PRIMARY eye care
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Painful watery red eye

A 60-year-old male patient presents complaining of a painful, watery and red right eye of one day's duration. A rash of vesicles and crusts on the right forehead has been present for approximately 3 days, with some associated pain. This has occurred previously. He is taking panadeine forte and oral acyclovir 800mg 5 times a day.

The rash is on the right forehead and respects the midline. It extends to the end of his nose indicating involvement of the nasociliary branch of the ophthalmic division of the trigeminal nerve. There is upper lid involvement but the lower lid does not appear to have any vesicles. There appears to be chemosis and hyperaemia of the lower tarsal conjunctiva.

Vision in the right eye is 6/30 compared to 6/7.5 in the left. Ocular motility is full with no diplopia reported.

Fundal examination shows no abnormalities but intraocular pressure is elevated in the right eye at 23mmHg compared to 16mmHg in the left.

Slit lamp examination confirms mild conjunctival oedema and injection in the right eye. Corneal defects exhibited include extensive superficial punctate keratitis, with a large dendritic lesion. There is poor tear film structure in the right eye. The anterior chamber is quiet with no cells or flare seen.

DIFFERENTIAL DIAGNOSIS

The three suggested diagnoses are: Herpes Zoster Ophthalmicus (HSO), Varicella Zoster and Herpes Simplex Keratitis (HSK). The clinical pictures of the suggested diagnoses are as follows:

Herpes Simplex Keratitis (HSK)

The primary infection with Herpes Simplex Virus (HSV) occurs in children typically between 6 months and 5 years of age mainly from droplet infection and occasionally by direct inoculation.

The most common site of primary infection in humans is the skin and the mucous membrane innervated by the trigeminal nerve. Blepharoconjunctivitis, which may be the only manifestation of the primary herpetic infection, is usually benign and self-limiting. Often, the presentation is unilateral and acute and exhibits follicular conjunctivitis with watery discharge and preauricular adenopathy.

HSV has two variants. HSV1 is responsible for orofacial and ocular infections and HSV2 is responsible for genital infections.

At the time of primary infection the virus is also transported via the nerve axon to its cell body in the sensory ganglion where it persists in a latent state until later reactivation. Some indication exists that the human cornea also may harbour latent virus. Recurrent disease, including HSK, is the result of reactivation of this latent virus.

Recurrent HSK infection has symptoms of red eye, photophobia, tearing, reduced visual acuity, skin rash, a history of previous episodes, and is usually unilateral.

The rash involves the skin and eyelids with initially clear vesicles progressing through to crusting. The conjunctiva is injected with the presence of follicles. Corneal involvement varies from fairly mild conditions such as reduced corneal sensitivity, superficial punctuate keratitis, stellate keratitis, dendritic keratitis and geographic ulcer; through to more severe forms such as disciform keratitis and necrotizing interstitial keratitis.

Signs of a dendritic ulcer follow the formation of coarse punctate or stellate keratitis. Central desquamation causes the linear branching of the ulcer. The bed of the ulcer will stain well with fluorescein and the margins, where cells contain the virus, stains with Rose Bengal.

Disciform keratitis appears as a disc shaped area of oedema with the overlaying epithelium intact. Localized granulomatous keratitic precipitates with mild iritis are typically present. Raised intraocular pressure may also be present.

Necrotizing interstitial keratitis is another serious corneal condition with multiple or diffuse white/grey stromal infiltrates with accompanying epithelial defects. Often, stromal inflammation, thinning and neovascularization are present. Other conditions that may be present include iritis, hypopyon and glaucoma.

> Corneal defects exhibited included multiple superficial punctate keratitis, with a large dendritic lesion.

Kanski (2002) suggests that topical antiviral ointment, applied approximately 5 times a day for approximately 20 days, is an appropriate treatment. Kaufman (2000) suggested acyclovir as an effective antiviral, also trifluridine which has been the treatment of choice in the United States. The Auckland Eye Manual suggests acyclovir as Zovirax ointment, 5 times a day for two weeks in the treatment of HSV keratitis.

