

Periorbital Rash

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The patient is a 47-year-old white female who presents to the clinic with right eye pain and redness of two days duration. She describes the pain as burning and constant with an intensity of 8/10. The eye problem was preceded by congestion in the ipsilateral maxillary sinus as well as pain in the ipsilateral ear and throat. She also reports a headache localized to the right periorbital region with intermittent, stabbing pains radiating to the right ear. She has tried OTC decongestants and analgesics with only temporary relief. She also tried hot/cold compresses with no relief. She has no fever and no pain or rash anywhere else on the body. Medical and family histories are noncontributory. She works as a second grade school teacher. She reports no known sick contacts but does admit to increased stress lately due to family issues.

QUESTIONS:

1. What is the diagnosis?

- Viral conjunctivitis
- Ramsay-Hunt syndrome
- Impetigo
- Rhus dermatitis
- Shingles with ocular involvement

2. How is this condition diagnosed?

- HSV titers
- Slit lamp exam
- Thorough history and physical
- Tzank smear
- All of the above aid in diagnosis

3. How is this condition treated?

- Aggressive pain control
- Antiviral/anti-inflammatory ophthalmic formulations
- Supportive measures
- Systemic antiviral therapy
- All of the above

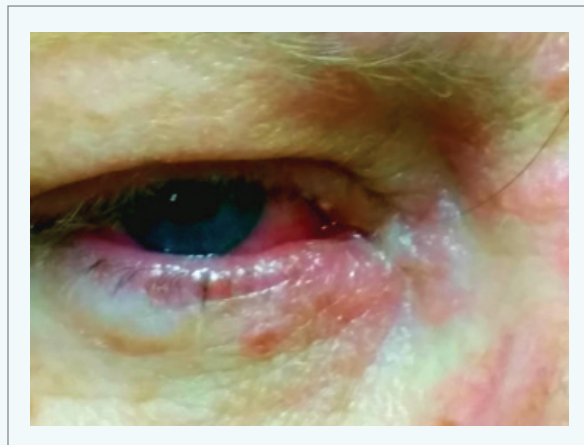
FIGURE 1:

V1 dermatomal distribution of vesicular rash on erythematous base



FIGURE 2:

Conjunctival injection with concomitant hyperemia and blepharitis



ANSWERS

1. What is the diagnosis?

The correct Answer is: E) Shingles with ocular involvement

The given clinical history is most suspicious for ocular shingles, also known as herpes zoster ophthalmicus (HZO). The involvement of the V1 dermatome is clearly seen (Figure 1). There is typically a flu-like prodromal phase that precedes the skin eruption. This phase can consist of fever, malaise, headache, and ocular pain.¹ Viral conjunctivitis does not usually have a significant skin rash and tends to be bilateral with significant lymphadenopathy, watery discharge, and fever.² Ramsay-Hunt Syndrome (RHS) typically presents with herpetic lesions involving the ear and cervical dermatomes and often is accompanied by facial hemiparesis on the affected side. Impetigo presents with pathognomonic, “honey-crusted” lesions which are usually more prominent around the mouth and nose with regional lymphadenopathy being present in 90% of cases.⁴ Rhus dermatitis refers to an allergic phytodermatitis caused by exposure to the oils of plants in genus *Toxicodendron*. Most common in the US are poison oak, poison ivy, and poison sumac. Usually, there is a history of outdoor activities in the past 1-14 days in which the patient remembers having contact or could have had contact with these plants. The skin lesions tend to be intensely pruritic and linear in morphology. This patient had no such contact and did not complain of pruritus.⁵

2. How is this condition diagnosed?

The correct Answer is: E) All of the above

HZO is primarily a clinical diagnosis with a thorough history and physical being the key aspect. HZO is an ophthalmologic emergency, so prompt referral to an ophthalmologist for a full eye exam is recommended. A skin scraping can be performed using a 15 blade to scrape the base of the vesicle. Direct fluorescence antigen (DFA) testing can then be performed.⁶ With the advent of better serological techniques, Tzanck smears are not routinely performed anymore. If done, it would show the characteristic multi-nucleated giant cells upon microscopic examination.⁷ HSV titers can be helpful to rule out herpes infection in equivocal cases.

3. What is this condition treated?

The correct Answer is: E) All of the above

Aggressive pain control is often necessary due to the sometimes severe pain and disability associated with post-herpetic neuralgia (PHN). In a meta-analysis of PHN pain management options by Hempenstall et al, sufficient evidence was found to support the use of strong oral opioids, TCAs, gabapentin and pregabalin. Often, a combination of these drugs is necessary to provide ample relief.⁸ If ocular inflammation is present (Figure 2), then ophthalmic formulations of steroids (e.g. prednisolone), antivirals (e.g. ganciclovir), and cycloplegics (e.g. atropine) may be used.

