Herpes zoster: A case series with varied clinical presentations

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ABSTRACT

Herpes zoster (HZ) is a viral disease that clinically presents as a painful vesicular rash restricted to the distribution of a sensory nerve, unilaterally. It usually results from the reactivation of the DNA virus varicella zoster, which causes chicken pox. The condition is characterized by the occurrence of multiple, painful vesicles, and ulceration which shows a typical unilateral distribution. This case series of HZ infections is an attempt to present different clinical presentations of the disease, showing both the facial and oral manifestations, which are successfully managed by the appropriate medical management.

Key words: *Herpes zoster, Herpesvirus 3, Human, Shingles, Varicella zoster infection*

Herpes zoster (HZ), also known as shingles, is an acute infection of viral origin resulting from the reactivation of the varicella zoster virus (VZV), which causes chicken pox [1]. HZ typically erupts within one or two adjacent dermatomes, with thoracic (50–60%), cervical (10–20%), and trigeminal (10–20%) being more commonly involved, while lumbar (5–10%) and sacral (5%) are other less commonly involved dermatomes. In immunocompetent patients, the involvement of non-contiguous dermatomes is never seen, although overlapping of adjacent dermatomes can be shown in 20% of cases [2]. The involvement of maxillary and mandibular branches without the involvement of the ophthalmic branch accounts for 1.7% [3] –2% [4] of total cases of HZ, which is comparatively rare [3].

This case series is an attempt to highlight the various clinical presentations of HZ infections with the rarity of involvement of more than one division of the trigeminal nerve showing manifestations both in the orofacial region and in the intraoral site in the affected individual.

CASE REPORT

Case 1

A 42-year-old female patient reported with the complaint of pain in the upper left side of the jaw for 2 days and also discomfort with burning sensation during food intake. The patient gave a history of the appearance of 4–5 vesicles 3 days back on the hard palate following their rupture to form ulcer which was associated with pain. The pain was mild, continuous, and radiating in nature; aggravated while eating, drinking, and swallowing but did not get relieved. The pain was also associated with fever of low grade for 5 days. She also gave a history of chicken pox in the childhood. Extraoral examination showed no significant findings. Intraoral examination revealed multiple ulcers in relation to the left side of the hard palate, measuring approximately 0.5–1 cm in diameter, irregular in shape surrounded by an erythematous halo, and not crossing the midline (Fig. 1a). The ulcers were tender on palpation. Based on the above findings, a provisional diagnosis of HZ infection of the left maxillary division of the trigeminal nerve was considered.

Case 2

A 34-year-old male patient reported to the clinic complaining of painful blisters on the left side of his face and painful ulcers in the mouth for the past 5 days. Detailed history revealed that the lesions were preceded by the fever of low grade. 2–3 days after the fever, he developed fluid-filled blisters on the left side of his face. Initially, the blisters were small in size and few in number, but later, they increased in number covering the entire left half of the face with a watery discharge. It was also associated with pain which was severe, continuous, and radiating in nature. He also gave a complaint of difficulty in eating and swallowing. The patient gave a history of chicken pox infection in the childhood. No relevant drug, dental, and family history were recorded. Extraoral examination revealed clusters of vesicles on the left half of face extending from the temple region to the left chin region, which stopped abruptly at the midline. The surrounding skin was very tender on palpation (Fig. 2a). Intraoral examination showed numerous ruptured vesicles, which coalesced to form large ulcers that measured approximately 1–2 cm in size on the left half of the hard palate, not crossing the midline (Fig. 2b). The ulcers were irregular in shape with sloped edges and were surrounded by an erythematous halo. There was tender on palpation. Vitals

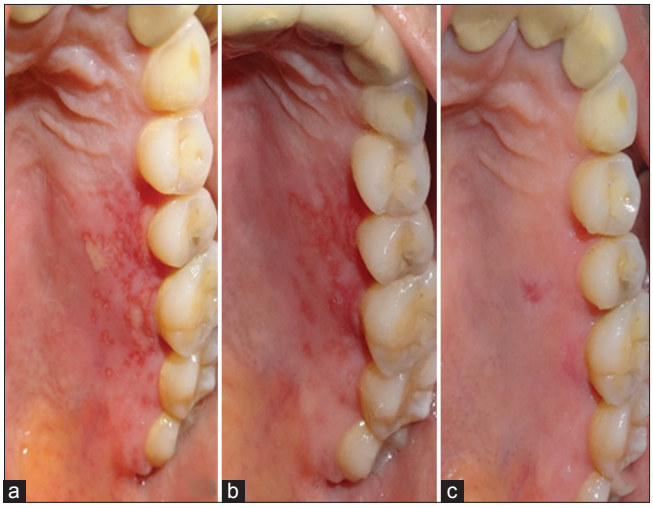

Figure 1: Case 1 - (1a) Pre-treatment intraoral photograph; (1b) after 7-day follow-up visit; (1c) after 1-month follow-up visit

