BMJ 2016;353:i3221 doi: 10.1136/bmj.i3221 (Published 13 June 2016)

ENDGAMES

CASE REVIEW

Photophobia and a painful rash

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A 62 year old woman presented to eye casualty with a 10 day history of a left sided headache. Two days after her headache started she developed a painful and pruritic left sided rash. During the 24 hours before presentation, her left eye had become injected, painful, and photophobic.

On examination she had a well demarcated, unilateral area of erythematous and mildly oedematous skin, which extended from her left upper lid up across her forehead. Within this area were discrete tender scabbed lesions, which extended back into her hairline (fig 1). She had no lesions on the tip of her nose or in her auditory canal. No lesions crossed the midline to the right side of her forehead or scalp.

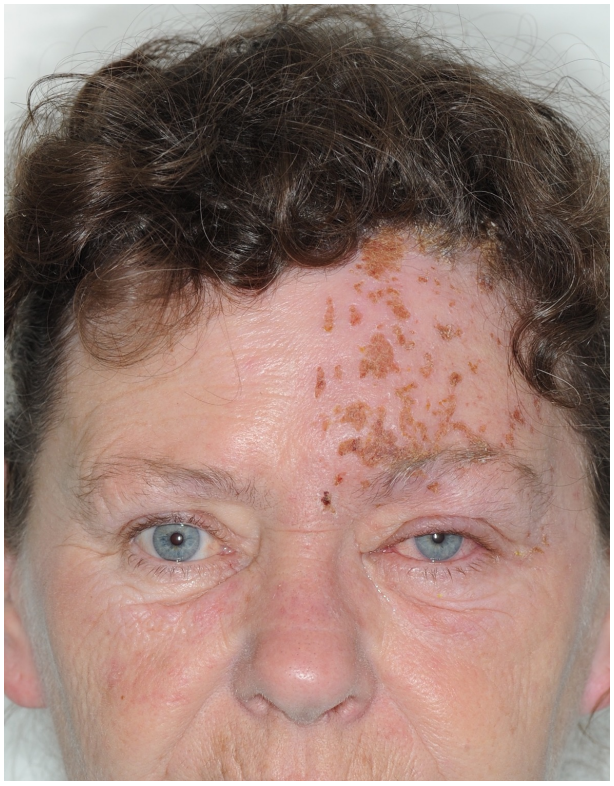

Fig 1 Left side scabbed skin lesions respecting the midline with associated left lid swelling and conjunctival injection

Ocular examination showed an unaided visual acuity of 6/6 in the right eye and 6/9 in the left eye. Ocular motility was full. Intraocular pressures were 10 mm Hg in the right eye and 12 mm Hg in the left. Her left cornea was clear and did not stain with fluorescein, while her conjunctiva was diffusely injected. Slit lamp examination of her left anterior chamber showed 1+ for cells and flare. Dilated funduscopy showed a clear vitreous and healthy fundus. Her right ocular examination was normal.

Questions

1.What is the most likely diagnosis?

2.How is the diagnosis confirmed?

3.How is the condition managed?

4.What complications might occur?

Answers

1.

What is the most likely diagnosis?

Short answer

Left herpes zoster ophthalmicus (HZO) with associated anterior uveitis.

Discussion

HZO occurs when latent varicella zoster virus (VZV), residing in the ganglion of the trigeminal nerve, reactivates and affects the ophthalmic nerve (V_1). Primary infection with VZV commonly occurs in childhood as chickenpox. Anterior uveitis occurs in 40-50% of all cases of HZO.[1]

The typical features of HZO include a viral prodrome (lethargy and weakness), followed by preherpetic pain in the region of skin where the rash later appears.[2] The pain, often described as burning or stabbing, can range from mild to severe. Two to three days later a papular rash appears, which becomes vesicular before finally scabbing over. In rare cases no rash appears (zoster sine herpete). The skin lesions are tender to touch and occur in the V1 dermatome. This area stretches from the upper lid on the affected side, through the hairline, and back to the lambdoid

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suture. In immunocompetent patients, the rash respects the affected dermatomal boundaries and does not cross the midline. In patients who are immunocompromised or elderly, the rash can become widespread and the infection more serious, which can make the diagnosis more difficult.

