Alveolar bone necrosis and spontaneous tooth exfoliation associated with trigeminal herpes zoster: a report of three cases

Nam-Kyoo Kim, Bong Chul Kim, Jung-woo Nam, Hyung Jun Kim

1Department of Oral and Maxillofacial Surgery, College of Dentistry, Yonsei University, Seoul,
2Department of Oral and Maxillofacial Surgery, Daejeon Dental Hospital, College of Dentistry, Wonkwang University, Daejeon, Korea

Abstract (J Korean Assoc Oral Maxillofac Surg 2012;38:177-83)

Herpes zoster is a viral infection caused by the reactivation of the varicella zoster virus, an infection most commonly affecting the thoracolumbar trunk. Herpes Zoster Infection (HZI) may affect the cranial nerves, most frequently the trigeminal. HZI of the trigeminal nerve distribution network manifests as multiple, painful vesicular eruptions of the skin and mucosa which are innervated by the infected nerves. Oral vesicles usually appear after the skin manifestations. The vesicles rupture and coalesce, leaving mucosal erosions without subsequent scarring in most cases. The worst complication of HZI is post-herpetic neuralgia; other complications include facial scarring, motor nerve palsy and optic neuropathy. Osteonecrosis with spontaneous exfoliation of the teeth is an uncommon complication associated with HZI of the trigeminal nerve. We report several cases of osteomyelitis appearing on the mandible, caused by HZI, and triggering osteonecrosis or spontaneous tooth exfoliation.

Key words: Human herpesvirus 3, Herpes zoster, Osteonecrosis, Tooth exfoliation

I. Introduction

The varicella zoster virus (VZV) produces two clinical results: varicella or chickenpox and herpes zoster infection (HZI)\(^1\). Varicella caused by the primary infection of VZV is a benign childhood disease producing eruptive vesicles. As a result of primary infection in the varicella, a skin virus moves to a sensory nerve and remains in latent state in a ganglion\(^1,2\). When VZV in latent state is reactivated, it develops into HZI, which causes severe pain and painful vesicles in the skin and mucosa around the affected sensory nerve distribution\(^3,4\).

Thoracolumbar dermatomes (T3-L3) are most commonly affected by HZI\(^1,4\). HZI may also affect the cranial nerves, with the trigeminal nerve most frequently affected (18.5-22%)\(^7\). Herpes zoster affecting the trigeminal nerve is generally unilateral; it affects a single branch among three branches, mainly the first branch or optic nerve. Oral manifestation can be observed when the maxillary and mandibular branches are affected\(^6\).

Oral vesicles appear mainly after a skin manifestation\(^3,5\). Sometimes, however, there may be mucosal involvement without skin lesion\(^7\). The vesicles erupt and leave mucosal erosions but no scar in most cases\(^3\). The most significant complication of HZI is post-herpetic neuralgia\(^2\); other complications may include facial scarring, motor nerve palsy, optic neuropathy, blindness, encephalitis, and calcinosis cutis\(^6\).

The bony change in association with HZI was first reported by Rose in 1908\(^7\). According to Dechaume et al. (1955)\(^8\), Gonnet’s presentation in 1922 was the first report to establish interest in osteonecrosis and tooth exfoliation associated with HZI\(^2\). Complication such as osteonecrosis with spontaneous tooth exfoliation is very rare. Thus, we report some cases of osteomyelitis in the mandible caused by HZI affecting the trigeminal nerve.

II. Cases Report

1. Case 1

A 78-year-old male patient visited our hospital on February 12, 2010 with chief complaint of osteonecrosis of mandible
A skin lesion in the mandibular right area was observed, showing a healing pattern based on the clinical examination. (Fig. 1) The oral findings included exposure of necrotic bone in the mandibular right area, pus discharge through extraction sockets for canine, first and second premolar, and malodor. (Fig. 2) The patient’s oral hygiene was poor and there were many root rests observed in the maxillary right second molar, first molar, second premolar, first premolar, maxillary left first molar, mandibular left first premolar, second premolar, and first molar. There was no significant finding from the blood test and chemical test. Additionally, computed tomography (CT) scan was conducted. The radiological findings included a low attenuate intraosseous lesion with ill-defined border. Reactive osteosclerosis around the lesion, and sequestrum were seen in a lesion. Other findings included the bony destruction pattern of the buccolingual cortical bone near the lesion and multiple enlarged lymph node in the submandibular space. (Fig. 3)

When the patient visited the hospital again on the February 17, the exposure pattern of cortical bone in the right mandible showed no significant change compared to the first clinical examination, and the CT findings were explained to the
patient and his caregiver. We temporarily diagnosed it as mandibular osteomyelitis caused by HZI, hospitalized the patient on the 18th of the same month and year, and planned antibiotherapy, consultation with dermatologist, and sequestrectomy.