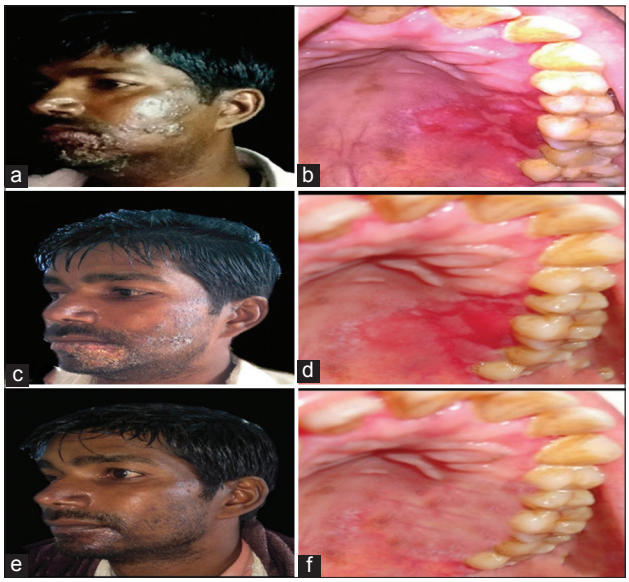

Figure 2: Case 2 - (2a) Pre-treatment extraoral photograph; (2b) pre-treatment intraoral photograph; (2c and 2d) after 1-week follow-up visit; (2e and 2f) complete resolution of lesion both extraorally and intraorally after 2 weeks

were normal at the time of examination. Routine hematological and serological investigations were performed for the patient. Complete blood count was found to be within normal limits except erythrocyte sedimentation rate and red blood cell which were slightly raised. The cytological examination was done after obtaining the smear from the lesions presented intraorally and extraorally. Acantholytic cells with few exfoliated squamous cells and inflammatory cells were revealed in the cytological smear. Based on the history, clinical findings, and cytological examination, a final diagnosis of HZ infection was given.

Case 3

A 57-year-old female patient reported with the chief complaint of ulcers on the left side of the palate for 7 days (Fig. 3a). The patient gave a history of pain in the left side of the palate for 7 days which got aggravated for the past 3 days. The pain was continuous and severe. There was no history of fever and malaise. There was no evidence of any vesiculation or ulceration extraorally. On intraoral examination, multiple small ulcers were observed on the left side of the palate with a unilateral arrangement in a linear pattern. The ulcers were irregular in shape extending anteroposteriorly from distal of the upper left second premolar to distal of the second molar and mediolaterally from mid of the hard palate to the interdental gingiva in relation to the upper left first molar, and the second molar. No such lesions were observed anywhere else in the oral cavity. Based on the above-mentioned clinical findings, a provisional diagnosis of HZ infection involving the left maxillary division of the trigeminal nerve was considered.

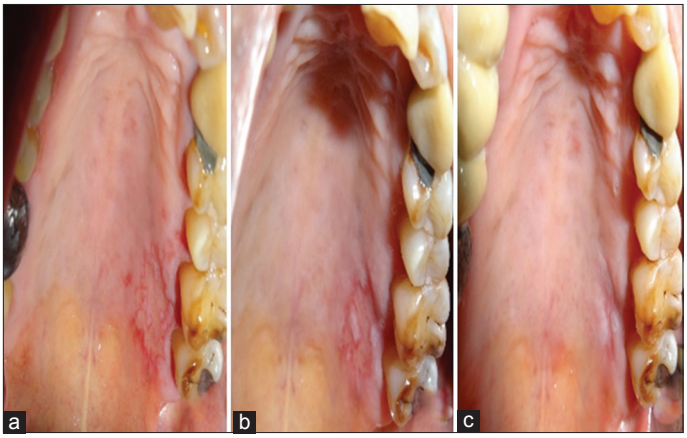

Figure 3: Case 3 - (3a) Pre-treatment intraoral photograph; (3b) after 1 week; (3c) after 3 weeks, complete resolution of the lesion

