

CLINICAL MANIFESTATIONS OF HERPES ZOSTER OPHTHALMICUS

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Abstract

Background: Herpes zoster ophthalmicus (HZO), which accounts for 10–20% of herpes zoster (HZ) cases, involves the first division of the trigeminal nerve. It is considered a medical emergency due to its potential to significantly affect visual function and quality of life.

The aim of this study was to evaluate the clinical manifestations of hospitalized patient with HZO and to identify potential factors associated with the time to improvement of skin rash and the duration of ocular symptoms at discharge.

Material and methods: Our case report is a 33-year-old man who presented with left-sided orbital and temporal stabbing pain, accompanied by swelling in the left frontal region that later extended to the left ocular area, with upper eyelid edema, burning, and tearing.

Due to the persistence of swelling and pain, the patient was referred to the Department of Infectious Diseases, hospitalized for further evaluation and treatment.

Results and Conclusion:

Varicella-zoster virus-specific cell-mediated immunity, which maintains latent VZV under control and is reinforced by periodic re-exposure, represents a key mechanism in preventing viral reactivation and the development of HZ.

Clinical manifestations include dermatomal vesicular rash, acute ocular pain, and prodromal symptoms. Slit-lamp biomicroscopy is necessary to identify ocular complications, while corneal sensation testing is recommended to detect neurotrophic keratopathy. Initial treatment consists of systemic antivirals, including acyclovir, with assessment for possible immunocompromise.

Advanced age is not the sole risk factor for HZO, as the disease may occur at any age. This case indicates that stress and other factors may contribute to VZV reactivation in middle-aged patients. Whereas older age appears to be mainly associated with delayed healing of skin lesions.

Keywords: Herpes Zoster Ophthalmicus, Clinical Manifestations, Acyclovir, Varicella-Zoster Virus, Trigeminal nerve.

Introduction

Herpes zoster ophthalmicus (HZO) is a special type of HZ, accounting for 10–20% of HZ cases, which involves the first division of the trigeminal nerve (ophthalmic division).[1] HZ or shingles, results from reactivation of latent infection with varicella-zoster virus, which also causes chicken-pox. Anyone who has had chickenpox, even in subclinical form, is at risk for developing HZ. It is estimated that the lifetime risk of HZ is 30%, and 1 million new cases are reported annually in the United States.[2] HZO is a medical emergency because it can significantly compromise visual function and quality of life.

The combination of vision loss and chronic pain creates a dual burden, with profound psychosocial and economic consequences. Patients with HZO often experience reduced productivity, higher healthcare utilization, and increased risk of depression and social isolation.[4]

Herpes zoster classically results in a unilateral neurocutaneous reaction in the dermatome served by a particular neurosensory nucleus, causing pain and a pustular rash; serious complications such as superinfection, long-term pain, and ophthalmic involvement can result in significant morbidity. Up to 4% of patients presenting with herpes zoster require hospitalization to aid in management of complications.[3]

Objective

The aim of this study was to evaluate the clinical manifestations of hospitalized patient with HZO and to identify potential factors associated with the time to improvement of skin rash and the duration of ocular symptoms at discharge, emphasizing the need for close multidisciplinary collaboration among infectious disease specialists, ophthalmologists, and dermatologists.

The specific objectives include:

To identify the main clinical, dermatological, and ophthalmological manifestations of herpes zoster ophthalmicus.

To describe the pathophysiological pathway of HZO.

To evaluate the clinical course and variability of symptoms in relation to age and associated risk factors.

To analyze the potential ocular complications arising from this condition.

To emphasize the importance of early diagnosis and timely therapeutic intervention in preventing permanent damage, particularly ocular sequelae.

Epidemiology, risk factors and prevention measures

Epidemiological study results indicate that the lifetime risk of herpes zoster is nearly 30%, with approximately 1 in 3 individuals expected to develop shingles during their lifetime. Among these, nearly one-quarter will experience ophthalmic involvement, translating into millions of individuals at risk for HZO-related complications worldwide. [5]

Global Burden

Worldwide, the incidence of herpes zoster is estimated at 3 to 5 cases per 1000 person-years, with rates increasing sharply in older populations to over 10 cases per 1000 person-years in individuals aged 60 years and older; approximately 10% to 20% of these manifest as HZO, equating to millions of cases annually. With global increases in life expectancy and a higher prevalence of immunosuppressive conditions, the burden of HZO is expected to rise significantly in the coming decades.[6]

