Clinical Diagnosis and Treatment of Herpes Zoster in an Immunocompromised Dental Patient: A Case Report

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Herpes zoster (HZ) is an acute, unilateral inflammatory viral infection characterized by a rash with painful blisters in a localized area of the body. HZ is often associated with intense pain in the acute phase and presents postherpetic neuralgia in the chronic phase. During the prodromal stage of the HZ from the trigeminal nerve, however, the only presenting symptom may be odontalgia, which could be particularly difficult to diagnose. This distinctive syndrome occurs predominantly in the immunocompromised or elderly individuals. In this article, we report a case of HZ developed in the trigeminal nerve of a 60-year-old immunocompromised female patient, whose symptoms including atypical, non-odontogenic odontalgia had improved after series of antiviral treatments.

Key Words: Herpes zoster; Toothache

Introduction

The herpes simplex virus type 3 of Herpesviridae, also known as varicella-zoster virus (VZV), is the infection agent for both varicella (chickenpox) and herpes zoster (HZ)¹. Typically, primary infection with the VZV causes varicella, illness with the acute onset, short-lived, generalized maculopapular skin rash. After development of immunity for the VZV, dormant virus persists in the dorsal root ganglia without any clinical symptoms². Years after the initial infection, the reactivated virus may spread from one ganglia to the another and infect the affiliated dermatome to cause a painful skin rash³. In one study, HZ has been reported to have the overall incidence of roughly 3/1,000 of the population/year rising to 10/1,000 per year by 80 years of age⁴. Although antibody levels of VZV in
advancing age are relatively constant, the elders experience the higher incidence and severity of HZ and postherpetic neuralgia (PHN) because of age-related progressive decline in cell-mediated immunity to the virus. Other circumstances such as malignancies, human immunodeficiency virus, use of immunosuppressant drugs, physical trauma including dental manipulation, and psychological stress also contribute to reactivation of the VZV.

Prolonged and disabling pain and discomfort could diminish the HZ patient’s quality of life. According to Lydick et al., the degree of discomfort could be equivalent to that in diseases such as congestive heart failure and myocardial infarction. However, the only presenting symptom of the HZ during prodromal stage may be odontalgia, which may be a diagnostic challenge even for experienced dentists. Thus, practicing dentists should be familiarized with manifestations of HZ since misguided emergency treatments for the atypical odontalgia may often result in irreversible damage or delay the appropriate treatment.

The following case presents the treatment of a 60-year-old immunocompromised female patient who had suffered from HZ with atypical, non-odontogenic odontalgia.

**Case Report**

In May 2013, a 60-year-old female patient with medical history of leukopenia, hypertension, and iron-deficient erythropoiesis visited Seoul National University Bundang Hospital (SNUBH)’s emergency room (ER) with complaints of headache and odontalgia (visual analogue scale, 10) on lower left molar area that started two days prior to the admission. The patient had visited a local dental clinic in the same morning and received root canal treatment (access open) on the lower left 2nd premolar (Fig. 1). The patient, however, had persisting pricking toothache after the dental treatment. Therefore, she was referred to the ER and tentatively diagnosed with trigeminal neuralgia by attending dentist and discharged with a prescription of carbamazepine 200 mg (Tegretol-CR Tab.; Novartis Korea, Seoul, Korea) and ultracet (Tramadol 37.5 mg/acetaminophen 325 mg; Janssen Korea, Seoul, Korea).

Four days later, the patient visited at Department of Oral and Maxillofacial Surgery (OMFS) in SNUBH with developed ulcerative lesions on lower left lip mucosa and erythematous multiple bullous lesions on left chin and ear area. The patient complained that the pricking pain (visual analogue scale, 10) persisted. Dentists in the department soon noticed that these symptoms may be manifestations of viral infections; HZ was ruled out subsequently for differential diagnosis and further examinations were arranged after the patient’s hospitalization. Throughout the hospitalization, ultracet tablet was prescribed as pro re nata.

