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Herpes zoster: An observational study and an overview

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ABSTRACT

Herpes zoster is a very common viral infection with disabling complications like post herpetic neuralgia in the affected dermatomes. Though this study was aimed to identify the most common dermatome involved, we also tried to find out the underlying triggers which herald the onset of this condition. Adequate treatment at appropriate time will prevent the complications associated with this disease, thereby enhancing quality of life for all patients.

1. Introduction

This is a novel type of study attempted by the authors to determine the type of involvement in Herpes Zoster[HZ] segment wise. Which helps us in turn to assess the pattern of disability in patients owing to development of delayed complications like post herpetic neuralgia [PHN]. In many of the patients PHN was so disabling that it was difficult for patients to carry out routine activities like wearing clothes(paresthesia owing to PHN) , brushing teeth, watering of eyes, inability to sleep on the affected side, even some of the patients experienced difficulty in raising hands over their heads (usually cervical segment involvement).

Authors were also interested in interpreting any of the underlying co morbidities which were triggering the herpes zoster onset.

2. Aims and Objectives

1. To determine the most common segment involved in the patients.
2. To assess retrograde /any underlying predisposing factors for the occurrence of zoster.

3. Materials and Methods

Patients were diagnosed as a case of HZ based on the classical appearance of lesions like grouped vesicles arranged in a particular segment of the body unilaterally.

The study was conducted for a duration of 2 years. A total of 187 patients participated in the study. Of these, 115 patients were males and 72 were females.

3.1. Inclusion criteria

1. All of those patients who were willing to participate in the study and come for regular follow up.
2. Patients who developed herpes zoster and consented for participation in the study.

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3.2. Exclusion criteria

Patients who were unwilling to participate in the study and come for regular follow up.

Patients were treated with Tab. Valacyclovir 1g tid for 7 days. To maintain uniformity of study participants; all were treated with the same regimen & hence patients were deferred from prescribing other drugs like acyclovir, Famcyclovir etc.

We preferred valacyclovir compared to other drugs owing to it's increased bioavailability.

4. Results

Table 1:

Male	Female	Total
115	72	187

As seen in the above table male patients were more in numbers than females. Findings of other studies with regard to male to female ratio is discussed subsequently.

Table 2:

Dermatome involved	Number of patients
Trigeminal	33
Cervical	27
Thoracic	54
Lumbar	64
Sacral	9

According to our study as recorded in the above table, lumbar segment (34.22%) was the most commonly involved, followed by thoracic (28.8%), trigeminal (17.64%), cervical (14.4%). Sacral segment (4.8%) was was the least affected.

Table 3:

Predisposing factors	Total patients
Surgery (pre and post-operative)	34
acute stressful episode	26
other infections	17
Immunosuppression	19
spontaneous	91

As we noted in this study, interestingly most of the patients didn't have any underlying predisposing element for HZ to occur; so disease appeared spontaneously (48.6%). Next majority was either pre or post operative surgery patients (18.1%), acute stressful events like loss of a loved one, divorce, professional setbacks were observed in 13.9%. Immunosuppression in HIV positive individuals, malignancy, post chemotherapy led to HZ in 10.16% of our patients. Other underlying systemic infections like cholecystitis, pulmonary koch's were seen in 9.09% of patients before onset of HZ.

5. Discussion

Studying Anatomy of the segments helps us to understand underlying limitations of that particular part involved during PHN. Hence a detailed study of dermatomes. [1]

Dermatomes of the Head and Neck.

5.1. Divisions of the trigeminal nerve (cranial nerve [CN] V1, V2, and V3)

Most of the skin of the face, including anterior aspect of lower jaw (CN V3); the area of skin in front of both ears; superior part of the lateral aspect of the auricle (CN V3)

5.2. Cervical plexus (ventral rami of C2-C4)

Skin over the angle of the mandible, anterior to and behind the ear, the anterior neck and back of the head and neck; inferior part of the lateral aspect of the auricle and skin on medial aspect of the auricle; the lateral and anterior aspects of the neck

Greater occipital nerve (dorsal ramus of C2), third occipital nerve (dorsal ramus of C3), and the posterior divisions of C4-C6:

The posterior aspect of the head (C2) and neck (C3) with C4-C6 innervating the back of the neck.

