An Unusual Case of Osteonecrosis and Spontaneous Tooth Exfoliation Following Trigeminal Herpes Zoster in a HIV Seropositive Patient

Nagaraju Kamarthi, Guru Eraiah Narasimha, and Ashok Lingappa

1Department of Oral Medicine & Radiology Subharti Dental College, Subhartipuram, India
2Department of Oral Medicine & Radiology Vinayaka Mission’s Sankarachariyar Dental College, Salem, Tamilnadu State, India
3Department of Oral Medicine & Radiology Bapuji Dental College, Davangere, India

Correspondence to:
Kamarthi Nagaraju
E-mail: drnagranil977@gmail.com

Abstract
Oral lesions associated with human immunodeficiency virus (HIV) are often the first overt clinical features of HIV infection. Reports of HIV-associated herpes zoster infection with alveolar bone necrosis and spontaneous tooth exfoliation are extremely rare, with only four cases reported in the literature. The exact mechanism of osteonecrosis induced by herpes zoster infection remains uncertain. An altered oral environment, decreased host immunity, or immune reconstitution inflammatory syndrome (IRIS) could further compromise the viable periodontal status, leading to alveolar bone necrosis and tooth exfoliation. We report a case of herpes zoster infection involving two divisions of the trigeminal nerve in an HIV-seropositive patient who further manifested with mandibular and maxillary osteonecrosis and spontaneous mandibular and maxillary tooth exfoliation. The occurrence of such infection in immunosuppressed individuals, its etiopathogenesis, and associated clinical features are briefly reviewed and discussed.

Keywords:
HIV, herpes zoster, tooth exfoliation, immune reconstitution inflammatory syndrome (IRIS)

Introduction
Herpes zoster is an acute viral infection of the dorsal root ganglion of the spinal cord or extramedullary cranial nerve ganglia due to reactivation of the varicella zoster virus and is characterized by unilateral vesicular eruption localized to the skin and mucous membrane of the dermatome innervated by the affected nerve (1).

Oral manifestations of herpes zoster appear when the mandibular or maxillary divisions of the trigeminal nerve are affected (2). Herpes zoster infection has been commonly recorded in cases of human immunodeficiency virus (HIV) infection; however, manifestations with extensive alveolar necrosis and spontaneous tooth exfoliation are rare (3).

Case Report
A 43-year-old male patient came to the Department of Oral Medicine and Radiology, Bapuji Dental College and Hospital, Davangere, Karnataka, India, with a burning sensation on the right side of his mouth of 15 days’ duration and pain in the lower right back tooth region beginning the previous day. He was apparently asymptomatic 15 days earlier, when he developed an itching sensation of the skin overlying the right side of his face and the right buccal mucosa, followed by spontaneous development of fever, rash, and vesicles over the right side of the face that eventually ulcerated and became encrusted. The condition was associated with difficulty chewing and swallowing, a burning sensation of the eyes, blurring of vision, and spontaneous exfoliation of apparently firm teeth #27, #28, and #29 (right mandible).

The patient’s past medical, dental, and family histories were insignificant. Physical examination revealed vesicles and pustules with crusting on the skin overlying the external ear and upper and lower
Fig. 1. Clinical photograph showing hypopigmented, hyperpigmented, and encrusted lesion areas of the right side of the face (frontal view).

Fig. 2. Clinical photograph (lateral view).

Fig. 3. Intraoral photograph showing erosions of the right hemipalate.

Fig. 4. Intraoral photograph showing erosions of the right buccal mucosa in the retromolar area.

Fig. 5. Intraoral photograph showing the alveoli with denuded, dry, and yellowish bone devoid of blood clots and missing teeth #27, #28, and #29.
lips superimposed over areas of healing with scar formation. The lesions were confined to the distribution of right trigeminal nerve, sparing the eyes and an area over the angle of the mandible. There was no involvement of the tip of nose, conjunctiva, or other regions of the body (Figs. 1 and 2).

Intraoral examination revealed poor oral hygiene and halitosis with erosions over the right retromolar area and right hemipalate that were restricted to the midline (Figs. 3 and 4). The alveolar bone missing teeth #27, #28, and #29 was denuded, dry, yellowish, and devoid of blood clots (Fig. 5). Tests for sensitivity to heat and cold and the electric pulp vitality test showed negative responses by all teeth in the first and fourth quadrants; intraoral periapical and panoramic images revealed the outlines of the sockets of the exfoliated teeth with no evidence of sequestration (Figs. 6 and 7). Based on the history and clinical features, a diagnosis of osteonecrosis and spontaneous

Fig. 7. Panoramic images (orthopantomography) showing mild interdental bone loss and exfoliated teeth #27, #28, and #29.