In all the three cases, the patients were treated with antiviral drugs and supportive therapy for 1 week. Acyclovir 800 mg (5 times a day for 7 days) was prescribed to control the active viral phase. Topical application of acyclovir cream (5%), 3 times a day, was also advised to apply in the affected region till complete resolution of the erythema. Aceclofenac (100 mg) in combination with acetaminophen (325 mg) and serratiopeptidase (15 mg) was prescribed, twice daily for symptomatic relief of pain and fever. Lignocaine gel (2%) was prescribed for local application before meals and betadine mouthwash to improve oral hygiene.

After 1 week of follow-up, in case one, the number of intraoral lesions was regressed (Fig. 1b). No fresh vesicles were reported. The patient was then again reviewed after 1 week and complete resolution of the lesions was noticed (Fig. 1c). After 1-month follow-up, the patient was totally asymptomatic and no post-therapeutic complications were reported. In case two, after 1 week, significant regression of a number of extraoral lesions was noted with the formation of scar tissue (Fig. 2c). Furthermore, resolution of the lesions was noticed intraorally (Fig. 2d). On further follow-up, after 2 weeks, the lesion was completely resolved, both extraorally and intraorally (Fig. 2e and f); and the patient was completely asymptomatic. In case three, on follow-up examination, significant regression in the lesion was observed 1 week after the institution of treatment (Fig. 3b). The ulcers were completely resolved on further follow-up visit after 3 weeks (Fig. 3c).

DISCUSSION

VZV is responsible for two major clinical infections of humans: the chicken pox or varicella (primary infection) and shingles or HZ. HZ is caused by reactivation of latent virus acquired during varicella [5]. Reactivation of VZV may occur spontaneously or when host immunity is compromised. Increased age, physical trauma (including dental procedures), psychological stress, malignancy, radiation therapy, and immunocompromised states including transplant recipients; steroid therapy and HIV infection are the predisposing factors for VZV reactivation [6]. The pathogenesis of the VZV infection has been depicted in Fig. 4. To get up-to-date information, a web-based search was initiated using PubMed/Medline database, searching for recent and relevant case reports of HZ written in English (Table 1).

The disease is more common in adult life and affects males and females in equal frequency. This is also evident from the cases reviewed (Table 1) that the age ranged from 23 to 80 years with the majority of HZ cases occurred in patients above the age of 40 years. HZ may affect any sensory ganglia and its cutaneous nerve; predominantly, the dermatomes innervated by spinal cord segment T3–L2; however, approximately 13% of the patients present with infections involving any of the three branches of the trigeminal nerve [5,7]. The ophthalmic division (V1) of the trigeminal nerve is most commonly affected presenting lesions on the upper eyelid, forehead, and scalp. Involvement of maxillary division (V2) shows lesions on the midface, upper lip, on the hard palate, and/or, buccal gingiva on one side which is preceded by prodrome and with mandibular division (V3) shows lesions on the lower face, lower lips, on mandibular gingivae, and tongue [8]. Among the case reports summarized in Table 1, the incidence of involvement of maxillary division is found to be predominant, followed by mandibular division. In our cases also, maxillary division of the trigeminal nerve was involved in case 1 and 3; while both maxillary and mandibular division are involved in case 2.