The dermatologist decided not to require additional antiviral treatment because the skin lesion had already entered the healing stage, and just recommend the administration of non-steroidal anti-inflammatory drug (NSAID) and pregabalin to provide relief from post-herpetic neuralgia. With antibiotherapy, sequestrectomy and extraction of root rests were performed under local anesthesia on February, 26. The bony defects were dressed with Vaseline gauze, which was replaced on a daily basis. The postoperative radiological findings showed normal healing pattern of the area where the bone was removed.

(Fig. 4) The lesion was overlapped with soft tissue in good condition nine days after the operation, and the patient discharged the hospital on the 16th day after the operation. As a result of monitoring until eight months after the surgery, the patient did not complain of post-herpetic neuralgia, and there were no findings of recurrence.

2. Case 2

A 77-year-old male patient was referred to our hospital with chief complaint of sore gingiva and mandibular pain on December 17, 2010. A month before visiting our hospital, the patient complained of pain in the right ear area, vesicles and swellings with pain along the pathway of the trigeminal mandibular branch on the right side of the face, and consulted an otolaryngologist, taking antiviral agent medication. Two weeks before he visited our hospital, he felt pain from sore gingiva and exposure of cortical bone beneath the gum. He had used maxillary complete denture and mandibular removable partial denture for several years.

The clinical examination revealed findings of erythematous edema in the right chin and ulcer and post-inflammatory hyperpigmentation in the right chin and preauricular area. (Fig. 5) The oral findings included the extraction socket (considered to have been dropped recently) of the mandibular right canine, first and second premolar used as abutment of the removable partial dentures, exposure of neighboring necrotic bones, and inflammation of neighboring gingiva. (Fig. 6) The patient did not remember the exact time of

![Fig. 4. Case 1. Post-operative radiographic findings post-operative day 8; the necrotic bone and multiple hopeless teeth were removed, and normal healing was noted.](image1)

![Fig. 5. Case 2. Skin lesions of herpes zoster; erythematous swelling and ulcer with post-inflammatory hyperpigmentation. A. Skin lesion can be seen on the chin, right. B. Skin lesion can be seen on the preauricular area, right.](image2)

![Fig. 6. Case 2. Necrotic bone was exposed, spontaneous teeth exfoliation on #43, 44, 45.](image3)
Since post-herpetic neuralgia persisted, gabapentin 600 mg, tramadol 37.5 mg, acetaminophen 325 mg, and aminotriptyline 10 mg were administered to the patient.

On June 8, 2011, after continuous follow-up for six months, post-herpetic neuralgia subsided, and sequestrum formed and naturally exfoliated. Biopsy of the exfoliated sequestrum was performed, with the result reported as necrotic bone. On June 29, the area was overlapped with soft tissue around the lesion, healing well. (Fig. 8)

3. Case 3

On July 22, 2010, a 74-year-old male patient visited our hospital with chief complaint of swelling of the left side of the face and pain. He complained of pain in the upper anterior teeth for three days before he visited our hospital, and vesicles and edema were formed along the pathway of the left trigeminal maxillary branch two days before he visited our hospital. On July 22, he went to a private dental clinic; he was then referred to our hospital. He took prescription pills for high blood pressure, which was relatively well-regulated. He wore maxillary and mandibular partial dentures for five years. The clinical examination showed that the left side of the face had diffuse erythematous plaques and vesicles with tenderness. (Fig. 9. A); the oral findings included multiple mucosal vesicles and ulcer formation on the left palate together with mobility of the remaining teeth and alveolar bone resorption in edentulous state except the maxillary right and left central incisor, lateral incisor, and canine. (Fig. 9. B) HZI was considered to be in active phase, consultation were administered with a dermatologist and a periodontist to prevent osteonecrosis and loss of remaining teeth. After the tooth exfoliation, but it was estimated to be about one week earlier according to the opinions of his caregiver and the people around him. Assuming mandibular osteomyelitis in association with HZI, antibiotics were prescribed to prevent secondary infection, and CT scan was conducted. Consultation with the dermatologist and otolaryngologist was administered for the skin lesion and otalgia. The radiological finding showed a low attenuate intraosseous lesion with relatively ill-defined borderin the mandibular right area but no destruction of cortical bone or sequestrum. Some of the enlarged lymph node in the submandibular space was observed. (Fig. 7) Dermatologically, since one month had passed after HZI, antiviral treatment was not required. For post-herpetic neuralgia, pregabalin and acetaminophen were administered.

