

Dilemma in Diagnosing Herpes Zoster with Prodromal Odontalgia in Immunocompetent Patient: A Case Report

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ABSTRACT

Herpes Zoster (HZ) is an acute viral infection characterised by painful unilateral vesicular lesions, generally occurs in immunocompromised conditions, and progresses through three stages i.e., prodromal, active, and chronic stages. Odontalgia may occur when trigeminal nerve branches are involved during this prodromal stage. More than 53% of doctors have difficulty in diagnosing HZ on the prodromal stage before the emergence of the skin eruption. This report describes the HZ infection affecting all three branches of the trigeminal nerve which causes odontalgia on the prodromal stage. A-62-year-old male referred with the complaint of painful oral ulcers, multiple vesicles and crusts with swelling and pain on his left side of the face. Previously, it was only confined to the lips but gradually spreads to the eyes followed by odontalgia and pain on the left side of mandible. The diagnosis of HZ affecting three branches of trigeminal nerves was determined from the presence of unilateral lesions on the skin and oral cavity. The lesions healed completely after two months. Odontalgia in trigeminal HZ that occurs in the prodromal stage can pose a dilemma, be misdiagnosed, and become a diagnostic challenge for dentists. The presence of an unidentified cause of odontalgia should be an alarming sign of HZ infection, especially in the elderly.

Keywords: Shingles, Toothache, Trigeminal nerve, Varicella zoster virus

CASE REPORT

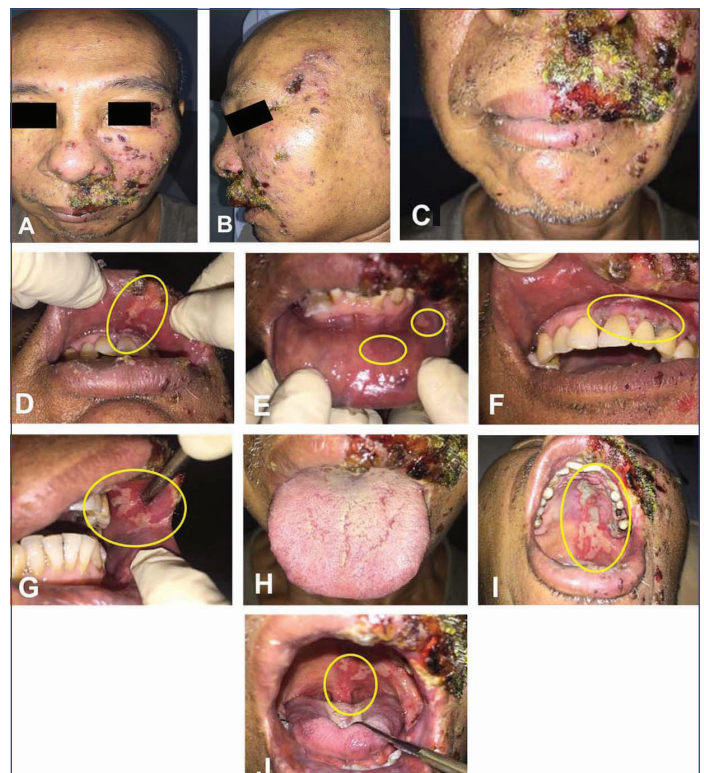
A 62-year-old male reported to the Department of Oral Medicine with a chief complaint of multiple vesicles, crusts and swelling over the left side of the face for the past 5 days as well as oral ulcer with severe pain since 4 days, leading to difficulty in eating, drinking, opening the mouth, and cleaning his oral cavity. The patient had been treated for 2 days by an Oral Surgeon for swelling accompanied by burning sensation and pain in the lips, eye and left lower mandible as well as blisters on the left upper lip and around the nose. Based on the clinical presentation, the patient was diagnosed with the left submandibular cellulitis due to pulp necrosis of tooth number 38 accompanied by Herpes Simplex Virus (HSV) infection. After one day of hospitalisation, many blisters were seen on the left side of the cheek, chin, eye; and ear, therefore the patient was referred to the Department of Dermatology and Venereology.