Initially a high frequency of dosage is used and as the ulcer heals. Tapering of the dosage to prevent local toxicity is recommended. The time frame for healing is generally two weeks. The formulation of acyclovir as an ointment may not be as convenient due to blurring of vision caused by its application.

These treatment regimes are equally appropriate to treat epithelial keratitis if present

The most common presentation of ocular HSV infection is a dendritic ulcer. Although not pathognomonic, its presence generally leads to a specific diagnosis of HSV infection. Signs of a dendritic ulcer follow the formation of course punctate or stellate keratitis. Central desquamation causes the linear branching of the ulcer. The bed of the ulcer will strain well with fluorescein and the margins, where cells contain the virus, stain with Rose Bengal.

Treatment of this form of ulcer is topical use of antivirals such as acyclovir, though disruptive to vision, or trifluridine. Initially a high frequency of dosage is used but as the ulcer heals tapering, to prevent local toxicity is recommended by Kaufman (2000). The time frame for healing is generally two weeks.

Oral acyclovir can also provide therapeutic concentrations in the tears as well as the aqueous humor. Valacyclovir is rapidly converted to acyclovir systemically and can be used in this manner. These systemic antivirals can be used as an alternative or supplement to topical therapy. This regime may be useful in children or dexterity compromised adults.

Occasionally ulcers will enlarge into a geographic or amoeboid configuration, especially if patients are using topical steroids alone. Other more serious corneal defects can occur including disciform keratitis through to necrotizing stromal keratitis. Treatment is generally a combination of topical antiviral and topical corticosteroids. Kaufman (2000) suggests that corticosteroids do not cure underlying hypersensitivity but only relieve symptoms. Typically corticosteroids must be continued for several months along with the antiviral treatment.

Necrotizing stromal keratitis is the most severe and prolonged type of herpetic keratitis and it is the least reliably treated. Treatment with topical antiviral with corticosteroids is still the best modality at present (Kaufman, 2000). Oral acyclovir does not appear to be useful.

Any corneal scarring resulting from stromal herpes will lead to reduction of vision and may lead to the requirement for penetrating keratoplasty. Unfortunately transplanting after damage due to viral recurrences appears less successful in the long term compared to transplanting from simple corneal damage (Kaufman, 2000).

Iritis tends to occur with stromal disease and is treated with topical corticosteroids. It is also necessary to treat concurrently with antivirals to reduce potential for the virus to exacerbate corneal disease.

Recurrence of stromal disease is a problem, as successive episodes tend to cause more corneal scarring. Approximately 25% of patients have a recurrence within 1-2 years. Low dosage oral acyclovir has been shown to reduce clinical recurrences by approximately one half (Kaufman, 2000).

Varicella-Zoster: Ocular Herpes Zoster most likely occurs as a secondary phenomenon of Zoster, involving the ophthalmic division of cranial nerve V. Varicella infection generally presents as chickenpox, predominantly in children under 8 years of age. Infection of the eye as a primary phenomenon is rare. Children with chicken pox may develop ocular signs that mimic those of Zoster infection in adults.

The symptoms include a facial rash, red eye and foreign body sensation. In the early stages the ocular signs can be acute conjunctivitis, vesicles on the limbus, eyelids or conjunctiva, presence of pseudodendritic lesions and possible stromal keratitis and anterior uveitis. Later stage signs include stromal or necrotizing keratitis. Treatment is as for any zoster ocular infections.

Herpes Zoster Ophthalmicus (HZO): This is generally the adult presentation of zoster infection and may be the result of recurrence of a childhood Chicken Pox or Varicella-Zoster infection. About 90% of the population has been infected by Varicella-Zoster at one time or another. The trigger to cause recurrence is unknown. Of all cases of Zoster infection, 15% of cases will affect the ophthalmic division of cranial nerve V and result in Herpes Zoster Ophthalmicus. (Cockburn, 2000: Kanski, 2002). The virus may affect any one of the three branches of ophthalmic division of cranial nerve V or may occur in all three. The branch most likely to cause ocular complications of Zoster infection is the nasocilary branch. This gives rise to the Hutchinson sign, lesions at the tip of the nose,(Cockburn , 2000).

