Original Research Article

Study of clinical features and management of herpes zoster ophthalmicus

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Abstract

Background: Herpes zoster ophthalmicus occurs when the varicella zoster virus is reactivated in ophthalmic division of trigeminal nerve. The aim of this study is to know the clinical profile and management of HZO. **Methods:** This study was carried out in Department of Ophthalmology, Mamata medical college and hospital, Khammam from January 2014 to January 2019. **Results:** 46 patients with herpes zoster ophthalmicus were examined and their clinical findings and response to treatment were noted. The disease primarily affects the elderly. Systemic and topical antiviral therapy is the mainstay of treatment. **Conclusion:** Early diagnosis and prompt treatment were key in preventing ocular complications.
Key Word: Acyclovir, Herpes Zoster Ophthalmicus, Keratitis, Postherpetic Neuralgia

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INTRODUCTION

Herpes zoster ophthalmicus (HZO) is reactivation of varicella zoster virus in the ophthalmic division of the trigeminal nerve. Herpes zoster affects about 20% of the world population atleast once in their lifetime, with nearly 20% of these showing an ophthalmic involvement. The prodromal phase of HZO usually includes an influenza like illness with fatigue, malaise and low-grade fever prior to the development of unilateral rash over the forehead, upper eyelid and nose. Dermatomal pain can precede the eruption. Subsequently, erythematous macules appear and progress to form clusters of papules and vesicles. These lesions then evolve into pustules, which quickly lyse and crust over. As with chickenpox, once crusting occurs, the lesions cease to be infectious. Scarring with hypopigmentation or hyperpigmentation may persist over a long period. Ocular complications from HZO include vesicular dermatitis, keratitis, neurotrophic keratopathy, uveitis, glaucoma, retinitis, choroiditis and optic neuritis. Persistent pain after disappearance of the skin rash at the involved dermatome, known as postherpetic neuralgia (PHN), can develop and is seen more frequently in older cases. The aim of this study was to know the clinical profile of HZO and management and effect of treatment on the course of the disease.

MATERIAL AND METHODS

A hospital based prospective study was conducted in 46 patients presenting with features of Herpes zoster ophthalmicus attending ophthalmology OPD, Mamata Medical College and Hospital, Khammam during January 2014 to January 2019. Evaluation of patients included taking history, asking for history of primary varicella infection (chickenpox), and complete vaccination history, and careful questioning to elicit potential immune compromise, as the disease entity is more severe and prolonged in immune compromised individuals. Varicella virus serologies are not part of the typical work-up because diagnosis can usually be made by history and physical examination alone. If testing is necessary, a Tzanck smear or Wright stain may be used to determine whether lesions contain a herpes- type virus, although they do not distinguish between varicella and herpes

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simplex infections. Physical examination included a thorough ophthalmologic examination including external inspection to evaluate for dermatomal involvement of herpes zoster, visual acuity, visual fields, extraocular movements, pupillary response, fundoscopy, intraocular pressure, slit lamp examination of anterior chamber and corneal examination with and without fluorescein staining. Investigations like blood sugar, HIV serology and complete haemogram were done in all patients. Patients with HZO were treated with oral Acyclovir 800mg, 5 times daily for 7 to 10 days. Patients with epithelial keratitis were treated with topical Acyclovir 3% eye ointment 5 times/day, cycloplegics and lubricating eye drops. Patients with uveitis received topical steroids and topical cycloplegics that were tapered according to the clinical response. Patients were followed up at regular intervals depending on the severity of involvement and the response to treatment was evaluated.

OBSERVATIONS AND RESULTS

This study was conducted on 46 patients presenting with herpes zoster ophthalmicus who came to Ophthalmology OPD during period of 5 years i.e from January 2014 to January 2019. In this study, it was found that the maximum incidence of HZO was in the age group of 51-60 years (47.82%).