Differential diagnoses in this patient include herpes simplex virus (HSV), which can also present with groups of painful vesicles. An important differentiating factor between the two infections is the location of the rash. Unlike in HZO, in HSV infection the vesicles are not limited to the ophthalmic nerve dermatome. Instead, they are typically periocular or genital in location. In addition, rashes caused by HSV often recur, whereas multiple attacks of HZO are unusual, unless the patient is immunocompromised.

Impetigo and contact dermatitis are other differential diagnoses. As with HSV, the rashes in impetigo and contact dermatitis are not dermatomal. Impetigo differs from HZO in that it typically affects preschool children, whereas HZO commonly affects older people. Contact dermatitis is often differentiated from HZO by a history of periocular contact dermatitis or exposure to a causative irritant or allergen. In addition, the predominant symptom of dermatitis is itching, whereas in HZO it is pain.

2.

How is the diagnosis confirmed?

Short answer

The diagnosis of HZO is based on a history of varicella zoster virus (VZV) infection and the presence of a characteristic painful dermatomal rash. Further diagnostic tests are not usually needed. If the diagnosis is in doubt, polymerase chain reaction (PCR) on vesicular fluid for VZV DNA is the most sensitive and specific test.

Discussion

The diagnosis of HZO is made clinically on the basis of a history of VZV infection and the presence of a characteristic painful dermatomal rash. In atypical presentations when the diagnosis is in doubt, PCR can be performed on the vesicular fluid to confirm the presence of VZV DNA.[1] This is the most sensitive and specific test for diagnosing VZV infection.[1] Alternative diagnostic tests are available, including PCR on samples taken from macular or papular lesions, cheek swabs, and oral fluid, all of which have a sensitivity of 95-100%. These tests may be particularly useful in patients who have had VZV vaccination, because in this situation the dermatomal rash is not always vesicular.[1] Direct fluorescent antibody testing, viral culture, and serology for VZV IgM or IgA are less sensitive tests and are now not widely used.[1]

3.

How is the condition managed?

Short answer

Uncomplicated HZO is managed with oral antivirals (aciclovir, valaciclovir, or famciclovir) and analgesia. Ophthalmic involvement warrants specialist ophthalmology review and management within 24 hours. Immunocompromised patients or those with severe systemic VZV infections may require hospital admission for intravenous antiviral treatment, supportive therapy, and monitoring.

Discussion

The management of HZO is aimed at reducing viral replication and acute and post-herpetic neuralgia, as well as minimising the risk of complications. In immunocompetent patients with localised disease, treatment with oral antivirals should be started as soon as the diagnosis is suspected. A 7-10 day course of oral antivirals is recommended. Aciclovir (800 mg five times a day) has been used most extensively and can be used in pregnant women with HZO infection. The use of alternative antivirals, including valaciclovir (1g three times a day) or famaciclovir (500 mg three times a day), may improve compliance owing to the reduced frequency of administration. A meta-analysis has also shown that valaciclovir and famaciclovir are more effective in reducing herpes zoster associated pain.[3] Early administration of oral antiviral treatment, within 72 hours of the rash appearing, is important and reduces the duration of disease, acute and post-herpetic pain, and ocular complications.[4 5]

In immunocompromised patients, HZO infection can result in severe disseminated disease with potentially life threatening complications. Early antiviral therapy is crucial. In severe disseminated disease, with neurological, respiratory, hepatic, or severe ocular involvement, inpatient admission should be arranged and early intravenous antiviral therapy started. In an immunocompromised patient with localised disease, oral antiviral therapy may still be appropriate.