The lesions initially began approximately 4 days before visiting the hospital, when he developed breakouts and swelling on the left upper lip. Then the next day, it spread to the eye followed by odontalgia in the lower left third molar and pain on the left mandible which pushed him to visit the nearest hospital. Pulpitis and abscess were suspected based on the symptoms, and antibiotics and non steroidal anti-inflammatory drug was administered. The pain still persisted, a rash appeared on the cheek and he was prescribed antibiotics, paracetamol, and acyclovir ointment. However, the breakouts were still spreading, and the patient went to another hospital and due to the severe condition, the patient was referred to present hospital.

There was no history of diabetes mellitus, hypertension, or any systemic illness, no family member had experienced similar lesions, patient had chicken pox when he was child. No routine drug consumption was recorded. It was admitted that the patient was physically fatigued due to road trip for approximately 24 hours.

On extraoral examination, unilateral multiple vesicular lesions and crustations were present on the left side of the upper and lower lips, chin, cheek, around the nose, eye, eyebrow, ear and temporal region but not crossing the midline followed by swelling and pain

on his left side of nose, cheek and around the eyes. On intraoral examination, there were painful multiple ulcerations of varying sizes covered with yellowish-white pseudomembrane, surrounded by erythematous margin with an irregular shape lesion affecting the left side of hard and soft palate to uvula, upper labial mucosa from 21 to 22 region, lower labial mucosa at 32 region, buccal mucosa from corner of the mouth to 25 region and upper gingiva from 21 to 23 region. White pseudomembranous plaque was seen in the two-third posterior dorsum of the tongue, that can be scrapped off without leaving an erythematous area. [Table/Fig-1].



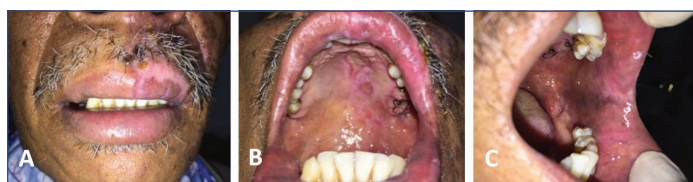
[Table/Fig-1]: (A-C) Extraoral and (D-J) intraoral images during the first visit (lesions at the left side area).

Serologic tests for Human Immunodeficiency Virus (HIV), Immunoglobulin G (IgG) anti HSV-1, IgM and IgG anti HSV-2 and Coronavirus Disease-2019 (COVID-19) (due to the pandemic situation) were negative except IgG anti-HSV-1 titer was more than 3 times above positive value, reaching 33.40 Units (U) (normal range: negative <9 U, equivocal 9-11 U, positive >11 U) [1]. On examination, blood pressure was 120/90 mmHg, pulse rate was 80 pulse/min, and respiratory rate was 21 breaths/min. Blood tests (haemoglobin 15.8 g/dL, leukocytes $8.03 \times 10^3/\mu\text{L}$, erythrocytes 4.98 million/ μL , platelets 163 thousand/ μL , urea was 22 mg/dL, creatinine 1 mg/dL, fasting blood sugar 91 mg/dL) showed a normal value.

Based on patient's history and clinical examination at the first visit, a provisional diagnosis of herpes simplex infection and herpes labialis was given, with a differential diagnosis of herpes zoster of trigeminal nerve. Differential diagnosis of pemphigus and pemphigoid were also given. However, these diagnosis were ruled out because pemphigus or pemphigoid is a chronic disease and does not show blisters or ulcers unilaterally [2]. Since, the characteristic clinical features were unilateral multidermatomal at the left side without crossing the midline, so the final diagnosis was HZ infection of ophthalmic, maxillary, mandibular branch of trigeminal nerve was made.