Table 1: Age -wise distribution of cases

Age in years	No. of cases	Percentage of cases
21-30	1	2.17%
31-40	1	2.17%
41-50	9	19.56%
51-60	22	47.82%
61-70	11	23.91%
71-80	2	4.34%

18 cases (39.13%) were female and 28 patients (60.86%) were male. 43 cases (93.47%) had past history of chickenpox. Although 35 patients (76.08%) had no co-morbid disease, 11 cases (23.91%) had predisposing factors including diabetes mellitus in 4 cases(8.69%) , malignancy in 3 cases (6.52%), immunosuppressive medication in 2 cases (4.34%), HIV infection in 1 case (2.17%), radiotherapy in 1 case (2.17%) and tuberculosis in 1 case (2.17%). Skin lesions and acute neuralgia were the most common presenting symptoms which were present in all of the patients studied (100%). Ocular involvement was seen in 37 patients (80.43%) while 9 (19.56%) had only skin lesions.

Table 2: Sex distribution, Predisposing features, Ocular involvement and Presenting Features

		No. of Cases	Percentage
Gender Distribution	Male	28	60.86%
	Female	18	39.13%
Predisposing Factors	Age >50 yrs	35	76.08%
	Diabetes Mellitus	4	8.69%
	Malignancy	3	6.52%
	Immunosuppresive medication	2	4.34%
	HIV	1	2.17%
	Radiotherapy	1	2.17%
	Tuberculosis	1	2.17%
Ocular Involvement	Present	37	80.43%
	Absent	9	19.56%
Presenting Symptoms	Acute Neuralgia	46	100%
	Skin Lesions	46	100%
	Watering	22	47.82%
	Lid Swelling	13	28.26%
	Diminution of Vision	12	26.08%

In this study, conjunctiva was involved in 39 (84.78%) cases, cornea was involved in 37 (80.43%) cases. Anterior uveitis was seen in 12 (26.08%) cases. Ocular involvement in patients with HZO is shown in table. Postherpetic neuralgia was reported in 14 patients (30.43%) in three months of follow-up and 2 cases (4.34%) in one year follow-up.

Table 3: Ocular Involvement seen among HZO patients

Clinical Features	Number of Patients	Percentage
Lid Lesions	40	86.95%
Follicular Conjunctivitis	39	84.78%
Punctate Epithelial Keratitis	20	43.47%
Dendritic Keratitis	11	23.91%
Nummular Keratitis	4	8.69%
Disciform Keratitis	1	2.17%
Neurotrophic Keratitis	1	2.17%
Uveitis	12	26.08%
Secondary Glaucoma	10	21.73%
Postherpetic Neuralgia	14	30.43%

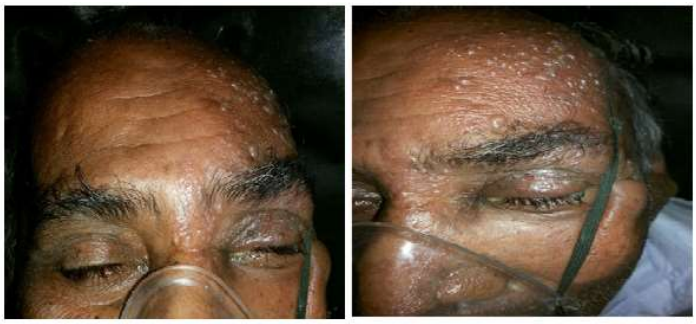

Figure 1: Images showEruptive Vesicular Skin Lesions showing Dermatomal Distribution in patient with Herpes Zoster Ophthalmicus

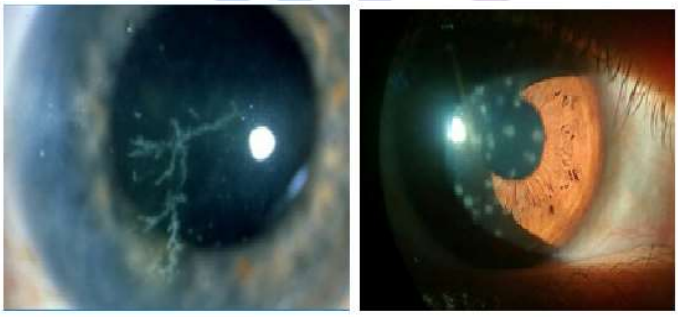

Figure 2: Herpes Zoster Dendritic Keratitis; **Figure 3:**Nummular Keratitis

Patients with HZO were treated with oral Acyclovir 800mg, 5 times daily for 7 to 10 days. Patients with epithelial keratitis were treated with topical Acyclovir 3% eye ointment 5 times/day, cycloplegics and lubricating eye drops. Patients with uveitis received topical steroids and topical cycloplegics that were tapered according to the clinical response. Patients were followed up at regular intervals depending on the severity of involvement and the response to treatment was evaluated. It was observed that patients in whom Oral Acyclovir was started within 72 hours of onset of skin rash recovered completely.