When he visited the hospital again, the exposure pattern of the right mandibular cortical bone had no significant change compared to the first clinical examination. Since there was neither sequestrum nor acute inflammation, we only use antibiotics and antimicrobials (Chlorhexidine Gluconate Solution) for prevent secondary infection. Surgical sques-trectomy was planned in case of sequestrum develops in the future. Continuous follow-up and disinfection were perfor-

---

**Fig. 7.** Case 2. Radiographic findings; diffuse radiolucent lesion and extraction sockets area seen on the mandible, right. A. Orthopantograph. B. Mandibular computed tomography (CT) view; coronal. C. Mandibular CT view; axial.

**Fig. 8.** Case 2. Soft tissue covering previous lesion.
Alveolar bone necrosis and spontaneous tooth exfoliation associated with trigeminal herpes zoster: a report of three cases

Risk elements may include external damage of the affected dermatomes, psychological stress, and race. The thoracic dermatome is most commonly affected, accounting for 50% of the total cases. The cranial nerve may also be affected, with the trigeminal nerve most commonly affected (18.5-22% of the total cases) followed by the glossopharyngeal nerve and the hypoglossal nerve. In case of trigeminal nerve involvement, it is unilaterally limited to a single branch, mainly affecting the optic nerve.

Oral symptom is observed when the trigeminal maxillary and mandibular branches are affected and skin lesion is mainly preceded, but a case starting with paresthesia of mental nerve was also reported. The erythematous vesicle is developed in the oral cavity; it ruptures, forms an ulcer, and gets covered by white pseudomembrane. Lymphadenopathy may appear in the submandibular area. In addition, patients may complain of symptom similar to acute pulps of the affected tooth and toothache; root resorption and periapical lesion may also occur. Since histological findings that are not significantly different from the osteomyelitis pattern show necrotic bone and inflammatory cell infiltration, the diagnosis of the relationship with herpes zoster can hardly be confirmed only by such histological findings; the diagnosis should take into account the clinical findings. Among the findings, osteonecrosis of the jaw and natural tooth exfoliation are very rare complications. Jain et al. conducted a review of literature on 41 cases of osteonecrosis of the jaw caused by HZI. The onset age range was from 6 to 85, with 8 cases of patients under the age of 40.

III. Discussion

The prevalence rate of HZI in all ages is reported to be 1.2-4.8 per 1,000 people every year, with 7.2-11.8 people over the age of 60. The prevalence rate and seriousness increase with age. 40-50% of the patients with HZI are over the age of 60 every year, with 50% of persons over 85 years old recording prevalence rate of at least once. As to the reason for such prevalence rate increase, natural immunity decline according to age increase may be considered; the decline in VZV-specific cellular immunity according to age increase is supported. The prevalence rate also increases among immunocompromised patients such as patients infected with human immunodeficiency virus, hematologic malignant disease, and immune-mediated disorder and organ transplant patients, and the risk of HZI for such immune-suppressed patients also increases according to age. Other risk elements may include external damage of the affected dermatomes, psychological stress, and race.

Fig. 9. Case 3. Lesions of herpes zoster (active phase). A. Extraoral view; diffuse erythematous plaques and vesicles were seen on the upper side of the face (V2 area) with tenderness. B. Intraoral view; multiple mucosal vesicles and ulcer formation observed on the maxilla, left.

Fig. 10. Case 3. Lesions of herpes zoster (healing phase). A. Extraoral view; clusters on the skin on the upper side of the face (V2 area) were seen. B. Intraoral view; normal healing state on mucosal lesion. No visible scar formation.

10 cases of those between 40 and 60, and 12 cases of those over 60. The prevalence rate increased according to age, with no difference by gender. It mainly appeared unilaterally in the maxilla or mandible of the affected skin. 13 patients had it in the maxilla, and 18 patients, in the mandible. There were 31 lost teeth in the maxilla and 44 teeth in the mandible, making the mandible a predilection site. Since the anterior teeth numbered 64 and the posterior teeth were 61, there was no significant difference in the anteroposterior position. The exfoliated teeth per patient were 0-7; in five cases, all the teeth of the affected quadrant were lost.

