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Treatment of medication-related osteonecrosis of the jaw around the dental implant in a patient with multiple myeloma: a case report

Minyeong Youn, Youngjae Yee, Jun-Young Kim

Department of Oral and Maxillofacial Surgery, Yonsei University College of Dentistry, Seoul, Korea

The management of medication-related osteonecrosis of the jaw (MRONJ) around a dental implant is difficult. Conservative treatment is recommended, but patients do not exhibit improvement. Thus, several adjunctive therapies have been introduced. This paper describes a case of MRONJ around a dental implant in a 68-year-old man. Treatment with teriparatide was contraindicated because of the patient's history of multiple myeloma. Successful results with hyperbaric oxygen therapy and surgical intervention were achieved. Clinicians treating patients with MRONJ should conduct a thorough examination before selecting the modalities of adjuvant therapy, thereby establishing a solid treatment strategy. (JOURNAL OF DENTAL IMPLANT RESEARCH 2020;39(4):43-47)

Key Words: Osteonecrosis of the jaw, Dental implant, Multiple myeloma, Bisphosphonate

INTRODUCTION

Bisphosphonates (BPs) are a class of drugs commonly used for bone disease owing to their osteoclast-inhibition properties. They have been indicated for various diseases, including osteoporosis, metastatic bone cancer, Paget's disease, and osteolytic lesions in multiple myeloma[1,2].

However, their use might lead to significant complications. Marx first recognized and described medication-related osteonecrosis of the jaw (MRONJ) decades ago[3]. In its 2014 position paper, the American Association of Oral & Maxillofacial surgeons classified MRONJ into five stages according to the clinical features and suggested treatment strategies based on disease stages[4]. There have also been studies investigating the association between MRONJ risk and the serum levels of bone turnover markers such as serum C-telopeptide of collagen type 1 (CTx), procollagen type 1 N-terminal propeptide (P1NP), and osteocalcin[5-7]. For the serum CTx level, Marx classified <100 pg/ml as high risk, 100 pg/ml to 150 pg/ml as moderate risk, and >150 pg/ml as minimal risk[5]. However, it remains quite challenging for clinicians, and there is currently no gold standard treatment. In addition to BP administration and surgical intervention, various adjunctive treatments with laser, ozone, growth factors (platelet-rich plasma or recombinant human bone morphogenetic protein-2), pentoxifylline and tocopherol (PENTO), hyperbaric oxygen (HBO), and teriparatide have been suggested[8-13].

Teriparatide, a recombinant human parathyroid hormone, simultaneously stimulates osteoblasts and osteoclasts, thus reactivating bone remodeling[14]. Since Harper and Fung first described a case of a patient with MRONJ who was successfully treated with teriparatide in 2007, there have been several reports on the effectiveness of teriparatide in the treatment of MRONJ[12,14-16]. However, owing to its ability to promote osteoclastic bone resorption, teriparatide is contraindicated in patients with cancer and known bone metastasis[17]. There have also been reports on the occurrence of adverse effects with the use of ter-

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Correspondence to: Jun-Young Kim, Department of Oral and Maxillofacial Surgery, Yonsei University College of Dentistry, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea. Tel: +82-2-228-3134, Fax: +82-2-227-7825, E-mail: jyomfs@yuhs.ac

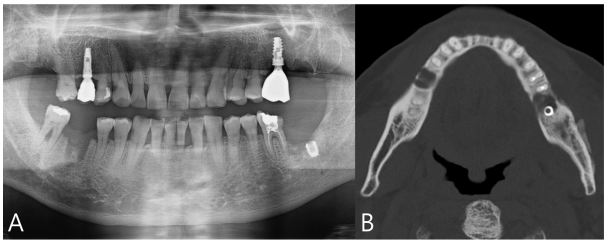

Fig. 1. Initial panoramic radiograph (A) and computed tomography (B) depicting an osteolytic lesion around extraction socket and dental implant.