5.3. Dermatomes of trunk

The dermatomes of the trunk are relatively evenly spaced out; however, considerable overlap of innervations between adjacent dermatomes often occurs. Thus, a loss of afferent nerve function by one spinal nerve would not generally cause complete loss of sensation, but decrease in sensation may be experienced.

T3 dermatome: Runs along the third and fourth interspace

T4 dermatome: Nipple line

T6 dermatome: At the level of the xiphoid process

T10 dermatome: Level of the umbilicus

T12 dermatome: Just above the hip girdle

Remaining thoracic spinal nerve dermatomes: Relatively evenly distributed between the above mentioned thoracic dermatomes

L1 dermatome: The hip girdle and the groin/inguinal area

Dermatomes of the Upper Extremity

Third and fourth cervical nerves: Limited area of skin over the root of the neck, upper aspect of the pectoral region, and shoulder

C5 dermatome: Lateral aspect of the upper extremities at and above the elbow.

C6 dermatome: The forearm and the radial side of the hand.

C7 dermatome: The middle finger.

C8 dermatome: The skin over the small finger and the medial aspect of each hand.

T1 dermatome: The medial side of the forearm.

T2 dermatome: The medial and upper aspect of the arm and the axillary region.

Dermatomes of the Lower Extremity and Genitalia.

L1 dermatome: The skin over the back lateral to the L1 vertebra; wraps around the lower trunk/upper part of lower extremity to the hip girdle and the groin area.

L2 dermatome: Anterior aspect of each thigh; the skin over the medial aspect of the mid thigh.

L3 dermatome: Anterior aspect of each thigh; anterolateral thigh and continues down to the medial aspect of the knee and the medial aspect of the posterior lower leg, proximal to the medial malleolus.

L4 dermatome: Posterolateral thigh and the anterior tibial area; it crosses the knee joint over the patella and also covers the skin over the medial malleolus and the medial aspect of the foot and the great toe.

L5 dermatome: Posterolateral thigh (just inferior to L4 dermatome) and wraps around to lateral aspect of the anterior lower leg and dorsum of the foot; it crosses the knee joint on the lateral aspect of the knee; also covers the plantar aspect of the foot and the second through fourth toes.

S1 dermatome: The heel, the lateral aspect of the foot, the lateral aspect of the posterior thigh, and most of the posterior lower leg.

S2 dermatome: Most of the back of the thigh and a small area along the medial aspect of the posterior lower leg; the penis and scrotum.

S3 dermatome: The medial aspect of the buttocks; perianal area; penis and scrotum.

S4 dermatome: Skin over the perineal region (along with S5); perianal area and genitals.

S5 dermatome: Skin over the perineal region (along with S4); the skin immediately at and adjacent to the anus.

Bhavsar et al noted that COVID-19 diagnosis in middle aged to elderly patients was associated with a significantly elevated risk of developing HZ, hence revealing the relevance of regular HZ vaccination[2].

Similar to our study, wherein we also encountered few patients with HZ reactivation after covid 19 vaccination, agarwal et al also found around 10 patients who presented in a same manner to their OPD.[3] But this shouldn't defer patients from vaccinating themselves against covid 19 vaccine. Hence the underlying predisposing factor (Covid19 vaccine) should be kept in mind by all dermatologists.

Elderly patients have a very high incidence of HZ. Varicella zoster virus during primary infection leads to varicella, during that period it lodges into dorsal root ganglion. Those patients who have reduced immunity usually have occurrence of HZ more frequently than normal population. Post herpetic neuralgia is very common and intolerable symptom leading to activity limitation and extreme pain in affected part. Varicella sometimes can cause meningoencephalitis or meningitis, cerebellitis, or the Ramsay Hunt syndrome, multiple cranial nerve palsies (polyneuritis cranialis), vasculopathy, myelopathy, isolated cranial nerve palsies that produce ophthalmoplegia and other inflammatory disorders of other organs and eyes. For cases which are not responding to drugs; psychological, interventional and physical therapies may be used. Pulsed radiofrequency can also be put into use. Researchers are contemplating about prevention of infection because eradication of the virus is difficult. Quality of life becomes poor in patients worldwide due to HZ infection and it's aftermath.[4]

