A Rare Case of Herpes Zoster Ophthalmicus Secondary to Methotrexate Induced Immunosuppression

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INTRODUCTION

Herpes zoster ophthalmicus (HZO) is defined as herpes zoster (HZ) due to involvement of the ophthalmic division of the fifth cranial nerve.[1] It is the second most common type of herpes zoster, after thoracic zoster. Herpes zoster affects about 20% of the world's population at least once in their lifetime, with nearly 20% of these showing an ophthalmic involvement.[2] It is estimated that 1 million adults in the USA are afflicted with herpes zoster every year. The risk of developing herpes zoster increases considerably with age, reaching 50% in those aged 85 or older. Advanced age and dysfunctional cell-mediated immune responses are two well-established risk factors for varicella zoster virus reactivation. Other risk factors, such as female gender, Caucasian ethnicity, diabetes mellitus, psychological stress, mechanical trauma, heavy metal exposure, as well as family history, have also been postulated. It causes debilitating pain, neuropathy and inflammatory complications.[3] Herpes zoster ophthalmicus may present with ocular involvement such as conjunctivitis, keratitis, iritis, and uveitis. It can also present without ocular involvement (where only the skin of the V_1 dermatomal region is affected). Herpes zoster infection may rarely present without any cutaneous manifestation, also known as "zoster sine herpete," with or without ocular involvement, rendering the diagnosis more difficult.[4] Timely diagnosis of herpes zoster ophthalmicus, with an early recognition of its various associated complications as well as their management, along with an early referral to an ophthalmologist are all critical in limiting visual disability. We report such a rare case of herpes zoster ophthalmicus due to methotrexate induced immunosuppression.

Herpes zoster also called shingles, occurs due to reactivation of varicella-zoster virus (VZV) or the human herpes virus 3 infection. Herpes zoster ophthalmicus is herpes zoster characterized by usually unilateral radicular pain and vesicular eruption limited to the dermatome involving the ophthalmic branch of the trigeminal (Vth cranial) nerve. It may lead to ocular complications including blindness. It is seen more commonly among individuals aged more than 50 years, those with immunocompromised status, and those on immunosuppressant drugs. Herpes zoster occurring due to immunosuppression caused by drugs such as methotrexate, infliximab, azathioprine, corticosteroids, mesalamine has been rarely reported. We are reporting one such rare case of herpes zoster ophthalmicus occurring due to methotrexate induced immunosuppression.

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PRESENTATION OF CASE

A 45-year-old female patient presented with few painful grouped blisters with surrounding redness over the left forehead and the left eye region since 2 days (figure 1a and 1b). There was no history of chronic weight loss, chronic diarrhoea and chronic fever or malaise. Patient was a known case of palmoplantar psoriasis (figure 2 and 3) for which oral methotrexate 5 mg once a week was advised by a dermatologist. Patient inadvertently took oral methotrexate 5 mg daily once for 4 days. Within a week she developed these painful grouped vesicles. She was not a known case of hypertension/diabetes mellitus/hypothyroidism/bronchial asthma. Appetite was normal. Diet was mixed. Bowel and bladder habits were regular. On general examination, Patient was moderately built and nourished. There was no pallor, icterus, cyanosis, koilonychia, lymphadenopathy or pedal oedema. Vitals were stable. Cutaneous examination revealed few grouped vesicles with surrounding erythema and few erosions on left side of the forehead (in distribution of ophthalmic division of trigeminal nerve) extending to involve the nose and fronto-temporal areas (figure 1a and 1b). Left eye showed conjunctival congestion and watering. Laboratory parameters were within normal limits. HIV status was nonreactive.

Differential diagnosis of herpes zoster ophthalmicus, irritant contact dermatitis, and Insect bite were considered. A clinical diagnosis of herpes zoster ophthalmicus due to immunosuppression caused by methotrexate was made based on the characteristic clinical manifestation of grouped painful vesicles in the distribution of ophthalmic division of trigeminal nerve with intense pain. Patient was treated with oral acyclovir (antiviral drug) 800 mg 5 times a day for 5 days and symptomatic treatment. Patient recovered in 10 days (figure 4) without any complications. There was no associated bone marrow suppression such as pancytopenia.