During first visit, the patient was treated by Oral Surgeon with Ringer's lactate infusion, ceftriaxone 1g intravenously (i.v.) (2 times daily for 7 days), metronidazole 500 mg i.v. (3 times daily for 7 days, ketorolac 30 mg i.v. (2 times daily for 7 days, omeprazole 40 mg i.v. (2 times daily for 7 days). After the emergency condition correction, the necrotic pulp of teeth 38 was extracted to ruled out submandibular cellulitis in consideration of preventing the sepsis. There was no postextraction complaint. For the HZ infection, the patient was prescribed acyclovir (800 mg orally 5 times/day for 5 days), methyl prednisolone (8 mg orally 2 times/day for 5 days), and mecobalamin (500 mg orally 3 times/day for 5 days). In Department of Oral Medicine, he was instructed to apply 0.9% NaCl on a gauze to moisten the lips, 0.2% chlorhexidine digluconate spray (3 times daily), maintain oral hygiene, and follow a soft diet. The Potassium hydroxide (KOH) staining examination was done on the second day of the visit, and the result was negative.

Upon two weeks control, the ulcers had significantly recovered, and the patient felt more comfortable when eating and drinking. However, the ulcer on the palate and hypopigmentation on the upper lip was still visible [Table/Fig-2]. The ulcers on the palate were completely healed after 2 months [Table/Fig-3].



[Table/Fig-2]: Extraoral and intraoral examinations on two weeks control.



[Table/Fig-3]: Extraoral and intraoral images of the recovered patient (after two months of follow-up).

DISCUSSION

Herpes Zoster (HZ) or "shingles" results from the reactivation of a latent infection of Varicella Zoster Virus (VZV), that also causes varicella (chickenpox) [3,4]. As within the western population, within Asia-Pacific countries the incidence of HZ is around 3-10/1000 people per year, with high occurrence within people over 40 years of age and peaks within population of 70 to 80 years of age [5]. In a study of 2232 HZ patients in 13 university hospitals in Indonesia

(2011-2013), a peak of 851 cases (37.95% of total HZ cases) was found in people between the age of 45-64 years old [6]. Studies in Indonesia and other Asian-African countries showed higher incidence of HZ in women compared to that of men [5,6]. With regards to dermatome involvement, the most commonly affected ones by HZ are thoracic (50-60%), cervical (10-20%), trigeminal (10-20%), and lumbar (5-10%) and sacral (5%) [7], while with maxillofacial manifestations, the most commonly affected cranial nerves are trigeminal nerves (18.5%-22% of total cases), followed by glossopharyngeal and hypoglossal nerves [8,9].

HZ can affect either ophthalmic, maxillary, or mandibular branches of the trigeminal nerve. Ophthalmic branch involvement occurs 20 times more often than the others branches [3]. Oral manifestation presents when HZ attacks either maxillary or mandibular branches of the trigeminal nerve [4]. Multidermatomal involvement of the trigeminal nerve, mostly occurring with immunocompromised condition, uncommon in immunocompetent patients [3] but has been reported by Naveen KN et al., [10], and this article also presented a case of HZ infection that affected all three branches of the trigeminal nerve, and produced extraoral and intraoral lesions in immunocompetent condition. Lesions around eyebrows, eyes, and the bridge and sides of the nose indicates the involvement of ophthalmic branch [4,11]. Meanwhile, lesions on the middle third of the face, beneath the eyes, nose, cheeks, and intraorally on the palate, buccal and upper labial mucosa, and uvula indicates the involvement of maxillary branch [4,11], and the presence of lesions on the lower third of the face, lower lip, temporal regions, around the ears, and buccal mucosa indicates the involvement of the mandibular branch [4,11].

Predisposing factors for viral reactivation are HIV, malignancy, cytotoxic drug therapy, steroids, radiation therapy, stress, alcohol abuse, and physical trauma, including dental trauma [3,4,8,10,12]. For the case being reported here, all the patient's laboratory results were normal, indicating that the condition was not caused by immunocompromised conditions. Nevertheless, the patient's advanced age may have caused a decline in immunity [13]. Based on the patient's history, it was also recognised that the patient experienced stress or physical fatigue due to long-distance travel, which could also cause a decrease in immunity. Physical or psychological stress can stimulate Hypothalamic-Pituitary-Adrenal (HPA) axis; the released corticosteroids can influence immunity and impair immune cells function [14].

