Herpes Zoster of orofacial region- A review

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Abstracts: Herpes zoster is a disease of adulthood caused by reactivation of varicella zoster virus which lies dormant in sensory ganglia. Immunocompromised patients i.e. with malignancy/organ transplantation/AIDS; patients taking immunosuppressive drugs are more susceptible for herpes zoster infection. Various prodromal features like pain, odontalgia, fever and regional lymphadenopathy precede the active lesions of herpes zoster- i.e. unilateral vesicles (cutaneous/oral) and ulcerations follows pathway of dermatome and this clinical appearance is sufficiently distinctive to make clinical diagnosis of herpes zoster accurately without any other investigations. Antiviral drugs e.g. Acyclovir, Famcyclovir and Valacyclovir with symptomatic treatment are treatment of choice for herpes zoster infection.[Mehta D et al NJIRM 2013; 4(1) : 112-116]

Key Words: Herpes zoster, varicella, vesicles

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Introduction: Herpes zoster is a secondary infection caused by reactivation of endogenous latent virus-varicella zoster virus, that exists in the host from an earlier primary infection varicella (chickenpox).[1-4] The herpes zoster infection however is generally restricted to a sensory ganglion, its peripheral nerve processes and the epithelial surfaces innervated by that nerve(dermatome)[4]

OCCURRENCE:

Age: Incidence of herpes zoster increased with age. In USA it had been reported that more than 66% of affected patients are older than 50 years. Of all patients with herpes zoster infection, less than 10% are younger than 20 years and 55 are younger than 15 years. Although it is primarily a disease of adults, it had been noted as early as the first week of life due to primary Varicella Zoster Virus (VZV) infection during pregnancy.[5,6,] **Sex:** Certain studies showed that men and women are equally affected with herpes zoster infection [6] while various other studies suggested that herpes zoster had a slight male predominance.[7-13]

ETIO-PATHOGENESIS:

Risk Factors: The cause for reactivation of latent virus is not known**.** Patients with following conditions are considered risk factors for herpes zoster virus infection. They are age >50 years, deficiency in cell-mediated immune defense i.e. Malignant lymphomas, Leukemia and HIV infected patients (25%), patients taking immunosuppressive drugs (i.e. corticosteroids) and cytotoxic drugs, patients having organ transplants–renal, cardiac and bone marrow transplantations (7-9%),in utero varicella exposure, primary varicella zoster infection , stress ,trauma ,local irradiation. [1,6,13]

Pathogenesis: Varicella zoster virus which lies latent in the ganglionic neuron is reactivated from time to time, but the host's immune defense prevents clinical illness. Humans are infected with varicella zoster virus when comes in contact with mucosa of upper respiratory tract/conjunctiva, virus disseminated throughout the blood stream to the skin in mononuclear cells and producing generalized rash. Incubation period is 14 days. Other organs are also infected occasionally including Central nervous system. Virus infects, becomes latent in dorsal root and cranial nerve ganglia, limits its expression of viral proteins during latency.[2],[6] According to recent theory, virus remain in both neuron and satellite cells. Infection with varicella zoster virus induces production of cytotoxic-T cells that recognize and destroy virus infected cells. So cellular immunity is more important than humoral immunity both for limiting the extent of primary infection with varicella zoster and for preventing reactivation of virus with Herpes Zoster. Children with congenital T cell defects and HIV infected patients are more likely to develop disseminated chickenpox and zoster than B-cell abnormalities.[2]

PRODROMAL FEATURES:[1,3,7,13-16]

Pain- burning, itching or sharp, odontalgia(pulpitis),headache, chills, fever

,malaise, gastro-intestinal disturbances, photophobia , regional lymphadenopathy, pruritus. Pain in a dermatomal distribution is a classical finding of herpes zoster,[5] often preceding the eruption by days to weeks and occasionally the only manifestation. Most patients report a deep aching or burning pain, altered sensitivity to touch (paresthesia) that may be painful (dysesthesia), exaggerated responses to stimuli (hyperesthesia) or electric shock like pain. Itching / tingling sensation may present.[16] The pain associated with acute zoster is neuropathic and results from injury of the peripheral nerves and altered CNS signal processing. After the injury, peripheral neurons discharges spontaneously, have lower activation thresholds and display exaggerated responses to stimuli. The excessive peripheral activity is thought to lead to hyperexcitability of the dorsal horn, resulting in exaggerated CNS response to all input. Dermatomal pain without a rash referred to as zoster sine herpete.[11]