Generally HZO is a condition that affects more elderly patients. If the patient is less than 45 years of age then they should be considered as possibly suffering from an immunosuppression condition, such as HIV infection. (Kanski, 2002).

HZO infection can be classified into three phases; acute, chronic and recurrent.

The acute phase is preceded by flu like symptoms; malaise, fever and headaches. The presence of neuralgia follows with sensations varying from itching/burning and tingling through to boring or lancing pain along the distribution of the affected nerve. Initial presentation is a rash progressing from papules, vesicles and pustules, which crust in approximately 6 days. Any or all branches of the ophthalmic division may be affected. The frontal division is predominantly affected but nasocilary branch involvement poses greatest risk of ocular complications. (Cockburn, 2000)

Ocular lesions vary. Commonly these are lesions on the eyelids, resulting in ptosis from oedema, inflammation and conjunctivitis, always associated with lid vesicles. Episcleritis is relatively common and resolves spontaneously, but may be concealed by overlying conjunctivitis. Scleritis is rather uncommon but might occur at the end of week one and can involve the cornea. A common lesion is acute epithelial keratitis, which occurs within 2 days of the rash onset and resolves spontaneously. It consists of small, fine dendritic or stellate intraepithelial lesions. These lesions are differentiated from those of HSK by the lack of distinct bulbar ends to the dendrites (Kanski, 2002).

Nummular keratitis is less common but may appear approximately 10 days after the rash onset as multiple, fine, granular deposits beneath Bowman's membrane. These can resolve spontaneously but may become indolent. Disciform keratitis is uncommon but may appear approximately 3 weeks after the rash onset and can become chronic if left untreated.

Anterior uveitis is common within the first 2 weeks of rash onset and may result in iris atrophy. From 40% to 60% of sufferers have iridocyclitis within two weeks and 10% of sufferers have elevated intraocular pressures (Cockburn, 2000).

The chronic phase of HZO involves such changes as ptosis due to scarring, trichiasis, loss of lashes and lid notching. Mucus secreting conjunctivitis is a common chronic lesion, as is scleritis that may lead to patches of scleral atrophy. Nummular and disciform keratitis may persist for months and result in significant corneal scarring.

The relapsing phase can result in recurrent lesions for up to 10 years. It is frequently precipitated by sudden withdrawal or reduction of topical steroid treatment. Commonly it will result in the occurrence of episcleritis, scleritis, iritis, glaucoma or one of the several forms of keratitis.

The therapy for HZO is similar to treating any Zoster infection. Oral antivirals, such as Valacyclovir, Valtiex or Famvir, are most effective if commenced within the first 72 hours of the infection (Kaufman, 2000). It is important to try and limit post-herpetic neuralgia and secondary ocular complications. Although oral acyclovir shows a reduction in the severity of the skin rash, its ocular protective effect is not that impressive.

The use of topical corticosteroids with antiviral cover is the mainstay of treating the resultant keratitis and inflammation in HZO, but doubts persist over the effectiveness and safety of these treatments (Cockburn, 2000). Mydriasis is suggested if uveitis is present to prevent synechiae occurring. Artificial tears should be used to improve ocular comfort and prevent drying of the cornea. Great care should be taken to prevent exposure keratitis, which can be hidden by lid swelling. Lubricating ointments, use of bandage lenses, and possibly a tarsorrharphy may be considered (Kaufman, 2000; Cockburn, 2000).

