis (2 weeks-years)

- Isolated or associated with keratitis
- Frequently causes elevation in IOP at presentation
- Late iris atrophy and an irregular pupil

Trabeculitis

- Associated with high IOP

Posterior segment

Acute retinal necrosis (ARN)

- Peripheral patches of retinitis that rapidly coalesce, occlusive vasculitis and vitreous inflammation
- Retinal detachment common

Progressive outer retinal necrosis (PORN) a risk in immunocompromised patients

Other complications

- Cranial nerve palsies: 7th, 3rd (most common), 4th and 6th nerve palsies occur rarely
- Orbital inflammation/myositis
- Optic neuritis: rare
- Post-herpetic neuralgia (PHN; dermatomal pain persisting > 3 months after rash), allodynia (pain on light touch), reduced sensation, paraesthesia.

ENT referral (herpes zoster oticus/Ramsey Hunt syndrome) if:

- Otalgia
- Vesicular rash in or around the ear or on the face, mouth, tongue
- Vertigo, nausea, vomiting
- Hearing loss, hyperacusis, tinnitus

On Investigation:

- This is a clinical diagnosis most often not requiring confirmatory laboratory tests.
- Consider swab of vesicular fluid of skin lesions or inflamed conjunctiva for viral PCR if the diagnosis is unclear.
- Consider corneal scrape for MC+S if corneal infiltrate is present.

ACUTE MANAGEMENT

- Please note that the following recommendations do NOT directly apply to the management of ARN or PORN – please contact the Medical Retina Fellow who will direct treatment of these cases, in consultation with an Ocular Immunology Clinic (OIC) consultant.
- Oral antivirals preferably within 72 hours of rash onset, or within 7 days if still has active vesicles or in debilitated/immunocompromised patient. Greatly reduces risk of ocular complications, may reduce risk of PHN.
    - Options:
        - Valaciclovir 1000mg TDS oral, 7 days
            - PBS approval code 5962 for HZ, 72 hours of rash onset
            - PBS approval code 5968 for HZO (no time limit with regards to rash onset)
            - Medication of choice as easier dosing regimen, less expensive to purchase in community for non-concession card holders.
        - Aciclovir 800mg 5 times per day oral, 7 days
            - Not on RVEEH formulary
            - PBS approval code 5967 for HZ, 72 hours of rash onset
            - PBS approval code 5959 for HZO (no time limit with regards to rash onset)
        - Famciclovir 500mg TDS oral, 7 days
            - Not on RVEEH formulary, non-PBS
            - PBS codes exist for treatment of HZ only, i.e. 250mg TDS oral, 7 days (5951). Confirm patient with HZO is on correct dose (Famciclovir 500mg TDS oral, 7 days.
            - Costly for patient to fill non-PBS script, therefore Famciclovir is not ideal for treatment of HZO.
- All 3 antivirals are equivalent in terms of efficacy and safety.
- No apparent role for topical acyclovir in the management of HZO.

Skin lesions:

- Keep lesions clean and dry
- Symptomatic relief with warm compress to periocular skin TDS

Ocular involvement

General management

- Chloramphenicol:
    - Ophthalmic ointment TDS to lid vesicles to prevent secondary bacterial infection
    - Drops if significant corneal epithelial defect
- Lubricants: drops/ointment:
    - Conjunctivitis, SPK, pseudodendrites, neurotrophic keratitis

- Topical steroids:
    - Use for stromal keratitis and uveitis (see also CPG AAU)
    - Options: Fluorometholone, Prednisolone acetate 1% / phenylephrine
    - Selection and dosage depending on severity of disease
    - Slow taper guided by clinical progress
    - NOTE: uveitis may require prolonged treatment

Specific management

- Episcleritis/scleritis: treat as per episcleritis/scleritis, with topical steroids, oral NSAIDs, etc. in addition to systemic anti-virals.
- Neurotrophic keratitis: consider Cornea consult
    - Lubrication with preservative-free artificial tears every 1-2 hours and ointment at night
    - If corneal infiltrate is present, obtain a corneal scrape
    - Address lid malposition, trichiasis
- Elevated IOP: may be due to uveitis, trabeculitis or steroid response
    - Treatment guided by aetiology and severity of elevated IOP
    - If uveitis present, increase frequency of topical steroids
    - Avoid concurrent use of prostaglandin analogues (potentially pro-inflammatory but this is controversial)
- Retinitis, choroiditis, orbital inflammation, optic neuritis, or cranial nerve palsy
    - Consult appropriate subspecialty clinic
    - Consider admission, depending on severity
    - Consider switch from oral to IV Aciclovir 5-10 mg/kg TDS for 1 week
    - Some conditions may benefit from oral prednisolone
- Pain management: involve the patient's General Practitioner (GP)
    - First line: over the counter analgesics
    - Amitriptyline can be introduced at low doses with close GP follow-up
        - Amitriptyline 10 to 25 mg orally, at night.
    - Pain may be severe in the first 2 weeks and narcotic analgesics may be required. Consult Neurology consult if pain intractable/severe.
- Recurrent/chronic HZO
    - Can manifest as corneal lesions, interstitial keratitis or iritis
    - Oral antivirals likely to be of benefit. Length of course of antivirals often extended in practice. No clinical trials to date.
    - Topical steroids as per indication
    - No role for topical antivirals

FOLLOW UP

No ocular involvement

- Follow up at 2-3 weeks
- If no ocular involvement at follow up visit, discharge to GP or optometrist.