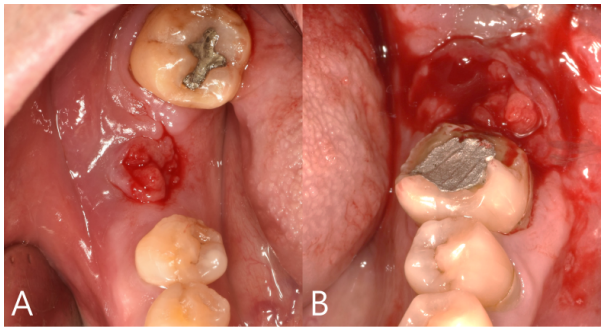

Fig. 2. Intraoral photograph after 6 weeks of conservative care. Soft tissue erythema and swelling are shown (A: right side, B: left side).

iparatide in multiple myeloma, which suggest that the use of teriparatide should be restricted in patients with multiple myeloma[18,19].

Herein, we describe the successful treatment of MRONJ around dental implants in a patient with multiple myeloma.

CASE REPORT

A 68-year-old man was referred to the department of oral and maxillofacial surgery owing to an unhealed wound on the mandible. The patient had previously undergone extraction of the right mandibular molar 6 months prior and curettage around the left mandibular molar implants 9 months prior to his visit. The patient was diagnosed with multiple myeloma and treated with zoledronate (Zometa®) for the preceding 14 months, after which the treatment was discontinued. Clinical examination revealed gingival redness, swelling, and purulent discharge from both mandibles. Panoramic radiography and computed tomography revealed delayed healing of the extraction socket on the right mandible, diffuse osteolysis, and periosteal new bone formation on the left mandible (Fig. 1). As there was no exposed necrotic bone, and the osteolytic lesion was not extended to the inferior border of the mandible, the patient was diagnosed with stage 2 MRONJ[4]. Serum levels of CTx, P1NP, and the parathyroid hormone were examined to evaluate the bone turnover rate. The initial serum levels of CTx and P1NP were 149 pg/ml and 16.5 ng/ml, respectively. Conservative care with oral antibiotics, pentoxifylline 400 mg twice daily (Trental®, HANDOK, Seoul, Korea), tocopherol 200 mg twice daily (Welltamin®, Samjin Pharm, Seoul, Korea) (PENTO), and an antibacterial mouth rinse were planned. There was no significant improvement or symptom relief, even after 6 weeks of administration; therefore, adjuvant therapy was planned (Fig. 2). As teriparatide was contraindicated owing to multiple myeloma, treatment with hyperbaric oxygen (HBO) was performed as adjuvant therapy. After HBO therapy, the gingival swelling and redness subsided (Fig. 3). Three months after his first visit, the serum CTx level was 181 pg/ml and the osteocalcin level was 8.29 ng/ml. Panoramic radiography and computed tomography revealed the formation of a sequestrum on the bilateral mandible (Fig. 4). Surgical intervention was planned, and sequestrectomy was performed on both sides of the mandible under general anesthesia, and platelet-rich fibrin (PRF) was applied to the surgical defect to promote wound healing. PRF was exposed at the time of stitch-out, but the healing pattern was favorable. HBO therapy was performed postoperatively, and the patient showed good soft tissue healing (Fig. 5), and radiographic examination revealed the progression of bone healing (Fig. 6).

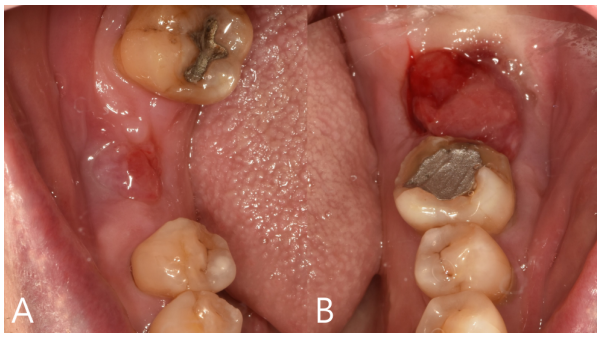

Fig. 3. Intraoral photograph after hyperbaric oxygen treatment showing subsided soft tissue lesion (A: right side, B: left side).