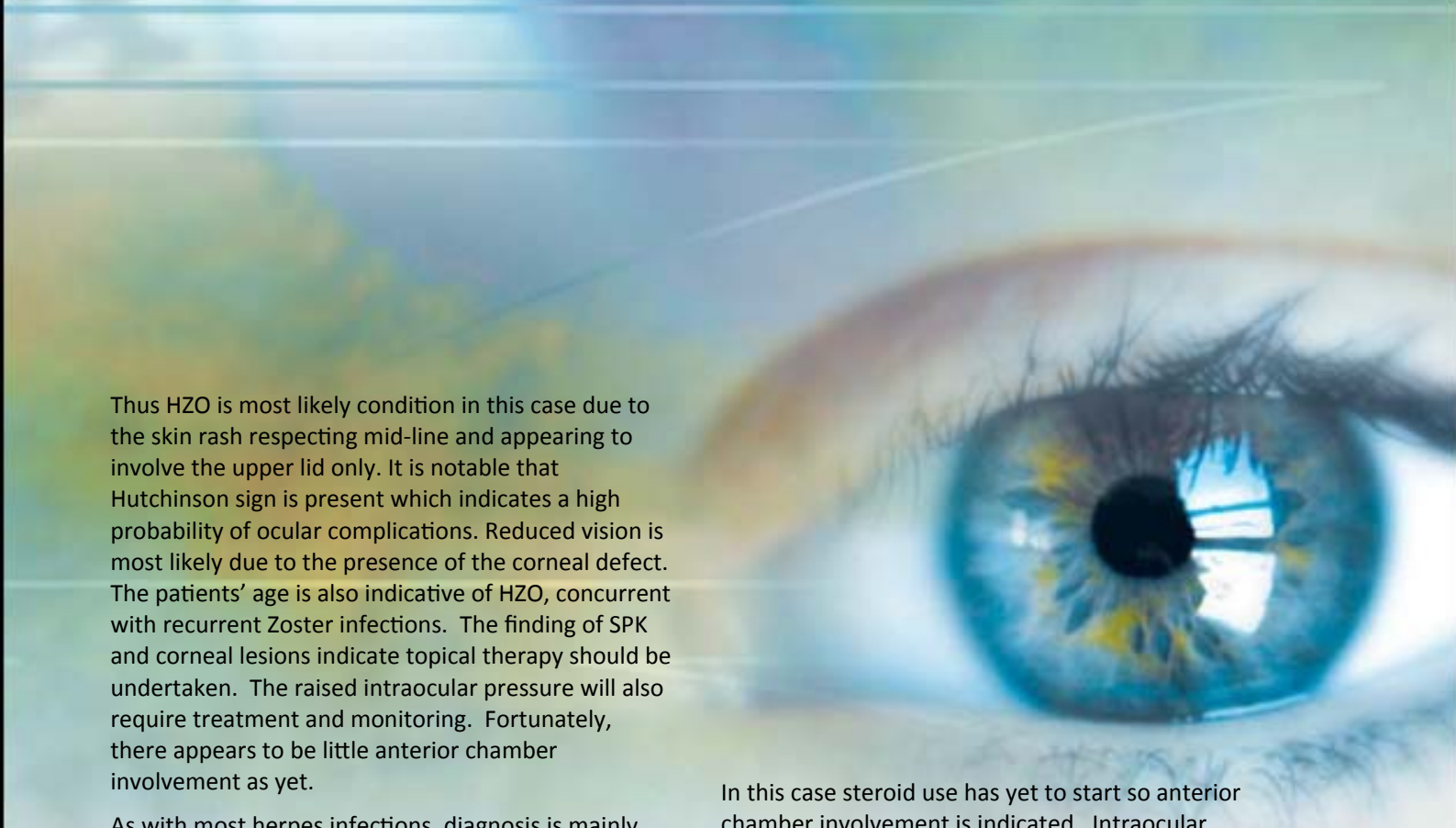
All patients need assessing for anterior chamber involvement, keratitic precipitates and raised intraocular pressure. Where intra-ocular pressure is raised, treatment with topical beta-blocking drugs may be necessary.

Although antiviral treatment does cure 95% of epithelial lesions, care should be taken. Antivirals such as trifluorothymidine are more toxic to epithelium than acyclovir. If treatment of ulcers with antivirals and tropical steroids are not effective, debridement should be considered with antiviral cover.