On day 1 after the hospitalization, antiviral agent acyclovir (Zoylex; Korea United Pharm., Seoul, Korea) was injected intravenous (IV) 250 ml every 8 hours with dexamethasone 10 mg IVS (Yuhan, Seoul, Korea). A 5% acyclovir cream (Vivir; Hanmi Pharm., Seoul, Korea) was also applied on the bullous lesion and further consultation letters were sent out to Department of Dermatology and Division of Infectious Diseases electronically.

On the following day, the patient complained difficult in eating because of intra-oral and...
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neck pains. Oropharyngeal and ear invasions were suspected, a consultation was sent out to Department of Otolaryngology. A 75 mg pregabalin (Lyrica; Pfizer Korea, Seoul, Korea) twice a day and 1% lidocaine gargling were prescribed. Complete blood cell count (CBC) result showed white blood cell (WBC) of 1.78×10^3 μl and absolute neutrophil count (ANC) of 125 μl at the time. The patient was quarantined in an isolated ward and consultation with Division of Hematologic Oncology was preceded.

Use of acyclovir was maintained for the seven days and Burrows solution of 1 : 40 wet dressing three times a day and application of 2% mupirocin ointment (Bactroban; Hanall Biopharma, Seoul, Korea) were confirmed by a dermatologist. Further steroidal use was discouraged because it could lower neutrophil level and mask heatness. A 300 μg filgrastim (Grasin; Jeil Pharm., Seoul, Korea) was injected hypodermically to compensate the lowered neutrophil level.

On day 3, the patient had relieved pain with CBC report showing WBC 14.01×10^3 μl, ANC 10,648, and C-reactive protein (CRP) 3.97 mg/dl. The patient was prescribed with ofloxacin drops (Tarivid Otic; Jeil Pharm.) application on inner ear following Department of Otolaryngology’s recommendation. The steroidal use was reduced.

On day 4, the pain vanished almost completely with WBC 15.28×10^3 μl and CRP 3.41 mg/dl. The lesion showed clinical healing state with a formation of multiple crusts. The steroid was finally discontinued. The patient was discharged from the hospitalization on the next day with a prescription of valacyclovir (Valcivir; Hanmi Pharm.), aceclofenac (Asec; Hanmi Pharm.), and pregabalin (Lyrica) (Fig. 2).

At the fourth day of follow-up, the patient received simple dressing and low-intensity laser therapy on the crusts to accelerate healing process (Fig. 3). Seven

Fig. 2. Clinical photographs during the hospitalization. Rash becomes vesicular and forms blisters; crusts eventually take over. (A, E) On day 2. (B, F) On day 3. (C, G) On day 4. (D, H) On day 5.
days after the discharge, the patient complained of hypoesthesia on lower left lip, anterior teeth, and jaw (visual analogue scale, 5). The laser therapy was carried out again. Ten days after the discharge, the patient consistently complained of paraesthesia on the left facial area with minor headaches (Fig. 4). Consultation with otolaryngology was scheduled. Further follow-up by OMFS was discontinued after the patient showed improvements in the symptoms.

Discussion

The early symptoms of HZ include generalized headache, photophobia, and malaise, usually without constitutional symptoms[2]. Itching, tingling, and burning or stinging pain in the affected dermatome commonly follows until a strip or small area of maculopapular and vesicular rash appear several days later. The rash will later form small blisters filled with serous exudates, then scab, until

Fig. 3. Low-intensity laser therapy performed on left chin and ear areas.