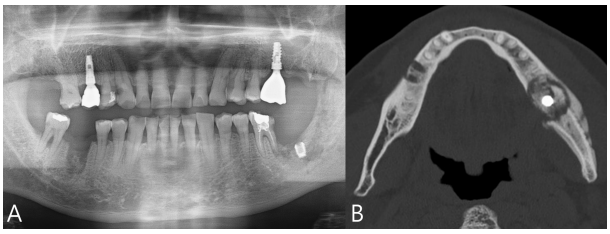

Fig. 4. Panoramic radiograph (A) and computed tomography (B) showing formation of sequestrum around dental implant on left side of mandible and extraction socket on right side of mandible.

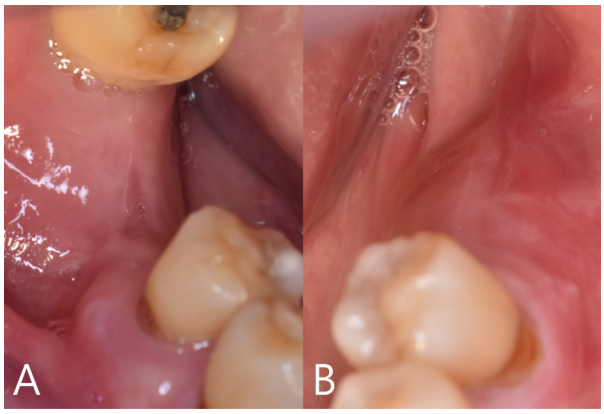

Fig. 5. Intraoral photograph showing excellent soft tissue healing 6months after surgical intervention (A: right side, B: left side).

DISCUSSION

As it is known that anti-resorptive and anti-angiogenic agents can induce avascular osteonecrosis of the jaw, this has become a concern for clinicians. The correlation of MRONJ and the presence or placement of dental implants has been discussed in the literature[20-22]. Currently, the treatment strategy for MRONJ is determined according to the disease stage based on the 2014 consensus of the American Association of Oral and Maxillofacial Surgeons[4]. However, patients do not respond to exclusive conservative treatment. Accordingly, various attempts at adjuvant therapy have been made, and among them, teriparatide seems to be promising, as it affects osteoblast function and exerts an anabolic effect. Despite its advantages, the use of teriparatide might be limited. The patient described here was unable to use teriparatide owing to multiple myeloma. In addition to conservative treatment recommended by AAOMS, PENTO and HBO were used as adjuvant therapies. Pentoxifylline improves

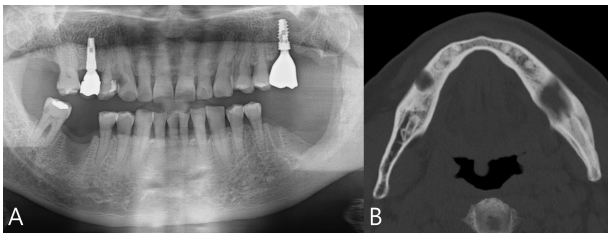

Fig. 6. Radiographic image showing progression of bone healing.

peripheral blood flow by increasing erythrocyte flexibility and vasodilation[23]. It also has an anti-tumor necrosis factor effect, thus inhibiting inflammation and decreasing fibrosis[24,25]. Tocopherol is a potent oxygen radical scavenger that reduces free radical damage to tissues. The combination of these (PENTO) has been reported to demonstrate an effect on MRONJ[11,26,27]. Meanwhile, HBO therapy generates reactive oxygen species (ROS) and reactive nitrogen species (RNS) that affect signaling processes critical to wound healing[28]. ROS and RNS also influence osteoclast differentiation and activity and could possibly counteract a BP-induced suppression of osteoclast activity[29,30]. After the formation of sequestra, surgical intervention with sequestrectomy, including dental implant fixture removal was performed. Excellent treatment results were achieved through a series of procedures.

In conclusion, although teriparatide is a promising treatment modality for MRONJ, a thorough examination should be performed prior to such treatment, and if it is contraindicated, other forms of adjuvant therapy should be considered.

CONFLICT OF INTEREST

We have no conflicts of interest.

ORCID

Minyeong Youn, https://orcid.org/0000-0003-2081-8953
Youngjae Yee, https://orcid.org/0000-0002-7954-948x
Jun-Young Kim, https://orcid.org/0000-0002-6596-6135

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