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Successful treatment of osteonecrosis-induced fractured mandible with teriparatide therapy: A case report



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ABSTRACT

INTRODUCTION: The management of medication-related osteonecrosis of the jaw (MRONJ) is controversial. To date, there is no established treatment for cases of advanced stage 3 MRONJ osteoporosis in elderly patients.

PRESENTATION: An 87-year-old osteoporotic woman with osteonecrosis-induced left mandible fracture related to minodronate therapy was referred to us for treatment. She had a vertebral compression fracture concurrently and had started subcutaneous injection of teriparatide. After 18 months of treatment with teriparatide the pathological mandible fracture was healed and functional recovery of the occlusion was obtained by complete dentures.

DISCUSSION: Teriparatide may have a powerful anabolic effect on bone, and promote bone regeneration against pathologic mandible fracture induced by MRONJ.

CONCLUSION: Based upon these findings, teriparatide might be beneficial for advanced stage 3 MRONJ osteoporosis in elderly patients.

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1. Introduction

Since bisphosphonate-related osteonecrosis of the jaw (BRONJ) was first reported [1], numerous cases have been identified [2]. The American Association of Oral and Maxillofacial surgery (AAOMS) updated their position paper on BRONJ in 2014, in which the term BRONJ was replaced with “medication-related osteonecrosis of the jaw” (MRONJ) [3]. Management of advanced MRONJ is both challenging and controversial. An AAOMS position paper described that these patients benefit from debridement, including resection, in combination with antibiotic therapy, which can offer long-term palliation with resolution of acute infection and pain. Symptomatic patients with stage 3 disease may require resection and immediate reconstruction. However, there is occasionally a case in which mandilectomy is not indicated because of age and primary illness.

Teriparatide (recombinant human PTH 1–34) is an osteoanabolic agent which induces bone formation [4], and is approved for the treatment of postmenopausal osteoporosis, male osteoporosis and glucocorticoid-induced osteoporosis. Administration of teriparatide for the treatment of MRONJ resistant to conventional

treatment was first introduced by Harper and Fung [5]. Subsequently, several case reports have disclosed favorable therapeutic outcomes from teriparatide in MRONJ [6–8]. We report here an 87-year-old osteoporotic woman with an MRONJ-induced mandible fracture that was successfully treated with teriparatide.

2. Case presentation

An 87-year-old woman with a 2-year history of minodronic acid hydrate (50 mg/4 w orally) for the treatment of osteoporosis was referred to us in 2013 for treatment of a pathological mandibular fracture. She had undergone extraction of the left mandibular first molar 5 months earlier, and underwent oral irrigation for the intraoral fistula at another hospital. She had an incomplete occlusion of the denture, and movement of the mandible bony fragment. The infection of the soft tissue and mandible had extended to the inferior border of the left mandible and emerged as an extraoral fistula (Fig. 1). Computed tomography revealed osteolysis extending to the inferior border resulting in a pathological fracture of the left mandible (Fig. 2). A biopsy was done and the histology revealed chronic inflammation and sequestrum. She was diagnosed with stage 3 BRONJ. She had a vertebral compression fracture concurrently and had started subcutaneous injection of teriparatide (56.5 µg/week) 1 month earlier. After discussion with the family physician, teriparatide treatment was continued and conservative treatment including amoxicillin hydrate administration (750 mg/d) initiated. Six months after the initiation of teriparatide therapy,

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Fig. 1. Extraoral view showing left submandibular extraoral fistula.



Fig. 3. Computed tomography after 18 months of teriparatide treatment.



Fig. 2. Computed tomography at the first medical examination.



Fig. 4. Extraoral view after 18 months of teriparatide treatment.

bone sequestration of the left mandible had occurred, and the patient was receiving intraoral sequestrectomy under local anesthesia. After 7 months of the treatment, her symptoms had resolved and the intraoral and extraoral fistula had been converted to normal mucosa and skin respectively; therefore, administration of the antibiotic was discontinued. After 18 months of treatment with teriparatide, computed tomography showed significant bone regeneration and recovery of the mandible bone continuity (Fig. 3). Thereafter, she obtained functional recovery of the occlusion by complete dentures (Fig. 4).

3. Discussion

Teriparatide has been approved for osteoporosis management [9]. In addition to its effect on osteoporosis of increasing bone mineral density and bone strength, it has the potential to allow correction of unstable vertebral fractures without surgical intervention [10], and it promotes typical femoral fracture healing after long-term bisphosphonate administration [11]. Teriparatid is able to reverse the anti-resorptive effect of bisphosphonates. It has been shown to stimulate the activity and viability of osteoblasts from the alveolar bone of chronic bisphosphonate users [12], while indirectly increasing the metabolic activity and number of osteoclasts by affecting osteoblast function [13]. Therefore, teriparatide therapy has the effect of improving bone formation and modulating

bone resorption at bisphosphonate therapy-induced pathological fractured sites of the mandible. In this case, mobile bone sequestrum was revealed 6 months after the teriparatide therapy was initiated. These results suggested that teriparatide can effectively enhance bone remodeling and separate the bone sequestrum for up to 6 months.

Successful cases of surgical resection of the mandible were reported by Carson and Basile in 2009 [14]. Recently, resection of MRONJ produced healing in patients taking oral bisphosphonate more successfully than conservative management [15]. However, aggressive resection of the jaw creates a difficult problem of delayed soft tissue coverage because osteoporosis patients are usually elderly and their wound-healing ability impaired. Elderly persons especially, i.e., those more than 80 years, have a characteristic decrease in body functions and various kinds of coexistent underlying disease. Therefore, when complications occur once, there is the risk that a vital organ will fall into malfunction in a chain reaction, and particularly careful operative adaptation and perioperative care are required.

In conclusion, teriparatide therapy can provide an important treatment option for advanced MRONJ stage 3 osteoporosis in elderly patients.

Conflict of interest

None.

Source of funding

None.

Ethical approval

N/A.

Consent

Informed consent was taken.

Author contribution

Tsuyoshi Shimo and Mayumi Yao contributed to data and writing. Yuko Ono, Kyoichi Obata, Norie Yoshioka, and Akira Sasaki contributed to data collectio'ns.

Guarantor

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