Sex Distribution

Most population-based studies show a slightly higher incidence in females than males, mirroring trends in herpes zoster more broadly. This difference may reflect both immunological and healthcare-seeking factors. However, no strong sex predilection is consistently observed in all cohorts.[7]

Of all risk factors, reactivation along the trigeminal nerve has been implicated in developing HZO. Of the branching fibers (nasociliary, frontal, and lacrimal), frontal nerve involvement is the most frequently documented. Risk factors for both acute and recurrent HZO include immunocompromised status, female sex, autoimmune disorders, and an age of 50 years or older. Additional risk factors for recurrence of disease include 30 or more days of zoster-associated pain during acute infection, ocular hypertension, and uveitis following acute infection.[2]

The CDC recommends use of varicella zoster immune globulin preparation for postexposure prophylaxis in patients at high risk of severe disease who lack immunity to varicella or for whom vaccination is contraindicated. This includes neonates or those who are immunocompromised or pregnant. The CDC recommends administration of immune globulin as soon as possible after exposure to varicella and within 10 days. Patients affected by herpes zoster are advised to remain under contact and respiratory isolation until full crusting of lesions is achieved, to prevent transmission to others.[8].

The first line of defense against HZO is prevention through vaccination. Compared to the live attenuated vaccine (Zostavax), the newer subunit vaccine (Shingrix) is more effective at reducing the incidence of HZ (51% vs. 97%, respectively, over three years). [9]

Pathophysiology

VZV is a double-stranded DNA virus that initially invades the upper respiratory tract via virus-laden respiratory droplets, replicating and invading adjacent lymph nodes. [10]

During primary infection, viral particles are believed to spread from the infected skin along sensory nerve endings, ultimately reaching the nerve ganglia. An alternative hypothesis suggests that hematologic spread during the viremic phase leads to access to the ganglia. [11] Following primary infection, the host's immune system suppresses viral replication; however, viral particles can then remain dormant for years, most commonly in spinal root and cranial nerve ganglia. The virus moves anterograde toward superficial tissue in the reactivation phase, reemerging as herpes zoster. [10]

After latency, when cell-mediated immunity declines due to aging, immunosuppression, or stress, the virus reactivates and spreads centrifugally along the ophthalmic branch of the trigeminal nerve, reaching the skin, cornea, conjunctiva, and ocular adnexa. [12]

Reactivation results when host immunity fails to suppress the virus and the reactivation leads to the classic dermatomal rash and neuropathic pain in the distribution of the dermatome of the involved cranial or spinal nerve. Additionally, inflammation in the ganglion itself can lead to neuronal necrosis. At the time of reactivation, the immune system demonstrates a T-cell proliferation with subsequent production of interferon-alfa and herpes virus-specific antibodies. [13]

The ophthalmic division of the trigeminal nerve provides sensory innervation to the cornea, conjunctiva, sclera, iris, eyelids, and forehead. Viral reactivation in this distribution explains the dermatomal rash and high frequency of ocular manifestations. Viral replication in the affected nerves causes neuritis, leading to acute pain and neuralgia. Inflammatory mediators and immune cell infiltration further contribute to nerve injury, predisposing to chronic postherpetic neuralgia. [14]

The ophthalmic division gives rise to 3 terminal branches: the lacrimal, frontal, and nasociliary branches. The nasociliary branch innervates the skin of the tip of the nose and divides further into the long ciliary nerves, which provide sensory innervation to the globe, including the cornea and uvea. For this reason, involvement of the tip of the nose, or Hutchinson sign, is highly correlated with ophthalmic involvement. [15]

As the virus replicates, viral particles migrate peripherally along the sensory nerves, triggering a local inflammatory immune response. In the early stages of replication and inflammation, this pain is often mildly neuropathic in nature, with sensations of burning and tingling; however, as the virus continues to replicate, the inflammation becomes severe, leading to intense pain in the affected dermatome. Once the virus reaches the skin, it penetrates the epidermis, resulting in a pustular lesion. Ophthalmic involvement follows a similar paradigm, as viral replication along the long ciliary nerves results in inflammation that can involve the cornea, sclera, conjunctiva, iris, retina, and optic nerve. As the virus migrates along these nerves, inflammatory sequelae can cause optic neuritis, retinal necrosis, and uveitis, as well as corneal stromal and epithelial sequelae. [16].

Case presentation

We conducted an observational study on a 33-year-old male who presented with left-sided orbital and temporal stabbing pain, accompanied by additional symptoms that began three days

prior to examination. The initial presentation included swelling in the left frontal region, which subsequently extended to the left ocular area, associated with upper eyelid edema, burning sensation, and tearing. The patient had no significant past medical history and no known drug allergies, and presented with dermatological and ocular symptoms. His chief complaint was a rash and pain localized to the left frontal and orbital region.