DISCUSSION

Primary infection by varicella zoster virus mostly occurs during childhood and early years of adult life. Varicella zoster virus (VZV) is a highly contagious infection and spreads both by respiratory droplets and direct contact. Primary infection begins with oropharyngeal infection followed by viremia, which leads to diffusion into the skin (chickenpox) and the nervous system where VZV may ultimately establish a latent infection. In our study, 43 cases (93.47%) had past history of chickenpox. In our study, it was found that the maximum incidence of HZO was in the age group of 51-60 years (47.82%). A recent case series reports that the most common decade of onset of HZO is between age 50 and 59 years.[1].Whereas,in a recent study, the incidence rate for the subgroup of population older than 65 years was approximately five times that of the rest of the population.[2,3] This relationship with age has been demonstrated in many geographical area[4,5]and is attributed to the fact that cellular immunity declines as people grow older. HZO was found to be an early clinical marker of HIV infection especially in patients aged <45 years. The study in Ethiopia[6] supported

this finding which showed 95.3% of total population and 100% of patients aged <45 years were HIV seropositive. In our present study, 1 patient (2.17%) was tested positive for HIV infection. In our study, skin lesions were present in all patients i.e in 46 (100%) cases. The skin manifestations of herpes zoster ophthalmicus strictly obey the midline with involvement of one or more branches of the ophthalmic division of the trigeminal nerve, namely the frontal, lacrimal and nasociliary branches. Because the nasociliary branch innervates the globe, the most serious ocular involvement develops if this branch is affected. Classically, involvement of the tip of the nose (Hutchinson's Sign) is considered to be a clinical predictor of ocular involvement[7]. In the present study, ocular involvement was seen in 37 patients (80.43%) which was similar to Liesgang *et al*[2] study. In our study, conjunctiva was involved in 39 (84.78%) cases. Conjunctivitis is one of the most common complications of herpes zoster ophthalmicus. In our study, cornea was involved in 37 (80.43%) cases, whereas in a study in Ethiopia[6] corneal involvement was seen in 65% and in a study United Kingdom[8] it was seen in 49%. Corneal involvement can result in significant vision loss. The earliest corneal finding is punctate epithelial keratitis. These lesions may either resolve or progress to dendrite formation. In our study, punctate epithelial keratitis was present in 20 (43.47%) cases. Herpes zoster virus dendrites appear as elevated plaques and consist of swollen epithelial cells. They form branching or 'medusa-like' patterns and have tapered ends in contrast to herpes simplex virus dendrites, which often have terminal bulbs. In our study, dendrites were seen in 11 (23.91%) cases. Nummular keratitis is characterised by multiple fine granular infiltrates in the anterior corneal stroma. In our study, nummular keratitis was seen in 4 (8.69%) cases and neurotrophic keratitis was seen in 1 case (2.17%). Neurotrophic keratitis is the end result of decreased corneal sensation from herpes zoster virus mediated destruction, including susceptibility to mechanical trauma, decreased lacrimation and delayed epithelial healing. Corneal thinning is a serious complication that may lead to corneal perforation In our study, uveitis was seen in 12 (26.08%) cases. Patients with uveitis received topical steroids and topical cycloplegics that were tapered according to the clinical response. Zoster uveitis can result in iris atrophy and an irregular pupil. Herpes zoster uveitis may cause glaucoma and cataract formation. Chronic inflammation can lead to endothelial cell injury, resulting in corneal oedema. Herpes zoster virus is considered the offending agent in most cases of acute retinal necrosis and progressive outer retinal necrosis syndromes. Acute retinal necrosis is characterised by peripheral patches of retinal necrosis that rapidly coalesce, occlusive vasculitis and vitreous inflammation. Progressive outer retinal necrosis[9] is more severe viral retinitis observed in immunocompromised persons and it has extremely poor prognosis. Treatment includes long courses of oral and intravenous acyclovir and corticosteroids. In our study, postherpetic neuralgia was reported in 14 patients (30.43%) in three months of follow-up and 2 cases (4.34%) in one-year follow-up. It has been shown that patients with keratitis, conjunctivitis, uveitis had a higher risk of developing postherpetic neuralgia compared with patients who did not have these ocular features.