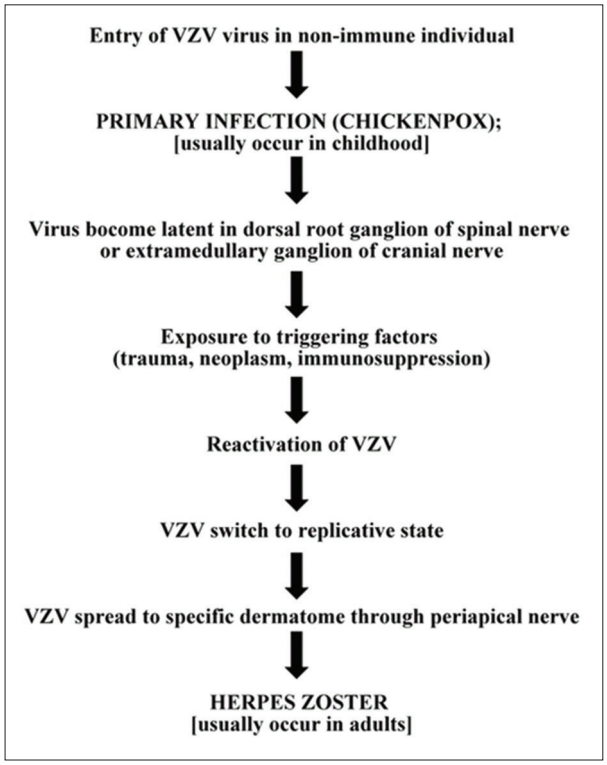

Figure 4: Pathogenesis of the varicella zoster virus infection

The common duration for shingle is a 2–3 days of prodromal phase characterized by deep intense pain over the affected nerve distribution. The prodromal phase begins 2–4 days before the appearance of the mucocutaneous rashes or vesicles. The presentation of prodromal pain is dermatomic in nature and may be associated with fever, malaise, and headache [9-11]. Similar findings were reported in all the three of our cases. This is followed by the acute phase, characterized by the development of clustered vesicles in a linear fashion alongside the affected nerve, unilaterally. Within a period of 3–4 days, the vesicles become pustular and ulcerate followed by the formation of scab usually in 7–10 days, although, it might take around 2–3 weeks for the lesions to go for complete resolution in otherwise healthy patients [9]. The active or "eruptive" phase of HZ is most contagious and can pose a significant risk of cross-infection [12].

Oral lesions occur with trigeminal nerve involvement, which may involve both the movable and bound mucosa, unilaterally [9]. Oral lesions appear as white opaque vesicles which rupture to form areas of shallow ulcerations, which are extremely painful. Ulcers are 1–5 mm in size and often coalesce to form larger ulcers with scalloped borders [8]. In all our cases, the patient came during the active stage of disease with the characteristic unilateral presentation of lesions. When trigeminal HZ occurs during tooth formation, pulpal necrosis and internal root resorption may occur [8]. Periapical lesions [13], tooth exfoliation [14], and alveolar osteonecrosis [15] have also been reported in association with HZ infection. Complete healing typically takes another 2–4 weeks. After complete healing ensues, scarring with areas of hypopigmentation or hyperpigmentation can be seen. When the dermatomal pain of HZ infections might occur without the appearance of rashes, it is being referred as zoster sine herpete [9].

The most common and debilitating complication of HZ infection is post-herpetic neuralgia (PHN), characterized by pain that lasts for almost 1–3 months after the lesions are cleared [15-18]. Secondary bacterial infection is another common complication of HZ [15]. If the geniculate ganglion is involved, it may result in James Ramsay Hunt's syndrome, which includes facial paralysis and painful vesicular eruptions of the external auditory meatus and pinna of the ear [19]. Other complications include scarring of skin, keratitis, retinal necrosis causing blindness, keratouveitis, cranial and peripheral nerve palsies, cerebral ataxia, and pneumonia may lead to death [19]. According to Whitley *et al.* [20], most frequent zoster-related complication, excluding PHN were neurological (1.4%) and ocular (0.7%) in non-vaccinated individuals, and cutaneous (0.7%) and neurological (0.5%) in vaccinated individuals.

Diagnosis of HZ infections can often be made from clinically by its unique unilateral distribution of the lesions. Identification of the virus in the cell culture of human fibroblasts is still the best diagnostic modality which reveals multinucleated epithelial cells,

Table 1: Cases of HZ reported in literature

Author	Year	Age/ Sex	Division of trigeminal nerve involved	Treatment	Recurrence on follow-up
Raj *et al.* [5]	2017	55/M	Right maxillary division	Acyclovir 800 mg 5 times daily for 5 days; Tab. prednisolone 5 mg 3 times daily for 5 days; Tab. paracetamol 650 mg	No
Tayde *et al*. [18]	2017	28/F	Left maxillary division	Acyclovir 800 mg 5 times per day for 7 days	No
		23/F	Right maxillary division	Acyclovir 600 mg 5 times per day for 7 days	No
		65/F	Right maxillary division	Acyclovir 800 mg 5 times per day for 7 days	
Ali *et al*. [22]	2016	50/M	Right maxillary and mandibular division	Acyclovir 400 mg/5 h for 2 weeks	No
Rai *et al.* [23]	2016	43/m	Left maxillary and mandibular division	Acyclovir 800 mg 5 times per day for 7 days	No
Chhimwal *et al.* [24]	2015	42/M	Left maxillary division	Acyclovir 800 mg 5 times per day for 10 days Aceclofenac 500 mg thrice daily Betadine mouthwash	No
Nair *et al.* [15]	2014	68/M	Left maxillary and mandibular division	Valacyclovir 1 g 3 times a day for 7 days	No
		50/M	Left maxillary, mandibular, and ophthalmic division	Acyclovir 800 mg 5 times per day for 10 days	No
Vineet *et al.* [6]	2013	53/M	Left maxillary division	Acyclovir 800 mg 5 times per day for 10 days	No
Mohan *et al.* [25]	2013	80/F	Maxillary division	Acyclovir 800 mg 5 times per day for 10 days	No