Three days prior to admission, the patient developed a rash in the left frontal region, which progressively spread to the left orbital area. The condition was associated with a burning sensation, itching, and severe pain. The patient was initially evaluated by an ophthalmologist and started on topical therapy with Tobramycin and Dexamethasone. He was subsequently assessed by a dermatologist and initiated on oral Acyclovir (five times daily). Despite treatment, the pain and swelling persisted, leading to referral and hospital admission to the Department of Infectious Diseases for further evaluation and management.

Prior to hospitalization, ophthalmological examination revealed no pathological changes in the cornea. Fluorescein staining (FLNA) was negative, and corneal sensitivity was preserved. Following the initial evaluations by the ophthalmologist and dermatologist, antiviral therapy with Acyclovir was initiated. Due to persistent symptoms, the patient was referred for inpatient care.

The patient reported no chronic diseases, and his family and epidemiological history were non-contributory.

The patient was in good general condition, conscious, afebrile, eupneic, and with a normal heart rate. The skin had normal coloration, while in the left frontal and orbital region a maculopapulovesicular rash was observed, accompanied by edema of the left upper eyelid.

On systemic examination, the respiratory system revealed normal vesicular breath sounds. The cardiovascular system showed a regular cardiac rhythm with normal heart sounds and no pathological murmurs. Examination of other systems did not reveal any pathological findings. The patient received combined multidisciplinary treatment, including both topical ophthalmic and systemic therapy. Local treatment consisted of moxifloxacin eye drops (Vigamox) administered four times daily, artificial tears (Proculin Advance) six times daily, chloramphenicol ophthalmic ointment once daily in the evening, and acyclovir 3% ophthalmic ointment applied three times daily.

Upon admission, systemic therapy was initiated immediately and included intravenous fluid replacement with 0.9% sodium chloride, parenteral third-generation cephalosporin (ceftriaxone 2 g/day), antiviral therapy with acyclovir, serrapeptase, as well as vitamin supplementation (pyridoxine and ascorbic acid) and additional symptomatic treatment.

Throughout hospitalization, the patient remained afebrile and demonstrated a favorable clinical course. Progressive improvement was observed, including reduction of eyelid edema and evolution of the skin lesions into the crusting stage. At discharge, continuation of therapy at home was recommended, including topical tobramycin/dexamethasone combination and systemic acyclovir.



Dg.herpess zoster ophthalmicus lat.sin

Figure 1&2. A 33 year old man with V1 dermatomal rash, ptosis, and periorbital edema.

* The images were obtained on the fifth day of hospitalization.

Clinical MANIFESTATIONS

The physical exam begins with an external evaluation of lesion distribution, including the eyelids and scalp. The rash often appears maculopapular before transitioning to vesicles and pustules that ultimately rupture and scab over. Although the rash is usually limited to a single unilateral dermatome, immunocompromised individuals may develop disseminated disease, with a

possible bilateral presentation. Particular attention should be paid to eyelid involvement, which is frequently associated with blepharitis, conjunctivitis, and episcleritis. A thorough ocular exam must include visual acuity, slit-lamp examination with fluorescein staining, and ocular tonometry; a thorough dilated funduscopy exam is also necessary.[17]

Depending on the severity of infection, patients may develop significant ptosis secondary to edema, resulting in inability to close the eyelid and dry eye. Red eye, excessive tearing, eye pain, blurred vision, photophobia, and decreased visual acuity are common complaints. The most common ocular presentations include mucopurulent conjunctivitis, anterior uveitis, and keratitis (nummular and disciform). Episcleritis and chemosis are often seen in acute disease, as well. [2]

The rash may involve the tip of the nose or nasal ridge, known as Hutchinson sign. This region is innervated by the nasociliary fibers, which also serve the conjunctiva, sclera, cornea, iris, and choroid. Hutchinson sign is associated with an increased risk of HZO. The absence of this sign does not rule out disease, however, as up to 30% of patients with HZ but without Hutchinson sign will develop HZO.[18]

Beyond ocular pathology, HZO is strongly associated with postherpetic neuralgia, a chronic neuropathic pain syndrome resulting from VZV-induced damage to sensory nerves. PHN can persist for months to years, significantly impairing quality of life. [4]