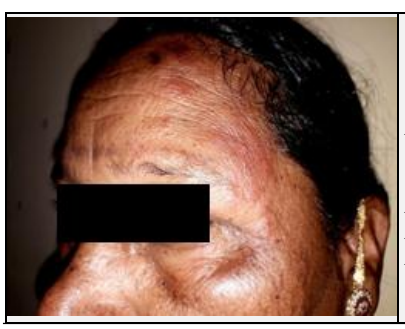

Figure 1a. Grouped Vesicles with Surrounding Erythematous Base Involving Ophthalmic Division of Left Trigeminal Nerve

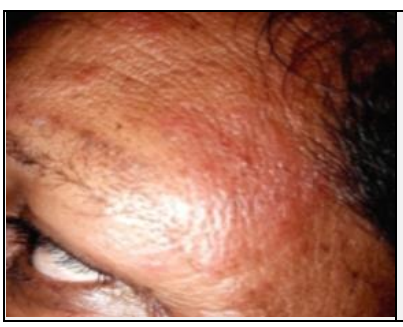

Figure 1b. Closeup View Showing Grouped Vesicles with Surrounding Erythema on the Left Side of Forehead Region

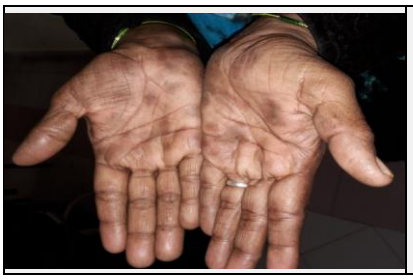

Figure 2. Multiple Discrete Well Defined Psoriatic Plaques and Post Inflammatory Hyperpigmentation over Bilateral Palms

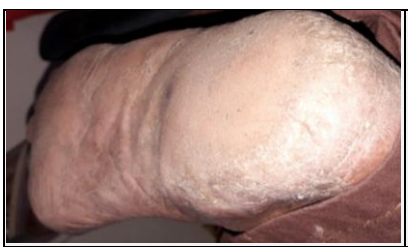

Figure 3. Multiple Discrete Well Defined Psoriatic Plaques and Post Inflammatory Hyperpigmentation over the Sole

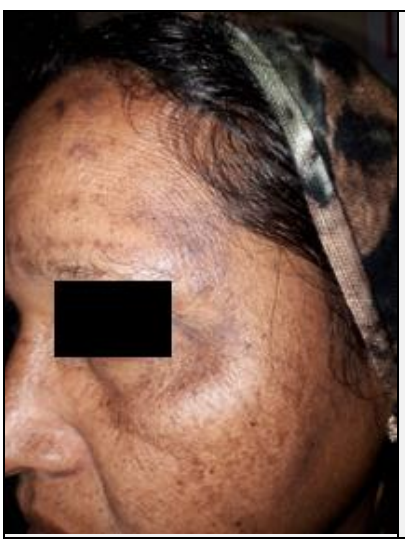

Figure 4. Post Inflammatory Hyper Pigmented Macules on the Left Side of Forehead Region after 10 Days of Healing of Herpes Zoster

DISCUSSION

Herpes zoster also called shingles, occurs due to reactivation of varicella-zoster virus (VZV) or the human herpes virus 3 infections.[5] following the primary varicella (chickenpox) infection, the virus remains dormant in the dorsal root or other sensory ganglia. Reactivation usually occurs due to a decline in the specific cell-mediated immunity to varicella zoster virus with aging, immunosuppression, or both. Role of cell mediated immunity is evident due to occurrence of herpes zoster more commonly in elderly black patients than in elderly whites.[6] Other risk factors for herpes zoster are elderly age, diabetes mellitus and also with immunosuppressant drugs such as methotrexate, infliximab, azathioprine, mesalamine, glucocorticoids.[7] Patients suffering with rheumatoid arthritis commonly suffers with herpes zoster because they are on immunosuppressant therapy.[8] Herpes zoster ophthalmicus was reported in a patient with Wegener's Granulomatosis due to oral cyclophosphamide treatment.[9] MDMA "ectasy" (3,4-Methylenedioxymethamphetamine) resulted in herpes zoster ophthalmicus has been reported.[10]