HZ: Herpes zoster

Table 2: Treatment modalities for herpes zoster infection

Antiviral treatment

Antiviral treatment (guanosine analogs) should be instituted within 72 h of cutaneous eruption because most virus replication ceases 72 h after onset of rash [5,11].

Acyclovir

- Drug of choice
- Dose - 800 mg, 5 times a day for 7–10 days
- Mechanism - shortens the duration of viral shedding, inhibits the formation of new lesions, hastens healing, and reduces the severity of acute pain.

Valacyclovir

- A prodrug of acyclovir
- Dose - 1000 mg, 3 times a day for 7 days
- It produces a serum acyclovir level 3–5 times as high as that achieved with oral acyclovir therapy

Corticosteroids [5,11]

- The use of corticosteroids in the treatment of HZ has been controversial. Their benefits are overshadowed by fear of reduced immune response, and hence, they are contraindicated in immunocompromised patients
- However, in combination with acyclovir, they show moderate but significant acceleration in the rate of cutaneous healing and also alleviate acute pain. However, no study demonstrated any effect of corticosteroids on the incidence or duration of PHN
- The use of corticosteroids for HZ without concomitant antiviral therapy is not recommended [26]

Tricyclic antidepressants[11]

- Capsaicin is the only topical preparation approved for temporary relief of pain associated with HZ infections
- It should not be applied until skin lesions have healed

Recent treatment modalities[5]

- Lysine/arginine - usually given at 300–1200 mg dosage per day
- Topical zinc treatment - applied as topical solution of zinc sulfate (4%) in water 4 times daily for 4 days
- Vitamin C - given as 200 mg ascorbic acid and 200 mg as water-soluble flavonoids (apparently from citrus) 3 times daily for 3 days
- Oral zinc treatment - which includes oral administration of 23 mg zinc sulfate and 250 mg Vitamin C, each twice daily for 6 weeks
- Vitamin E - topical application of Vitamin E relieved pain and aided in the healing of oral herpetic lesions. The affected area was dried and cotton saturated with Vitamin E oil (20,000–28,000 IU per ounce) was placed over it for 15 min
- Adenosine monophosphate is also given; each injection contained 1.5–2.0 mg/kg body weight and was administered every other day for a total of 9–12 treatments

Newer medications [6,11]

- CMX 001 hexadecyloxypropyl-cidofovir
- Valacyclovir nucleoside analog (H2G)
- ASP2151 helicase-primase inhibitor
- FV100 two bicyclic nucleoside analogs

although, it does not distinguish between herpes simplex virus and VZV. The other methods with higher sensitivity and rapid diagnosis are direct immunofluorescence antibody detection against VZV, giving positive results in up to 80% of the cases. Polymerase chain reaction detects viral antigen. In recurrent cases, increased immunoglobulin M (IgM) levels are detectable in serum 10 days after the appearance of the vesicles and increased IgG and IgA 4 days after the vesicles [9,10,21].

Although it is a self-limiting disease, early institution of antiviral and symptomatic therapy reduces the morbidity significantly (Table 2). Symptomatic treatment such as keeping cutaneous lesions clean and dry, use of sterile non-adherent dressing over skin to protect the lesions, topical applications (i.e. calamine lotion), sympathetic nerve blockades, and analgesics (aspirin and others) may be used, as was advised in both our cases and helped speedup recovery.

CONCLUSION

This case series signifies the importance of a thorough medical, dental case history, and examination of the patients with sporadic diseases such as HZ. Early diagnosis and prompt treatment by antiviral drugs in the acute stage of the HZ may aid in reducing the duration and the severity of pain of HZ infection and also prevent the complications.

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