Fig. 8. Clinical photograph at the second visit showing healed cutaneous lesions.
ous tooth exfoliation following herpes zoster infection of the right trigeminal nerve was made. Blood assays (enzyme-linked immunosorbent assay and Western blot assay) revealed that the patient was seropositive for HIV antibodies. The patient was advised to practice strict oral hygiene measures with 0.02% chlorhexidine mouthwash and was prescribed 800 mg acyclovir taken daily for 1 week and 200 mg tetracycline taken four times daily for 5 days. The patient was further referred to a general physician for the treatment of HIV, where he was counseled and prescribed highly active antiretroviral therapy (HAART).

At the second visit 10 days later, the patient had significant relief from the burning sensation and tooth pain. There was complete remission of the cutaneous lesions with healing by scarring, hypopigmentation, and hyperpigmentation (Fig. 8) and healing of the oral lesions (Fig. 9). However, the teeth in the right maxilla and mandible were becoming progressively mobile with spontaneous painless exfoliation of #7, #30, and #31, along with exposure of the alveolar bone and sockets (Figs. 10–12). Exposed alveolar bone was removed and sent for histopathological investigations and the margins were filed and sutured. Histological sections showed bone sequestra with necrosis and chronic inflammatory cell infiltrate (Fig. 13).

Within one month, patient returned with a severe
lancinating pain over the right side of his face, especially along the lower border of the mandible, which was suggestive of post-herpetic neuralgia. He was prescribed 100 mg carbamazepine (Tegretol) taken twice daily and 500 μg Diacobal (vitamin B12) taken twice daily for one month. Following this regimen, the patient had temporary relief within four weeks. Healing of the sockets was remarkable and radiographs showed healing alveolar bone (Fig. 14).

Discussion

The incidence of herpes zoster infection in the general population has been reported to be 5.4% (2, 4). Herpes zoster infection typically occurs in individuals older than 45 years of age, with the highest incidence among persons 60 to 90 years old (5, 6). Herpes zoster usually affects the cranial nerves; the trigeminal nerve is the most frequently affected (18.5% to 22%), followed by the glossopharyngeal nerve and hypoglossal nerve (5). Trigeminal nerve involvement is usually unilateral and limited to a single division. Oral manifestations appear when the second or third trigeminal division is involved (2). In our case, both the maxillary and mandibular divisions were involved, which was reflected both intraorally and extraorally.

Osseous alterations associated with herpes zoster infections were first reported by Rose in 1908 (7). Gonnett is credited with being the first to draw attention to herpes zoster infection–related alveolar bone necrosis and tooth loss, in 1922 (7). In a review of the literature to 2005 (8), 39 previous reports of bone necrosis after herpes zoster reactivation with a fairly common occurrence of spontaneous tooth exfoliation have been reported and in the past 4 years, four new cases have been added to the literature (8–11). One of these cases presented a co-infection with herpes zoster and cytomegalovirus (8). With the current case, a total of 44 cases of herpes zoster with osteonecrosis have been reported. Involvement of both jaws with exfoliation of the teeth in more than one quadrant, which occurred in the present case, is extremely rare.

An increased frequency of herpes zoster infection has been seen in cases of HIV infection. Reports of a similar manifestation in a seropositive individual have previously been reported only three times (3, 11, 12); our case is the fourth.

The exact mechanism by which herpes zoster causes bone necrosis is still unclear. Various hypotheses concerning the pathogenesis of herpes zoster–induced osteonecrosis have been postulated. Hall et al. suggested that decreased local host resistance, in the form of host irradiation obliteratorive endarteritis, may contribute to subsequent inflammatory and necrotic alterations due to avascular necrosis (13). Garty et al. (14) however disagreed, especially in the maxilla due to its rich vascular supply. Decreased host resistance fails to explain the localized effect to the jaws. Cooper et al. (15) postulated that adverse tissue reactions, possibly aided by local chronic inflammatory changes in the form of advanced per-
iodental diseases and delayed healing of extraction sockets, resulted in bone necrosis and tooth exfoliation. Wright et al. (7) postulated that local vasculitis caused by a direct extension of the neural inflammatory process to the adjacent blood vessels leads to infarction of the trigeminal vessels that accompany the trigeminal nerve supplying the jaws, leading to ischemic necrosis of the periodontal ligament and alveolar bone, which is well described in cases of herpes zoster infection involving the central nervous system. Mintz and Anavi postulated that denervation of the bones resulted in bone necrosis and tooth exfoliation (16), which seems unlikely.