The diagnosis of HZ can generally be made based on the patient's history and the presence of characteristically unilateral clinical features [15-17]. Clinical manifestations of HZ infection may show within (1) prodromal (pre-eruption), (2) acute (active), or (3) chronic phases, but some patients did not demonstrate any symptom within all the phases [4]. The prodromal stage presents as pain associated with mild fever, headache, and dysesthesia, accompanied by sensations such as burning, tingling, itching, or prickling which occur along the affected dermatome. This manifestation is believed to represent degeneration of nerve fibrils [4,12]. Viral reactivation along the maxillary or mandibular nerve branch may cause odontalgia and pulp vasculature leading to infarction and necrosis of the dental pulp [4,8,16,18]. The pain sensation on the prodromal stage commonly occurs within hours to a few days but can also last upto one month [8,18].

For the patient in this case report, there had been a difficulty in diagnosing the presence of herpes zoster, which could be seen from the patient's history of visitation. Before the patient came to our hospital, the patient had been seeking treatment twice but was only given analgesics, anti-inflammatory drugs, and antibiotics to treat the pain and swelling in the face and jaw. The patient was suspected of pulpitis and possible abscess. Suspicion of herpes simplex infection was made before the second treatment due to

the appearance of several vesicles around left side of the nose and upper lip, the patient was given additional acyclovir ointment to treat the condition. Sometimes a dentist may face difficulties in diagnosing HZ on the prodromal stage, especially before skin eruption occurs, which lead to treatment delay. Other possible diagnosis within the prodromal symptoms may include irreversible pulpitis, acute periapical periodontitis, or acute sinusitis [18,19]. Odontalgia and pulp necrosis had also been reported by Patil S et al., Brooks JK et al., and Fristad I et al., as a result of herpes zoster infection, which further complicate a proper diagnosis [18,20,21].

In this case, the patient experienced the prodromal stage for about three days, before hospitalisation. It was suspected that the source of the pain the patient experienced was from the third molar of the left lower jaw, during examination the tooth was diagnosed with pulp necrosis, thus causing a swelling of the surrounding region, and tooth extraction was performed. Paradoxically, there were reported cases in which VZV which might result in pulp necrosis and the formation of apical periodontitis was found in the absence of bacteria [22]. In addition, one study involving 24 patients seeking emergency treatment for the presence of an acute apical abscess found that 9% of apical abscesses contained VZV [23].

Thus, it is important to do a thorough clinical examination as well as an extensive pulp testing to decide on the appropriate treatment [8]. Laboratory tests such as the tzanck test or Polymerase Chain Reaction (PCR) method are required when the clinical finding is not conclusive [4]. On the other hand, toothache or pain mimicking pulpitis cannot be determined by a laboratory test, which makes a prodromal odontalgia hard to diagnose, especially without a history of previous herpes infection (zoster sine herpette) [21]. Fortunately, in this patient, the final diagnosis of herpes zoster with the involvement of all branches of the trigeminal nerve could be made based on the patient's history and after the appearance of characteristic clinical manifestation, i.e. unilateral dermatomal involvement.

After the diagnosis was established, the patient should be given therapy [8]. In this case, authors prescribed antibiotics, antiviral, corticosteroid, analgesic, multivitamin, and antiseptic. Delaying odontalgia treatment in HZ patients who experience irreversible pulpitis may be appropriate if there are no supporting findings such as sensitivity to percussion, active swelling, purulent drainage, or periapical pathology from radiographs examination [8]. Early diagnosis and treatment in HZ patients is important to reduce the duration and severity of the disease, for pain control, to prevent secondary infection, and to avoid the risk of complications [3, 18].

CONCLUSION(S)

Herpes zoster which affects the trigeminal nerve may manifest as odontogenic pain. The dentist must be aware that odontalgia may become a part of the prodromal stage of HZ on the trigeminal nerve before skin eruption (active stage). Therefore, the dentist needs to broaden their knowledge and be more careful in making an early diagnosis to prevent treatment delay, reduce the duration and severity of the disease, and also prevent the complications.

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