Fig. 4. Clinical photographs taken after the discharge. Crusts fall off and the skin gradually heals, with scarring and discolored skin remain. (A, D) After 4 days. (B, E) After 7 days. (C, F) After 10 days.
Infiltration of the virus in trigeminal nerve could cause neuritis, an inflammation of nerve derived from bacterial or viral infection and mimic odontalgia\textsuperscript{9,10}. Pain rising from neuritis may present relatively constant, dull, pricking or even burning pain. The pain could also accompany allodynia, pain resulting from a non-injurious stimulus. If branches of the trigeminal nerve are affected with viral degeneration, odontalgia and pulpal necrosis may also be observed\textsuperscript{7}. Hence, without any dermatomal or mucosal symptoms, viral neuritis can be particularly difficult to differentiate from other neuropathic or odontogenic pain even for experienced dentists.

When our patient first arrived in the ER, attending dentist prescribed carbamazepine, a common drug in the treatment of trigeminal neuralgia, because symptoms the patient displayed were not yet differentiable. However, when the patient visited our department four days later with developed ulcerative lesions and erythematous multiple bullous lesions on localized facial areas, HZ was subsequently ruled-out.

Once the HZ is diagnosed, the vast majority of patients is treated by symptomatic therapy with goals to decrease the viral dissemination, accelerate the healing process, restrain the pain, and minimize the debilitating complications\textsuperscript{31}. For this purpose, zoster vaccine, antiviral agents (\textit{i.e.}, acyclovir, valacyclovir, or famciclovir) combined with analgesics and sometimes steroids has been shown to be effective. Although zoster vaccine is proven to be safe, effective, and recommended for immunization of immunocompetent individuals over age 60 years, it is not recommended in treating immunocompromised individuals or patients with recent HZ\textsuperscript{12}. Antiviral drugs inhibit VZV replication and reduce recurrence of HZ with minimal complications, but they do not completely prevent risk of PHN.

Steroids are frequently used in treatment of the HZ. In one clinical trial involving immunocompetent patients older than 50 years of age with localized HZ, administration of prednisone with acyclovir improved the patients’ healing time and discomfort\textsuperscript{39}. However, steroids, the anti-inflammatory and immunosuppressive drugs, are not recommended in treating immunocompromised individuals, and oral steroids do not show protective effect against PHN. The options for treating PHN include topical agents to reduce allodynia, such as lidocaine patches, and systemic agents, such as the anticonvulsants gabapentin and pregabalin\textsuperscript{4}. The antiviral drugs are often used both as prophylaxis and as therapy during the acute phase. Acyclir has been the standard treatment for our patient but she was also administered with valacyclovir, a new drug known to demonstrate similar or even superior efficacy\textsuperscript{14}. The patient was also intravenously injected with acyclovir since it is known method to reduce complications in immunocompromised individuals with HZ.

Although the pain and rash diminishes after weeks of reactivation in healthy individuals, patients with reduced immunity may experience residual nerve pain lasting more than several months. Visceral dissemination of VZV to other vital organs such as the lungs, liver, and brain could occur in immunocompromised individuals\textsuperscript{50}. Our patient, who had medical history of leukopenia, was injected with filgrastim to compensate the lowered neutrophil level. Because blistering rash formed can be infected by bacteria, our patient was prescribed with antibacterial drugs such as mupirocin ointment and tarivid otic drop. The patient also received low-intensity laser therapy.
The laser therapy, with beneficial effects on tissue healing and pain relief, can be used in the treating both acute phase HZ or in chronic PHN\(^{15}\). Consultations with various medical specialties (i.e., dermatology, otolaryngology, infectious disease, and hematologic oncology) were also scheduled due to possible potential damages in affected, neighboring nerve segments and new infections.

We have reported a treatment case of immunocompromised patient who had suffered from HZ activated in the trigeminal nerve. With steady increase in geriatric population, it is important to detect HZ in early stages because prompt management of acute HZ with antiviral medication could reduce the duration and severity of the acute zoster. Considering that one of the key manifestations of HZ of the trigeminal nerve is non-odontogenic odontalgia, a role of dental professions in identifying onset of the virus are important for accurate differential diagnosis and treatment to decrease the duration and serious complications of HZ.

**Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

**References**

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