CLINICAL FREATURES:

Cutaneous Lesions: The lesion usually starts as an erythematous maculopapular rash which quickly evolves into a vesicular eruption. These vesicles are oriented along the track of dermatomal innervations and cutaneous eruption is unilateral and doesn't cross the midline. Pustules from in 3-4 days and they dry and develop a crust by day 10. After the lesions had crusted, they are no longer considered infective. However, crusting and new lesion formation may occur simultaneously. Therefore, the patient can still infect other individuals as long as active lesions are present. Skin lesions usually resolve into 2-3 weeks usually leave scars along the cutaneous distribution of nerve affected.[1]-[6],[8],[11]-[13,][16]-[18]Motor neuropathies had been reported in very few cases (5%) in herpes zoster infection.[3],[5] Herpes Zoster of sacral region may cause paralysis of the bladder. The extremities and diaphragm have also been paralyzed during episodes of Herpes Zoster infections.[17] Ramsay Hunt Syndrome is an infection of the geniculate ganglion of seventh cranial nerve seen in 50% of motor neuropathies characterized by Bell's palsy, unilateral vesicles of the external ear and vesicles of the oral mucosa.[17] This syndrome can lead to loss of taste perception hoarseness, tinnitus, hearing loss, vertigo. [5,18]

Oral Manifestations: According to various studies, the mucous membrane manifestations usually appear after the skin manifestations but oral mucosal lesions can appear with or without skin lesions and usually heal without scar. Various studies showed different oral manifestations of herpes zoster infection. It usually manifests as painful unilateral vesicles surrounded by erythematous zone, soon burst and coalesce leaving superficial fibrin -covered ulcerations. These lesions may present on the buccal mucosa, tongue, uvula, pharynx and larynx.(Fig 1) In various studies, other oral manifestations of Herpes Zoster like osteonecrosis, tooth exfoliation, devitalization of teeth, abnormal development of teeth, missing teeth, irregular shorter roots, calcified pulps, internal resorption of teeth also had been reported.[3,4,7,12,13,19-21]Cellulitis is one of complications of herpes zoster infection as a result of secondary bacterial infection- α-β hemolytic streptococcal.[2]

Spontaneous tooth exfoliation and mandibular osteomyelitis are the dental complications of herpes zoster infection. Possible etiopathogenesis of herpes zoster-bone necrosis.[17] Local vasculitis by direct extension of neural inflammatory process to the adjacent blood vessels, causing infraction of trigeminal vessels that accompany the trigeminal nerves supplying the jaws. A generalized infection of terminal nerves supplying the periosteum and periodontium is believed to cause avascular necrosis.

Denervation of bone: Systemic viral infection can injure odontoblasts and cause degenerative tissue changes that result in pulp necrosis. Preexisting periodontal or pulpal inflammatory conditions have the potential to contribute to a greater probability of tooth exfoliation and bone necrosis.

Dermatomal Involvement: Herpes Zoster typically erupts within one or two adjacent dermatomes, with thoracic (50-60%), cervical (10-20%), trigeminal (10-20%)[7] are most commonly involved

dermatomes. Lumbar (5-10%), sacral (5%) are other less common dermatomes.[2,6] Simultaneous involvement of noncontiguous dermatomes virtually never occurs in immunocompetent patients, although lesions overlap adjacent dermatomes in 20% cases, can also be seen in immunocompetent patients.[1] When 20% or more lesions fall out side the dermatomal pattern, disseminated herpes zoster infection is probable and severely disseminated disease may be the evidence of underlying lymphoma or other immunodeficient condition.[5] Although involvement of ophthalmic division is more common(15-20 times more) but oral and facial lesions due to herpes zoster infection are usually reported with involvement of maxillary and mandibular divisions of trigeminal nerve.(Fig. 2)

Complications: Postherpetic neuralgia (PHN) is most important complication of the Herpes Zoster infection. It results from injury of multiple sites in the peripheral and central nervous systems. It is the most common and prominent complication of Herpes Zoster. It has been variably defined as persistence of sensory symptoms for 1 month, 6 weeks, 2months, 3 months and 6 months after Herpes Zoster infection. Overall, 10-20% individuals had been reported with PHN after the acute phase of Herpes Zoster infection and had been reported to be more than 20% in elderly.[10] Secondary bacterial infection is another common complication of Herpes Zoster. In recent years, group A -ß hemolytic streptococcal infections-including cellulitis, necrotizing fascitis increasingly complicates the course of varicella**.** Other complications like scars of skin, keratitis,retinal necrosis causing blindness, keratouveitis, cranial and peripheral nerve palsies, cerebral ataxia, pneumonia may lead to death also occur.[2-5,7,9,12,13,15]