Treatment

Following a complete history and physical examination, management goals in the patient with herpes zoster ophthalmicus include shortening disease course, providing analgesia, and preventing potential complications. Treatment ultimately depends on the degree of ocular involvement. However, nearly all patients with acute manifestation of herpes zoster ophthalmicus require treatment with systemic antiviral medications, as the disease process is not limited to the ocular surface. Systemic antivirals have been shown to reduce viral shedding from skin lesions, reduce the chance of viral dissemination, and reduce the incidence and severity of ocular complications. Therapy started within 72 hours can also decrease the duration of postherpetic neuralgia, which may occur later in the disease process. [2]

Options for treatment include oral acyclovir, famciclovir, and valacyclovir. Famciclovir (500 mg 3 times a day) and valacyclovir (1 g 3 times a day) have been shown to be as effective as

acyclovir (800 mg 5 times a day),¹⁵ both in the treatment of herpes zoster and in reduction of complications. The simpler dosing regimen of famciclovir and valacyclovir may enhance patient compliance. Intravenous acyclovir is recommended in immunocompromised hosts, particularly to prevent disseminated disease such as encephalitis.[19]

The standard duration of antiviral therapy is 7-10 days. However, varicella DNA has been shown to persist in the cornea for up to 30 days, particularly in elderly individuals.[20]

In disseminated HZ or in immunocompromised patients, IV acyclovir is indicated; if the disease is resistant to acyclovir, IV foscarnet may be considered.

For HZO in particular, adjuvant therapy is used. Analgesics or steroids are given to reduce pain. If blinking is impaired, lubricating and antibiotic ophthalmic ointments may be used. Nonophthalmic topical antibiotics and dressings with adhesive are typically avoided, as they can exacerbate the rash and delay healing.

For stromal keratitis and uveitis, topical corticosteroids are used judiciously with close monitoring. Be aware that tapering prior to resolution of inflammation can prolong healing time. For optic neuropathy or orbitopathy, IV acyclovir is used at a dosage of 10 to 15 mg/kg three times daily for two to three weeks. The treatment for retinitis is similar, with the addition of several months of oral antiviral therapy.[21]

DISCUSSION

HZO is a serious condition characterized by various symptoms and complications, including postherpetic neuralgia, conjunctivitis, keratitis, uveitis, and even retinal vasculitis and necrosis. Previous studies have reported an incidence rate of ocular symptoms in HZO patients ranging from around 50% to 80%. This may be attributed to the fact that hospitalized patients generally have more severe symptoms. Patients with more pronounced and severe ocular involvement are more likely to be advised for hospitalization by doctors. Hence, the incidence rate of ocular symptoms among our patients is expected to be higher. Conjunctivitis, keratitis, and uveitis have been reported as the most common ocular manifestations of HZO.[22]

The evaluation of a patient suspected of having herpes zoster ophthalmicus begins with a complete history. When possible, a history of primary varicella infection should be solicited. Careful questioning to elicit potential immunocompromise should be undertaken, as the disease entity can be more severe and prolonged in immunocompromised individuals. The physical examination should be complete and thorough to evaluate for dermatomal involvement of herpes zoster. Varicella virus serologies are not part of the typical work-up because diagnosis can usually be made by history and physical examination alone. [8]

In developing countries, there are few studies on the prevalence of HZO infection, which allow the implementation of promotion and prevention strategies. It is important to create a higher awareness in the context of promotion to make an earlier diagnosis and avoid complications.

If there is a suspicion for ophthalmic involvement, a consultation with an ophthalmologist is recommended due to the significant morbidity that can occur.

In addition to the characteristic dermatologic findings, HZO can present with a variety of ocular findings, which occur in up to 50% of patients who do not receive antiviral treatment.

A trend of HZO occurrence at younger ages! However, previous studies have shown that specific cell-mediated immunity to VZV may decrease with age, leading to an increased incidence and severity of HZO.

CONCLUSION

This study provides the clinical manifestations and some risk factors of HZO patients. This review also describes the pathophysiology, evaluation, treatment, and prevention of herpes zoster ophthalmicus. First-line interventions include treatment with systemic antiviral medication, such as acyclovir, and testing to uncover potential immunocompromise.

Aging is not the only risk factor for HZO, since its occurrence does not know age and this case shows that stress with other factors help in the reactivation of VZ even in middle age as we

showed in our case. Therefore, we can say that advanced age is an independent risk factor for delayed healing of skin lesions.

Herpes zoster ophthalmicus causes significant ophthalmic morbidity if not adequately diagnosed and treated.

It can lead to serious sequelae, the most adverse involving the eyes, which may require more aggressive treatment for patients with severe facial rash.

For those whose symptoms persist after discharge from the hospital, further studies and follow-up are necessary.

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