Arikawa et al. (17) suggested that osteonecrosis in herpes zoster infection is probably due to compression of the alveolar artery due to edema caused by the inflammation of the alveolar nerve in the narrow maxillary or mandibular canal, resulting in ischemia and subsequent necrosis of the periodontal ligament and alveolar bone. Systemic viral infection can injure odontoblasts and cause degenerative tissue changes that result in pulp necrosis (18).

The theory put forward by Wright (7), which suggests that vasculitis following viremia from adjacent nerves in the alveolar bone leads to avascular necrosis, appears to be more appropriate. This initial infection, however, in the majority of cases is not sufficient to cause bone necrosis and tooth exfoliation, but contributing pre-disposing factors that reduce local and systemic host resistance may cause these aggravated responses (7).

Immune reconstitution inflammatory syndrome (IRIS) is defined as that circumstance in which pre-existing subclinical or mildly symptomatic infections or inflammatory conditions undergo paradoxical worsening with a substantial increase in inflammation during the initial months of host immunoreconstitution (19). This condition is an immunopathogenic or hyperinflammatory response to a pathogen that was already there as the host immune response is being rapidly reconstituted (19). Ortega et al. (20) reported a case of mandibular osteonecrosis in a HIV-seropositive patient who was on HAART therapy, signifying the effects of IRIS. In the present case, the patient first experienced exfoliation of the mandibular teeth and later, after he was started on HAART therapy, experienced exfoliation of the maxillary teeth and the early occurrence of post-herpetic neuralgia. In the present case, we believe that a correlation existed between IRIS and herpes zoster infection in an HIV-seropositive patient, which led to bone necrosis and tooth exfoliation in more than one quadrant.

Knowledge of complications related to this particular viral infection is necessary for comprehensive patient care. Here are the signs, symptoms, and radiographic and histological features of herpes zoster infection with oral manifestations.

Symptoms of osteonecrosis include fetor oris, deep boring pain, exposure of bone, mobility and painless exfoliation of teeth, and trismus in cases of superimposed secondary infection. Signs include denudation of alveolar bone that does not appear viable, recession of underlying soft tissues, mobility of teeth, soft tissue abscess, and persistently draining sinuses due to secondary infection (1, 3, 7, 12-17, 21).

Radiographic features may vary from clearly visible outlines of the sockets of exfoliated teeth to no demarcations of bone fragments adjacent to the remaining teeth to well demarcated sequestra from the surrounding healthy bone (1, 3, 7, 12-17, 21). Histopathological sections of bony sequestra usually reveal portions of necrotic bone tissue in the region of the bone marrow space and may show purulent exudates with bacterial colonies or superficial fungal invasion in cases of secondary infection (1, 3, 7, 12-17, 21).

This condition is managed mainly by a conservative approach: good oral hygiene instructions, frequent irrigation of the wound, and antibiotics to control secondary infections and prevent serious complications (13). Sequestrectomy with extraction of the involved teeth would be an ideal treatment, because the prognosis in these patients would be remarkable (21).

Mintz and Anavi (16, 22) have used a closed nasal vestibular double portal drainage system for the drainage and irrigation of the suppurative maxillary
bone. Two vertical incisions were made, one in the unattached mucosa in the canine fossa and the second at the zygomaticomaxillary buttress. The incisions were made down to the bone and a subperiosteal tunnel joining them was created with a periosteal elevator. The subperiosteal tunneling was extended anteromedially along the anterior maxillary wall and the nasal vestibule was penetrated with a hemostat. A 0.7×20-cm (Fig. 15) three-fourths perforated, flat silicone drain was inserted through the nostril and brought through the subperiosteal tunnel. An extramucosal U-turn was then made around the distal incision; the drain was brought forward through the anterior incision and then advanced submucosally until it was through the nasal vestibular hole. The nonperforated segment of the drain was inserted first so that it lay extramucosally, while the perforated segment was in the subperiosteal tunnel against the maxilla (Fig. 16). Two catheter adaptors were attached to the lumena of the drain tubes. With this drainage system in place, the necrotic maxillary alveolar bone was then irrigated with 2 gm cefazolin in 1000 ml of normal saline for 2 weeks.

**Conclusion**

The exact mechanism of osteonecrosis induced by herpes zoster infection remains unclear. It is possible that poor oral hygiene coupled with decreased host immunity or IRIS could further compromise an already fragile periodontal ligament status, thus leading to alveolar bone necrosis and tooth exfoliation.

Prompt antibiotic and antiviral medication along with oral hygiene measures may help to control bone destruction. More studies are needed to fully understand the pathophysiology and complications associated with this viral infection for improved prevention, early detection, and management.

**References**