Their specific dosage intervals and combinations are decided by the ophthalmologist after thorough slit lamp exam. Supportive measures such as avoiding stress and sunlight while applying cool compresses are recommended. Oral antiviral therapy has been shown to reduce the duration of active infection.⁶ If started within three days of the acute onset of rash, valacyclovir and famciclovir have also been shown to reduce the severity and incidence of PHN. An effective and accepted regimen for HZO consists of acyclovir 800 mg by mouth five times a day for one week. An additional advantage to this treatment is the low cost of acyclovir, particularly important for uninsured patients.⁹

DISCUSSION

The herpes virus and its “creeping” lesions have been described by humans since ancient times. However, it was not until the 1880s that the link between chicken pox and herpes zoster was suggested. This link was not definitively proven until the 1950s, leading to the development of a live, attenuated vaccine in 1974.¹⁰ Approximately 20-30% of the population is affected by herpes zoster at some point in their lifetime and herpes zoster ophthalmicus (HZO) affects roughly 10-20% of those individuals.¹¹ In 2006, Merck received FDA approval for Zostavax® a live vaccine for patients 60 and older. A 2005 NEJM study by Oxman et al demonstrated a reduction in herpes zoster of 51.3 % in the vaccinated group.¹² Given these innovations, one would expect to see the incidence of HZO begin to fall but long-term studies and post-marketing research are needed to further evaluate the impact of Zostavax® on HZO. The risk factors for HZO appear to be consistent with the risk factors for developing shingles, namely advancing age and immune compromise. Data on why some people with shingles develop eye involvement specifically is lacking and needs further study.¹

Herpes zoster ophthalmicus is caused by a reactivation of the varicella zoster virus (VZV) occurring in the ophthalmic branch of the trigeminal nerve (Figure 1). VZV is a member of the alpha-herpesvirus family and infects humans exclusively. Initial infection usually occurs in childhood and results in acute varicella or “chicken pox.” Afterwards, the virus establishes lifelong latency and remains dormant in the cranial nerve and dorsal root ganglia.¹³ Upon reactivation, the neurotropic herpes virus will travel from the trigeminal sensory ganglia up to the basal epithelium of the eye, emerging at the corneal surface where virus shedding occurs.¹⁴ Vesicular eruptions often occur on the skin throughout the V1 dermatome (Figure 1). Of note, lesions involving the nose often portend ocular involvement. This phenomenon is coined Hutchinson’s sign, and is due to the dual innervation of the nose and the globe of the eye by the nasociliary nerve.¹⁵

Patients usually present with a typical rash and history of a prodromal phase that preceded the rash. The prodrome typically consists of nonspecific symptoms such as malaise, fever, headache and pain in the affected eye and forehead. With the appearance of the vesicular rash, patients can exhibit conjunctival hyperemia (Figure 2), episcleritis, and drooping of the eyelid.^{8,16} If untreated, keratitis and iritis occur often, and can lead to permanent loss of function.^{8,13}

The potential for permanent loss of vision underscores the urgent nature of HZO and the need for early diagnosis and prompt ophthalmologic examination. The diagnosis of HZO is largely clinical and a high degree of suspicion must be maintained by the physician when evaluating periorbital skin lesions. Culture of herpes zoster is difficult due to the labile nature of the virus and thus is not routinely performed, especially with the advent of more effective laboratory techniques. Direct immunofluorescence assays can be helpful in differentiating herpes zoster infection from herpes simplex. Polymerase chain reaction (PCR) testing can be done on infected fluids and tissues to detect the herpes zoster virus.

Treatment for HZO is usually deferred to an ophthalmologist with expertise in managing corneal diseases. Systemic antiviral therapy remains the crux of therapy and is important to help reduce the progression of ocular complications. Oral acyclovir and its prodrug valacyclovir have been well studied in the setting of HZO and are the mainstays of treatment. Several randomized controlled trials (RCT) have shown that early treatment with these agents can mitigate pain and have a favorable effect on the incidence of post-herpetic neuralgia, one of the most feared complications of herpes zoster infection. Also, if taken within the first three days of the rash appearing, treatment with acyclovir has been shown to reduce the amount of viral shedding and accelerate the resolution of skin lesions.¹³ Oral steroids can be used in cases of significant ocular inflammation, such as uveitis. If ocular inflammation is significant, topical ophthalmic preparations including NSAIDs, steroids, and lubricating agents may also be used.^{12,13,17} The patient in this vignette was referred to an ophthalmologist and treated with oral acyclovir, ophthalmic ganciclovir and ophthalmic tobramycin/dexamethasone, to which she responded well.

HZO, while somewhat uncommon, is a very important entity to recognize. Failure to diagnose and treat this condition early can have devastating effects, including loss of sight. Although the advent of the shingles vaccine and newer antiviral medicines have decreased the occurrence of HZO, clinical suspicion must always be maintained when evaluating ocular and periorbital skin lesions. This particular patient was relatively young and otherwise healthy. Given her profession (2nd grade teacher) and somewhat subtle rash, it could have been easy to attribute the conjunctivitis to another cause, and in doing so, miss a vital diagnosis.

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