[3]Postherpetic neuralgia is characterised by varying degrees of constant and intermittent pain in the distribution of the affected dermatome, which may last for months to years. In severe cases, patients may be depressed and suicidal. Treatment includes topical capsaicin cream, analgesics, tricyclic antidepressants and anticonvulsants. Cranial nerve palsies involving 3rd, 4th and 6th nerves may occur rarely. Optic neuritis can occur, which is a rare complication of HZO. The main objectives of HZO treatment are lowering the viral replication, accelerating healing, limiting severity and duration of pain and reducing the complications. Patients with HZO are treated with Oral Acyclovir. It was observed that patients in whom Oral Acyclovir was started within 72 hours of onset of skin rash recovered completely. This correlates with prospective controlled clinical trials which have reported a beneficial effect of Acyclovir on ocular complications of HZO.[10] Acyclovir is a synthetic guanosine analogue whose activation requires three phosphorylations. Once activated, it becomes a potent inhibitor of the viral DNA polymerase, a key enzyme for VZV replication.[11] The first phosphorylation is mainly achieved by the viral thymidine kinase (TK), expressed in productively infected cells, thus conferring its selectivity to acyclovir. Nevertheless, acyclovir may also be activated to a lesser extent by cellular kinases, inducing toxicity in rapidly renewing tissues such as corneal epithelium. However, this toxicity is much lower than that of first generation, directly active, antiviral drugs. Acyclovir administered within 72 hours of onset has been found to speed resolution of skin lesions, reduce viral shedding and decrease incidence of dendritic and stromal keratitis as well as anterior uveitis. Valacyclovir has higher bioavailability and is equally safe and effective for the treatment of herpes zoster at a dosage of 1000mg 3 times daily for 7 to 14 days.[12] Famciclovir 500mg orally 3 times a day for 7 days, may also be used. Intravenous acyclovir is recommended in immunocompromised patients. The use of oral corticosteroids in conjunction with antiviral agents is recommended, as this has been shown to reduce duration of pain during the acute phase of the disease. Topical steroids are used to treat

inflammatory components of ocular complications such as stromal keratitis, uveitis, episcleritis and scleritis. It must be noted that use of topical steroids can have serious complications, including worsening of epithelial disease leading to corneal ulceration and perforation. Topical steroids should be used cautiously. Zostavax, a live attenuated varicella zoster virus-based zoster vaccine, has shown to reduce the incidence of herpes zoster among immunocompetent individuals of ≥ 60 years, worldwide. The vaccine boosts the varicella zoster virus- specific cell mediated immunity, thereby controlling the reactivation or replication of the latent varicella zoster virus and prevents herpes zoster infection or reduce its severity.[13]This live attenuated vaccine is not recommended for pregnant women, children and immunocompromised patients.[14] Zoster immune globulin is a gamma globulin fraction of plasma obtained from a patient recovering from herpes zoster.[15] It has to be administered within 72 hours of exposure to varicella.[16] Zoster immune globulin has provided an effective post exposure prophylaxis in preventing or modifying varicella zoster virus.

CONCLUSION

HZO can cause visual loss and debilitating post herpetic neuralgia. Early diagnosis and prompt treatment reduce the rate and severity of these complications. Antiviral medications like Acyclovir, Valacyclovir and Famciclovir remain the mainstay of therapy and are effective in preventing serious ocular complications of HZO when begun within 72 hours of onset of skin rash. In the future, a reduction in incidence and severity of HZO may result from a more widespread use of Zostavax vaccine.

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