INVESTIGATIONS: The distribution of vesicular rash on skin follows nerve pathway. Appearance of Herpes Zoster is sufficiently distinctive that a clinical diagnosis is usually accurate. In immunocompromised patient, cutaneous lesions may be atypical and thus require laboratory confirmation.[1,2,5,6.17,18]

Viral culture**:** It is possible but VZV is labile and relatively difficult to recover form swabs of cutaneous lesions, only 30-60% cultures are positive.

Tzank Smear**:**It is prepared from fluid contained in vesicular lesions and confirms the lesion is herpetic or not. The test does not differentiate among Herpes Zoster and Herpes Simplex.

Direct Immunofluorescence Assay**:**This is more sensitive than viral culture, having advantages of low cost, more rapid.

Polymerase Chain Reaction Techniques**:** These are useful for detecting DNA of VZV in fluid and tissues.

Concentration of a rising antibody titer is rarely necessary for diagnosis except in case of zoster sine eruptions when it is the only means of confirming suspected cases.[17]

Treatment: Antiviral drugs[1,2,4-6,9,16-19,22]Antiviral treatment should be started within 72 hours of cutaneous eruption, because most virus replication ceased by 72 hours after onset of rash. They are effective up to some extent. Three drugs are approved for the treatment of Herpes Zoster infection. They are: Acyclovir – 800mg 5times/day for 7-10 days; Famciclovir – 500mg 3 times/day for 7 days; Valacyclovir – 1000mg 3 times/day for 7 days. These three drugs are guanosine analogues that are selectively monophosphorylated by the viral thymidine kinase and are further phosphorylated by cellular kinases and thus inhibit the viral DNA polymerase.[2]Acyclovir (800mg 5times/day for 7-10 days) shortened the duration of viral shedding, halted the formation of new lesions, more quickly accelerated the rate of healing and reduced then severity of acute pain. Variable benefit are recorded with respect to reduction in the frequency and duration of postherpetic neuralgia (PHN).Valacyclovir, a prodrug of acyclovir produces serum acyclovir level 3-5 times as high as those achieved with oral acyclovir therapy. In a randomized trial of patients who are at least 50 years of age, Valacyclovir and

acyclovir resulted in equivalent rates of cutaneous healing. Famciclovir, a prodrug of pencicloivr is proved significantly superior to placebo. Valacyclovir and Famciclovir are compared for treatment of herpes zoster in immunocompetent patients and are shown to be therapeutically equivalent in terms of both the rates of cutaneous healing and pain resolution. There is no role for topical antiviral drugs in management of herpes zoster.In HIV infected patients, acyclovir is proved to be effective while Famciclovir and Valacyclovir are not systemically evaluated. In acyclovir resistant cases of HIV patients, Foscarnet had been proved effective. Other antiviral i.e. cidofovir, pencicloivr, vidarabine, cytarabine, ganciclovir had been tried for herpes zoster infection but not recommended for routine use.[5] The use of corticosteroids in the treatment of herpes zoster has been controversial. The benefits of therapy (i.e. limiting pain, inflammation) had been countered by the fear of a reduced immune response leading to disseminated varicella zoster infection and is contraindicated in many patients (e.g. diabetes mellitus, hypertension, immunocompromised patients).[5] It had been tried in combination with acyclovir and moderate but significant acceleration in the rate of cutaneous healing and alleviation of acute pain is noted. However, neither study demonstrated any effect of corticosteroids on the incidence or duration of PHN. The use of corticosteroids for herpes zoster without concaminant antiviral therapy is not recommended.[1]Capsiacin is the only topical preparation approved for the temporary relief of pain associated with herpes zoster infection. It should not be applied until the skin lesions have healed. [2,5]Symptomatic treatment like clean and dry cutaneous lesions,sterile nonadherent dressing over dermatome to protect the lesion, topical application (i.e. Calamine lotion),sympathetic nerve blockade, analgesics (aspirin and others) can be used. [1,5,6]

Prevention of herpes zoster infection: Studies are under way to determine whether administering the live vaccine to elderly persons can boost immunity specific to varicella-zoster virus and modify the course of zoster infection. Available data showed that immunologic boosting may reduce the herpes zoster incidence.[2]

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