Fever, pain, and itch are common symptoms before the onset of grouped painful vesicles. Post-herpetic neuralgia is the pain which persists after 6 weeks and is the most common complication associated with herpes zoster. Complications of

herpes zoster are more common among elderly individuals and immunosuppressed patients. An immunocompromised patient is more likely to have a prolonged illness, more likely to recur, and more likely to develop myelitis and vasculopathy.[11] The incidence of herpes zoster in HIV-positive individuals is seven times greater than that of the general population. Thus, HIV infection should be considered in individuals who develop herpes zoster, and especially in those who develop disseminated herpes zoster associated with immune-suppression.[12] disseminated herpes zoster is defined as more than 20 small widespread vesicles resembling varicella outside the area of the primary and adjacent dermatomes, and may or may not involve visceral organs. It has been mainly described in the elderly or persons with immunosuppression due to HIV infection, hematologic malignancy, or chemotherapy; in otherwise healthy individuals it is very rarely reported. But, disseminated herpes zoster may be the first manifestation of HIV infection. Therefore, it is important to recognize this disease as having a high predictive value for HIV infection, and therefore perform necessary laboratory work to ascertain HIV status.[13]

Herpes zoster and its complications can impact the patient's quality of life. The other complications noted include secondary bacterial infections, ophthalmic complications, cranial and peripheral nerve palsies, and segmental zoster paresis.[14] Herpes zoster ophthalmicus is a serious condition occurring in 8%–56% of all herpes zoster cases and the frontal branch of ophthalmic division of the trigeminal nerve is most frequently involved. With the onset of a vesicular eruption along the trigeminal dermatome, hyperaemic conjunctivitis, eviscerates, and lid droop can occur. The eye is usually spared when supratrochlear and supraorbital branches are involved. Ophthalmic complications include lid scarring, paralytic ptosis, conjunctivitis, neurotrophic keratitis, episcleritis, scleritis, iridocyclitis, choroiditis, acute retinal necrosis, glaucoma, ophthalmoplegia, and optic atrophy.[15] Corneal involvement may present as punctate epithelial keratitis or disciform stromal keratitis. Herpetic uveitis commonly presents as unilateral anterior uveitis.[16]

About 12% of all peripheral facial nerve palsies are caused by varicella zoster virus. The occurrence rate of associated cranial polyneuropathy has been reported to be 1.8-3.2% and cranial nerves VII, VIII, IX and X are the ones most commonly affected.[17] A diagnosis of HZ is made by characteristic clinical features. Rarely laboratory diagnosis is based on Tzanck smear from the base of the vesicles scrapings that reveal multinucleated giant cells on direct microscopy.[18] The other methods are by direct fluorescent antibody tests, presence of high or rising titers to varicella zoster virus, or by culture studies. Direct fluorescent monoclonal antibody test or detection of serum specific IgM by the indirect fluorescent antibody method is also used to confirm herpes zoster.[19]

Systemic antiviral therapy such as acyclovir, valacyclovir, and famciclovir remain the mainstay of therapy and are most effective in preventing ocular involvement when begun within 72 hours after the onset of the painful grouped vesicles is the mainstay of treatment.[20] However, consultation with an ophthalmologist is typically indicated. Topical acyclovir has no prophylactic effect in managing herpes zoster ophthalmicus. An 830 nm light-emitting diode (LED) therapy with famciclovir showed faster wound healing and decreased pain score among herpes zoster ophthalmicus patients compared to famciclovir alone.[21] Ganciclovir gel has shown a rapid healing effect in patients with persistent or recurrent pseudo dendrites in herpes zoster ophthalmicus. The drug acts only on the infected cells and hence has a good efficacy and is less toxic. In our case we treated the patient with systemic antiviral drugs (acyclovir 800 mg five times a day for 5 days) along with oral analgesics and antibiotics and methotrexate was withdrawn. Patient recovered in 10 days without any complications as there was no bone marrow suppression.

CONCLUSIONS

Herpes zoster ophthalmicus is an uncommon disease in healthy individuals and risk factors are elderly age, immunocompromised state including HIV/AIDS and immunosuppressant drugs. Herpes zoster ophthalmicus is more common in old age and can occur even at younger age usually due to immunosuppression caused by HIV/AIDS or immunosuppressive drugs. We are reporting a rare case of herpes zoster ophthalmicus due to methotrexate induced immunosuppression, given for palmoplantar psoriasis. Methotrexate was withdrawn and patient responded well to antiviral treatment.

Declaration of Patient Consent

The authors have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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