Ocular involvement

- Follow up interval dependent on type of ocular involvement and severity.
- Patient < 40 years old, refer to GP to evaluate for a possible immunocompromised state/immunodeficiency.

NOTE: Shingles is reportable to the Victorian Department of Health for epidemiologic data on infectious diseases, on the basis of clinical findings and/or laboratory results (see quick link on ED Intranet page).

DISCHARGE INSTRUCTIONS

- Give patient copy of Shingles Factsheet
- Education regarding:
  - Infectious precautions (see red flag)
  - Risk of late ocular complications
  - Importance of follow-up appointments for complications and monitoring treatment
- Patients advised to see eye care provider if develop ocular symptoms

ADDITIONAL NOTES

- The shingles vaccine, Zostavax®, has been shown to reduce the incidence of herpes zoster and post-herpetic neuralgia considerably. Zostavax® is now free of charge in Australia for people aged 70-79 years. Patients outside of this age group can pay to receive the vaccine.
- The vaccine is not indicated during acute disease.
- Caution is indicated regarding vaccination following HZO with ocular involvement. Several reports have described reactivation of ocular disease following administration of Zostavax®.
- It is suggested that vaccination may reduce the risk of recurrence following an episode of shingles elsewhere in the body and HZO without ocular involvement, but this has yet to be demonstrated in clinical studies. It is advised to wait at least one year following an episode of shingles before administering Zostavax® (National Centre for Immunisation Research and Surveillance, Australia).

Review Date: 08/06/2021

Authors: Dr Eamonn Fahy, CPG Working Party

References:

Ref no.	Author	Title	Source	Level of evidence (I – VII)
1	Cobo LM, Foulks GN, Liesegang T, *et al.*	Oral acyclovir in the treatment of acute herpes zoster ophthalmicus	Ophthalmology. 1986; 93: 763-770	II
2	Hoang-Xuan T, Buchi ER, Herbort CP, *et al.*	Oral acyclovir for herpes zoster ophthalmicus	Ophthalmology. 1992; 99:1062-1070	II
3	Tyring S, Engst R, Corriveau C, *et al.*	Famciclovir for ophthalmic zoster: a randomised aciclovir controlled study	BJO. 2001; 85: 576-581	II
4	Colin J, Prisant O, Cochener B, *et al.*	Comparison of the efficacy and safety of valaciclovir and acyclovir for the treatment of herpes zoster ophthalmicus	Ophthalmology. 2000; 107: 1507-1511	II
5	Beutner KR, Friedman DJ, Forszpaniak C, *et al.*	Valaciclovir compared with acyclovir for improved therapy for herpes zoster in immunocompetent adults	Antimicrobial agents and chemotherapy. 1995; 39: 1546-1553	II
6	Severson EA, Baratz KH, Hodge DO, *et al.*	Herpes zoster ophthalmicus in olmsted county, Minnesota: have systemic antivirals made a difference?	Archives of ophthalmology. 2003; 121: 386-390	IV
7	Watson PN	Postherpetic neuralgia	BMJ Clin Evid. 2010 Oct 8	I
8	Neoh C, Harding SP, Saunders D, *et al.*	Comparison of topical and oral acyclovir in early herpes zoster ophthalmicus	Eye (London). 1994; 8 (Pt 6): 688-691	II
9	Hu AY, Strauss EC, Holland GN, *et al.*	Late varicella-zoster virus dendriform keratitis in patients with histories of herpes zoster ophthalmicus	American Journal of Ophthalmology. 2010; 149: 214-220	V
10	Pavan-Langston D, Yamamoto S, Dunkel EC	Delayed herpes zoster pseudodendrites. Polymerase chain reaction detection of viral DNA and a role for antiviral therapy.	Archives of Ophthalmology. 1995; 113: 1381-1385	V
11	Hales CM, Harpaz R, Ortega-Sanchez I, *et al.*	Update on recommendations for use of herpes zoster vaccine	Morbidity and Mortality Weekly Report. 2014; 63: 729-731	I

The Hierarchy of Evidence

The Hierarchy of evidence is based on summaries from the National Health and Medical Research Council (2009), the Oxford Centre for Evidence-based Medicine Levels of Evidence (2011) and Melynk and Fineout-Overholt (2011).

I Evidence obtained from a systematic review of all relevant randomised control trials.

II Evidence obtained from at least one well designed randomised control trial.

III Evidence obtained from well-designed controlled trials without randomisation.

IV Evidence obtained from well designed cohort studies, case control studies, interrupted time series with a control group, historically controlled studies, interrupted time series without a control group or with case series.

V Evidence obtained from systematic reviews of descriptive and qualitative studies.

VI Evidence obtained from single descriptive and qualitative studies.

VII Expert opinion from clinician, authorities and/or reports of expert committees or based on physiology

CPG Suite General Disclaimer

These CPGs were written for use in the RVEEH speciality Emergency Department. They should be used under the guidance of an ENT or Ophthalmology registrar, and certain medications / procedures should only be undertaken by speciality registrars.

If you require clinical advice, please contact our admitting officer for assistance:
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