One of our patient went to medicine opd for chest pain, just the very next day lesions of HZ erupted in her in the left thoracic segment. One more patient who underwent radiation therapy for Ca Rectum, developed these lesions in the pelvic (lumbar) segment. Another patient came with watering and pricking sensation in the right eye, he developed HZ ophthalmicus after 24 hours. Rosamilia et al also noted that prodromal pain can mimic an episode of acute angle-closure glaucoma, costochondritis, myocardial infarction, renal colic, stroke, appendicitis, cholecystitis,, pulmonary embolus etc., to name a few of these pathologies.[5]

Out of overall cases of HZ, Disseminated HZ is seen in approximately 2%. It can be defined as at least 20 widespread vesiculobullous lesions which are found outside of the primary and adjacent dermatomes. And these lesions evolve for 1–2 weeks beyond the primary presentation. Pain is the most prominent feature of disseminated HZ and higher risk of neurologic, secondary bacterial infection complications and lung infections can be seen. This resembles primary varicella zosteremia.[5]

Besides early treatment of HZ which can significantly lower the complications like PHN, there's an interesting proposal by Bardach et al; vaccination of the elderly and at risk population. Because similar to our observations they also found a less incidence in the general population of HZ, with a constant progression n the rate of incidence among elderly people and high-risk population.[6]

We found male > female in our study in contrast to a study by patil et al wherein ratio of female to male was more[7]

Whereas Sharma et al found findings similar to our study that is male > female.[8]

Sharma et al noticed the dermatomal involvement in H Z patients to be in the order thoracic > ophthalmic.[8] In our study we found that highest number of involvement was seen in lumbar segment, followed by thoracic segment. Third most commonly affected was trigeminal, fourth was cervical. Lastly, the least affected was sacral segment. Whereas a study by koshy et al found that first was thoracic, second was lumbar, third most common was cervical and sacral segment was least affected. Increased HZ virus spread way beyond the isolated ganglion nerve

dermatome unit is seen among patients who have a deficient in macrophage-mediated immune defense and T lymphocyte functions. Sometimes which may lead to overlapping of few adjacent dermatomes. Disseminated HZ leads to involvement of cardiovascular system, lungs, skeletal system, gastrointestinal system, central nervous system (CNS), bladder, mucous membranes, liver and blood vessels can be seen. Mortality is high in patients with involvement of the CNS, lungs and liver.[9]

Pott junior et al have provided in a compact manner described the course of viral reactivation. From the dorsal ganglia peripheral and central spread of HZ virus is seen which produces intense inflammation of the skin, affecting the nerve roots and peripheral nerves. Spinal cord involvement is also seen. Pain is characteristically associated with vesicular rash and pain can occur before the onset of rash. Sometimes without the development of a rash in rare cases (herpes sine herpete).[10]

Wang et al noticed that most of the HZ was centered around trunk (thoracic & lumbosacral) followed by neck and upper limbs (cervical dermatome), lower limbs and perineum (sacral) & head(cranial nerves); whose findings are almost similar to our studies.[11]

As mentioned in Rook's dermatology textbook, 53% of involvement is seen in thoracic segment, 20 % of cervical segment cases are found;usually C2, 3 or 4. 15% of cases were having trigeminal involvement. Which included ophthalmic segment (most common) . Also lumbosacral dermatomal involvement was seen in 15% of cases; ophthalmic zoster increases in old age.

Incubation period of HZ is around 1.4 days in trigeminal zoster and 3.2 days in thoracic dermatome. The lesions erupt either continuously or in an interrupted pattern, but terminate exactly at the midline. Lesions are grouped vesicles, coalescing in nature; sometimes secondary bacterial infection can be seen leading to pustules formation. Single or contiguous dermatomal involvement can be seen. Oral and genital mucosal involvement is seen in particular dermatome which is affected. Eruption of new vesicles beyond a few days of primary eruption is also seen. Approximately 16% of patients, develop vesicles beyond the dermatome within the initial few days of the local eruption. Healing with scarring is seen in undernourished and elderly population, sometimes lesions may undergo necrosis. Regional lymphadenopathy is almost always present. In elderly patients recovery period is longer stretching upto 4 weeks, whereas in young adults and children it may take upto 3 weeks.