Given the background of the three diagnoses suggested with this case study, the final diagnosis is Herpes Zoster Ophthalmicus.

Varicella Zoster can be eliminated mainly due to the patient's age and the fact he suffers recurrent events, which indicates this is not a primary infection.

HSK can be eliminated due to the fact the infection follows the frontal and nasocilary branches of the ophthalmic division of cranial nerve V and respects the midline. Also the age of the patient would be contraindicated for this diagnosis.



Thus HZO is most likely condition in this case due to the skin rash respecting mid-line and appearing to involve the upper lid only. It is notable that Hutchinson sign is present which indicates a high probability of ocular complications. Reduced vision is most likely due to the presence of the corneal defect. The patients' age is also indicative of HZO, concurrent with recurrent Zoster infections. The finding of SPK and corneal lesions indicate topical therapy should be undertaken. The raised intraocular pressure will also require treatment and monitoring. Fortunately, there appears to be little anterior chamber involvement as yet.

As with most herpes infections, diagnosis is mainly clinical. However, if verifying laboratory tests were required or wished, the following would confirm the presence of herpes virus. Swabs from skin or lesions could be taken for Giemsa staining which shows the presence of multinucleated giant cells that produce the virus. Also confirmation using a viral culture could be undertaken. Swabs are taken from cornea, conjunctival or unroofed vessels and put in viral medium and the presence of herpes virus confirmed. Laboratory tests are definitely required if corneal ulceration worsens, to elimination the presence of secondary infection.

MANAGEMENT

Management of this patient requires early treatment of 800 mg oral acyclovir 5 times a day for 5 days (effective if HZO is diagnosed within a few days of onset) and concurrent topical corticosteroids to try and control the conjunctival and corneal lesions. A steroid such as prednisolone acetate (1%) is used to reduce inflammation in the keratitis present and antiviral cover is essential to prevent the exacerbation of the HZO epithelial infections that steroids alone can provoke.

The use of topical steroids may have to be tapered over months to years to prevent a relapse. Monitoring every 3 to 6 months following an acute episode resolves is recommended.

Use of topical lubricants would improve comfort for the patient. This is especially important if there is any risk of exposure keratitis.

The raised intraocular pressure would have to be treated; whether raised by steroid use or from anterior chamber involvement.

In this case steroid use has yet to start so anterior chamber involvement is indicated. Intraocular pressure monitoring, once the use of steroids commences, would indicate whether or not a B-blocker anti-oculohypertensive drug such as Timilol is required. Review is recommended on a weekly basis, initially for a month and longer if the condition doesn't improve.

Initial review should be in 2 to 5 days to evaluate the response of treatment. Effective treatment of the corneal lesions will require at least two weeks therapy. If there is no improvement by day 7, assume there is resistance to antiviral agent, thus a substitute agent or corneal debridement should be considered.

FINAL REMARKS

In this case study topical corticosteroids with topical antiviral cover, along with continuation of oral acyclovir and panadeine would be beneficial for the ocular and systemic symptoms as well as managing the skin rash and pain relief plus assisting in suppressing the ocular conditions. Frequent monitoring of the patient should continue for the next few months and every 6 months thereafter to ensure diagnosis and early intervention if reoccurrence occurs.

SOURCES

Auckland Eye Manual

Cockburn DM, Douglas IS. Herpes Zoster Ophthalmicus. Clinical and Experimental Optometry (2000); 83(2): 59-64

Graham RH, Ophthalmologic Manifestations of Herpes Simplex. Medscape - online

Kanski JJ. Clinical Ophthalmology. 4th Edition. Butterworth-Heinemann. 2002

Kaufman HE. Treatment of Viral Diseases of the Cornea and External Eye. Prog Ret Eye Res (2000); 19: 69-85

Graham RH, Ophthalmologic Manifestations of Herpes Simplex. Medscape - online