Pain control is an important aspect of the management of HZO. In the acute setting, paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs), with counselling on the risks and side effects, are suitable for mild pain. In severe pain, opioids should be considered. Lotions containing calamine or capsaicin can also be applied to the affected skin to reduce pain and itching. Post-herpetic neuralgia—in which neuropathic pain can persist for months to years after cutaneous healing—is the most common complication of HZO, and it often causes serious morbidity. Treatment is initially similar to that of acute neuropathic pain (paracetamol, NSAIDs, opioids). Patients who do not respond to this initial treatment should be offered tricyclic antidepressants (amitriptyline) or anticonvulsants (pregabalin, gabapentin). These have been shown to reduce pain from post-herpetic neuralgia and improve neuralgia affected sleep.[6 7] A study comparing gabapentin and amitriptyline showed no difference in the efficacy of pain relief between the two drugs.[8]

Ocular involvement, which may present in the form of pain, injection, photophobia, decreased visual acuity, or diplopia, warrants assessment and management by an ophthalmologist within 24 hours. Occasionally ocular complications require prolonged treatment and outpatient monitoring.

All patients should be informed about the risks of transmission of the virus. VZV can be transmitted from vesicular lesions to a patient who has not previously been exposed to the virus. Therefore, patients with acute vesicular lesions should avoid contact with:

- Pregnant women who have not had chickenpox or the VZV vaccine
- Newborn infants less than one month old whose mothers have not had chickenpox
- Immunosuppressed people.

Once the vesicles have scabbed over they are no longer contagious and these precautions are no longer needed.

4.

What complications might occur?

Short answer

Local ocular complications of HZO include conjunctivitis, keratitis, corneal scarring, uveitis, vitritis, retinitis, retinal necrosis, scleritis, optic neuritis, cranial neuropathies, eyelid

cicatrisation, trabeculitis with raised intraocular pressure, cataract, and orbital apex syndrome. Complications from disseminated disease can involve neurological (encephalitis, neuritis, myelitis), respiratory (pneumonia), hepatic (hepatitis), and gastrointestinal (oesophagitis, gastritis, colitis) systems.

Discussion

HZO can result in local ocular complications or widespread systemic complications from severe disseminated disease. A lesion on the tip of the nose indicates involvement of the nasociliary branch of the ophthalmic nerve. This is known as Hutchinson's sign and is a risk factor for developing ocular complications.[9] VZV can cause inflammation in any part of the eye. Ocular complications can therefore include conjunctivitis, keratitis, uveitis, vitritis, retinitis, retinal necrosis, scleritis, optic neuritis, eyelid cicatrisation, and trebeculitis with raised intraocular pressure. In addition, cranial neuropathies, chronic corneal scarring, and cataracts can develop. The most severe complication is acute retinal necrosis, which can rapidly result in blindness and often requires urgent intravenous and intravitreal antivirals and steroid treatment. The most common ocular complications in HZO are keratitis (76%), uveitis (47%), and conjunctivitis (35%).[10] Any sign of ocular involvement warrants an ophthalmology referral and review within 24 hours.

Severe disseminated disease can cause widespread cutaneous lesions and affect multiple organ systems. Neurological, respiratory, hepatic, and gastric systems are most commonly affected. Central nervous system involvement can result in encephalitis, meningitis, or myelitis. Respiratory involvement can manifest as pneumonia, pleuritis, or bronchitis. Gastric involvement can result in gastritis, oesophagitis, or colitis and hepatic involvement leads to hepatitis. Visceral involvement is more common in immunocompromised and elderly people. Severe disseminated disease requires hospital admission for monitoring, supportive therapy, and the administration of intravenous antivirals.

Patient outcome

Our patient was prescribed a seven day course of aciclovir 800 mg five times a day and paracetamol and ibuprofen analgesia as needed. The anterior uveitis in her left eye was treated with a five week course of a reducing dose of topical dexamethasone 0.1%. At review one week later her ocular symptoms had resolved, with her vision improving to 6/6 in the left eye. At this time her rash and neuralgia were improving. At final review (six weeks later), after finishing all treatment, there were no remaining cutaneous lesions, although she reported residual numbness on her forehead. Her ocular examination was normal.

Competing interests: I have read and understood BMJ policy on declaration of interests and declare the following interests: None.

Provenance and peer review: Not commissioned; externally peer reviewed.

Patient consent obtained.

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