

Different Treatment Applications of Medication-Related Osteonecrosis of the Jaw on Osteoporotic Removable Partial Denture Patients: A Clinical Report

^{id} Meryem ŞAHİN^{a,b}, ^{id} Sirmahan ÇAKARER^c, ^{id} Fatma ÜNALAN^{d,e}

^aDepartment of Prosthodontics, İstanbul University Faculty of Dentistry, İstanbul, Türkiye

^bDepartment of Prosthodontics, Biruni University Faculty of Dentistry, İstanbul, Türkiye

^cDepartment of Oral and Maxillofacial Surgery, İstanbul University Faculty of Dentistry, İstanbul, Türkiye

^dDepartment of Prosthodontics, İstanbul University Faculty of Dentistry, İstanbul, Türkiye

^eDepartment of Prosthodontics, İstanbul Kent University Faculty and Dentistry, İstanbul, Türkiye

This study was presented as a poster at the International Congress on Preventive Dentistry, March 5-8 2018, Erzurum, Türkiye.

ABSTRACT Bisphosphonates are highly effective medicines in preventing bone resorption in patients with malignant and benign bone diseases such as osteoporosis, multiple myeloma, hypercalcemia and Paget disease, which have intense bone resorption. However, it causes some complications by suppressing remodeling in the bone, and osteonecrosis in the jaws is becoming increasingly common in these complications. A 63-year-old woman was admitted with pain and swelling due to a removable prosthesis. She had used bisphosphonate 6 years ago and was diagnosed with Stage 2 medication-related osteonecrosis of the jaw by clinical, radiological and pathological examination. This clinical report describes the medical and surgical treatment used, along with hyperbaric oxygen therapy and laser therapy.

Keywords: Bisphosphonate-associated osteonecrosis of the jaw; osteonecrosis

Bisphosphonates (BPs) are prescribed to manage cancer-related conditions, skeletal-related events associated with bone metastases in the context of solid tumors, osteoporosis and osteopenia, Paget disease of bone and osteogenesis imperfecta.¹

Even though there are many benefits for patients with skeletal complications and this medication reduces the risk of fractures in postmenopausal osteoporotic women, side effects are also present and complications are increasing.¹

The American Association of Oral and Maxillofacial Surgeons (AAOMS) stated that there must be three criteria for diagnosis of bisphosphonate-related osteonecrosis of the jaw (BRONJ): Exposed bone in the maxillofacial region that does not heal for 8 weeks after diagnosis, ongoing or previous BP up-

take and an absence of radiation therapy in the craniofacial region.²

Because osteonecrosis seen in the jaws may also be caused by other medications, the BRONJ definition in 2014 was actually changed by medication-related osteonecrosis of the jaw (MRONJ).¹

Although the exact mechanism of MRONJ is unknown, it is thought to be multifactorial; oral surgery such as dental extraction, periodontal problems before tooth extraction, dentoalveolar trauma, implantation, dental prostheses and poorly fitting dentures are among the local factors.¹

In 2014, AAOMS was categorized according to the clinical status of patients, and the treatment plan for these classifications was determined (Table 1).¹

Correspondence: Meryem ŞAHİN

Department of Prosthodontics, İstanbul University Faculty of Dentistry, İstanbul, Türkiye

E-mail: mrym_ndr@hotmail.com

Peer review under responsibility of Türkiye Klinikleri Journal of Case Reports.

Received: 12 Dec 2021

Received in revised form: 07 Jan 2022

Accepted: 12 Jan 2022

Available online: 26 Jan 2022

2147-9291 / Copyright © 2022 by Türkiye Klinikleri. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