5.4. Trigeminal nerve zoster

In 66% of the cases of ophthalmic nerve zoster, ocular involvement is observed. When nasociliary nerve is involved, vesicular eruptions are observed on lateral aspect of nose; also called as Hutchinson sign. Ophthalmological involvement leads to complications like proptosis, conjunctival oedema, ocular muscle palsies, scarring and even necrosis of the lid, keratitis, uveitis, retinal vascular occlusion, conjunctivitis, scleritis, ulceration. Argyll–Robertson pupil is seen if ciliary ganglion is involved.

Motor involvement is seen in 5% of cases. Most frequently seen in carcinoma affected individuals and elderly population. Motor involvement is more common in cranial component affection rather than spinal. Pain and eruption precedes motor weakness by few days to weeks. 55% of patients undergo complete recovery and a further 30% have significant improvement. HZ in auricular segment leads to 10% of facial palsy cases. Recovery in Ramsay Hunt syndrome patients is only limited to 20%. Defecation or urination disturbances are found in HZ of the ano genital area.[12]

Acute, sub acute and chronic are the 3 stages of pain in cases of HZ. In the acute stage pain develops within 30 days of appearance of skin rashes. Whereas in the sub-acute stage pain persists beyond the acute stage, but resolved before PHN. The final stage is PHN itself, characterized by chronic neuropathic pain persisting at least > 1month in the pathway of the affected nerve, usually ranging between 1-6 months after skin rashes have healed and they may last for years.[13]

In pain accompanying acute herpes zoster the neuropathology and acute inflammation of acute herpes zoster are maximal within the dorsal root ganglion of the affected dermatome but extend peripherally along the length of the sensory nerve and sometimes proximally to the adjacent motor and sensory roots and the spinal cord. Peripheral sensitization is due to the damage to neurons secondary to VZV replication in acute herpes zoster. This results in an increase in the responsiveness and sensitivity of nociceptors. This is a consequence of the associated release of cytokines during initial inflammatory response to neuronal destruction. The pain associated with acute HZ is not produced by stimulation of the high threshold sensory receptors (nociceptors) and the functionally specialized nerve fibers that transmit sensations after noxious stimuli.

Deafferentation of dorsal horn neurons probably also plays a role in the pathogenesis of long-term central sensitization. As a cell loses its effective peripheral input (i.e., becomes deafferented), it compensates by becoming more excitable and increases the rate at which it spontaneously fires impulses in high-frequency bursts. The increased excitability eventually results in the cell responding to stimuli traveling in adjacent axons to nearby healthy cells within the spinal cord. This has the effect of enhancing the "receptive field" of the deafferented cell and their overreaction mimics the response to noxious stimuli.[14]

Though the diagnosis of herpes zoster can be made clinically, Polymerase chain reaction (PCR), direct immunofluorescence assay (DFA), skin biopsy, and viral

culture are the laboratory diagnostic tests of atypical herpes zoster. PCR can detect varicella zoster virus DNA in the vesicular fluid, and hence, is considered the most sensitive and specific diagnostic test for herpes zoster. PCR can be done on fluid from lesion, blood, plasma, cerebrospinal fluid (CSF), and bronchoalveolar lavage. DFA can be used as an alternative to PCR. It is preferred over viral culture due to its high sensitivity, low cost, and turnaround time compared to viral culture. In patients with herpes zoster myelitis, viral isolation cannot be done from blood or CSF fluid. Hence, diagnosis of herpes zoster myelitis can only be made by clinical appearance of rash on the particular dermatome with clinical features of transverse myelitis and magnetic resonance imaging (MRI) of the spine. In case of segmental zoster paresis, diagnosis can be confirmed by the presentation of painful dermatomal rash with muscle weakness. An electromyography can reveal acute denervation of the compromised area. [15]

In a study by munoz quiles et al, true post herpetic neuralgia has been defined as pain persisting beyond 90 days after HZ episode.

6. Conclusion

We need to ponder as to why specifically a particular Dermatome is involved in a patient sparing the other segments. As far as we have noticed usually an underlying triggering factor does exist for herpes zoster lesions to erupt. Inspite of availability of chicken pox vaccine, HZ infection still remains very high, and due to which patients all over the globe still have a quality of life which is low due to the infection and the sequelae. Also it's the responsibility of all dermatologist to spread awareness against local medicine, herbal concoctions, witch craft,..etc which are very commonly applied by uneducated patients in rural settings. Which leads to further prolongation of treatment and in turn greater complications of the disease.

7. Conflict of Interest

The authors declare no conflict of interest

8. Source of Funding

None.

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