With regard to the time interval between the outbreak of HZI and osteonecrosis accompanied by tooth loss, Mintz and Anavi presented in 1992 a report on the interval of an average of 21.2 days together with the occurrence of natural tooth exfoliation about 2-6 weeks after HZI manifestation through a review of 14 studies. Several authors reported that it occurred between two weeks after early infection with complication of osteonecrosis and tooth exfoliation, but other authors reported that it occurred between 3-12 weeks after HZI manifestation as a late complication. In the first case reported in this paper, the extraction of the mandibular right canine was performed about 4 weeks after HZI manifestation even though the mandibular first and second premolars were ruled out because those premolars were lost four weeks before the outbreak of skin lesion. In the second case, natural tooth exfoliation occurred about three weeks after HZI manifestation.

Taking into account the comparison of general osteomyelitis, in case of findings that show a medical history of herpes zoster recently affecting the trigeminal nerve and vesicular lesion in the related facial area with proper interval, and that the lesion is limited only to quadrant of jaw with the affected nerve distributed, it may be diagnosed as osteomyelitis of the jaw caused by trigeminal herpes zoster. Patients showing osteomyelitis of the jaw in Case 1 and Case 2 were old, taking prescription pills for high blood pressure and having medical history of coronary artery bypass surgery to avoid angina pectoris and cerebral artery infarction, respectively. Since they were old and weak patients with blood diseases, it might be diagnosed as general chronic pyogenic osteomyelitis caused by local dental infection. In Case 1, however, many remaining teeth were affected by dental caries or root rests; since the radiopaque lesions around the root apex were distributed in the maxilla and mandible, it could be judged that there was local dental infection causing chronic osteomyelitis. Taking into account the findings of the interval closely associated with the manifestation of herpes zoster affecting the trigeminal nerve and the progress of osteonecrosis and osteomyelitis accompanied by tooth exfoliation in the related quadrant only, we confirmed the diagnosis of osteonecrosis of the jaw to be associated with HZI. Since the patient in Case 2 had only mandibular right first and second premolars and canine as the remaining teeth, and there was no topical factor in the other quadrants, it may be more difficult to distinguish from general osteomyelitis. Nevertheless, considering the clinical history and patterns, we cannot rule out the relationship with herpes zoster.

The pathophysiological mechanism of osteomyelitis of the jaw caused by trigeminal herpes zoster is controversial, and several hypotheses are under discussion. The first hypothesis is that local vasculitis caused by the direct extension of neural inflammatory response to the adjacent blood vessels. This eventually may cause an infarction of the trigeminal vessels that accompany the trigemical nerves supplying the jaws and cause bone necrosis by triggering ischemia. The second hypothesis is that the generalized infection of terminal nerves supplying the periosteum and periodontium is believed to cause vasculitis of the periosteum and periodontium and avascular necrosis over a large area. According to Gilden et al., since VZV can also be invaginated to the vascular endothelial cell in the peripheral nervous system instead of being limited to the brain or spinal cord, it causes small ischemic lesion, possibly developing into necrosis and demyelination. The report can serve as grounds for the two hypotheses above. The third hypothesis can be a denervation of bone, but denervation only can hardly be thought to cause serious bone damage in a short time. The fourth hypothesis is that systemic viral infection renders damage to an odontoblast and brings about tissue denaturation, causing pulpal necrosis. The final hypothesis is that the existing pulps, periodontitis, or surgical procedure around the HZI area can cause serious necrosis of the alveolar bone. In comparing Case 1, Case 2, and Case 3 above, the regulation of initial response and topical factors is meaningful in preventing complications such as osteomyelitis and osteonecrosis of the jaw, and the local factor can be considered a cause of the mechanism in the development of osteomyelitis associated with trigeminal herpes zoster.

The cases above and literature review reveal that, in case of the outbreak of trigeminal herpes zoster, the prompt application of antiviral agents, active use of painkillers, and effective regulation of topical factors will be helpful in preventing such complications. If osteomyelitis and osteonecrosis
of the jaw occur as complications, such complications can be treated through the proper use of antibiotics to avoid secondary infection, squestrectomy, removal of inflammatory tissue, and regular follow up\textsuperscript{2,4,13-15}. In these cases, when osteomyelitis of the jaw and osteonecrosis accompanied by tooth exfoliation as rare complications after the outbreak of trigeminal herpes zoster occur, active use of painkillers, regulation of topical factors, and proper extraction of dead bone and affected teeth bring about good results.

References

7. Rose F. Postherpetic neuralgia; trophic lesions in hand’s bones similar to rheumatoid arthritis. Nouvelle Iconogr de la Salpêtrière, Soc Neurol 1908;9:64. [French]