TABLE 1: Categorization and treatment protocol of MRONJ according to AAOMS.¹

Staging of medication-related osteonecrosis of the jaw	Treatment strategies
At risk-no apparent necrotic bone in patients who have been treated with oral or intravenous bisphosphonates	No treatment indicated Patient education
Stage 0-no clinical evidence of necrotic bone but nonspecific clinical findings, radiographic changes, and symptoms	Systemic management, including use of pain medication and antibiotics
Stage 1-exposed and necrotic bone or fistulas that probes to bone in patients who are asymptomatic and have no evidence of infection	Antibacterial mouth rinse Clinical follow-up on a quarterly basis Patient education and review of indications for continued Bisphosphonate therapy
Stage 2-exposed and necrotic bone or fistulas that probes to bone associated with infection as evidenced by pain and erythema in the region of exposed bone with or without purulent drainage	Symptomatic treatment with oral antibiotics Oral antibacterial mouth rinse Pain control Debridement to relieve soft tissue irritation and infection control
Stage 3-exposed and necrotic bone or a fistula that probes to bone in patients with pain, infection, and ≥ 1 of the following: Exposed and necrotic bone extending beyond the region of alveolar bone (ie, inferior border and ramus in mandible, maxillary sinus, and zygoma in maxilla) resulting in pathologic fracture, extraoral fistula, oral antral or oral nasal communication, or osteolysis extending to inferior border of the mandible or sinus floor	Antibacterial mouth rinse Antibiotic therapy and pain control Surgical debridement or resection for longer-term palliation of infection and pain

MRONJ: Medication-related osteonecrosis of the jaw; AAOMS: American Association of Oral and Maxillofacial Surgeons.

Herein, a case of removable partial denture prosthesis-related MRONJ associated with BP was described.

CASE REPORT

A 63-year-old woman was referred to the Istanbul University Dentistry Faculty Department of Prosthodontics for the evaluation of right mandibular pain and swelling. In 2012, the patient was diagnosed with osteoporosis, and intravenous BP therapy (zoledronic acid) was initiated as a preventative treatment. During anamnesis, hypertension was also reported. Two years after BP treatment, the patient had a removable partial denture, and an ulceration had developed in the right mandibular lingual gingiva. An adjustment of the prosthesis by her dentist did not solve the issue. Thereupon, the patient discontinued the use of her prosthesis, and 3 years later, she was referred to the authors with the same complaints. The clinical examination showed swelling and purulent secretion on the right posterior mandibular area (Figure 1). Panoramic radiographs showed radiolucent areas in the same region (Figure 2).

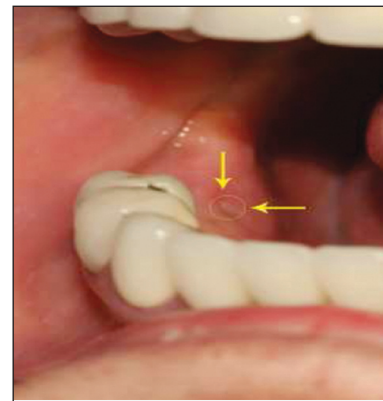


FIGURE 1: Presence of fistula in the right mandible.

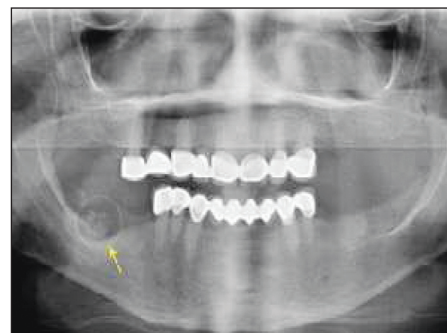


FIGURE 2: Panoramic radiography showed the affected area.

Computed tomography images were taken for more detailed examination (Figure 3). The initial treatment prescribed was penicillin VK and metronidazole, and the patient underwent an incisional biopsy, which found osteomyelitis. Based on the clinical, radiographic and histopathological examination and the patient's history of treatment with BP, MRONJ Stage 2 was diagnosed, which was caused by chronic irritation from the removable partial denture. The patient was recommended the use of chlorhexidine rinse 3 times a day for 2 weeks in the postoperative period and informed that 40 sessions of hyperbaric oxygen (HBO) therapy should be taken. After 32 sessions, she left the treatment voluntarily because of her need to get out of the city.

After 4 months, the patient's complaints were repeated, and intra-oral examination revealed a fistula in the same region (Figure 4). During the radiological reassessment, it was seen that the necrotic bone was separated from the healthy bone in the form of a line, and so surgical treatment was performed (Figure

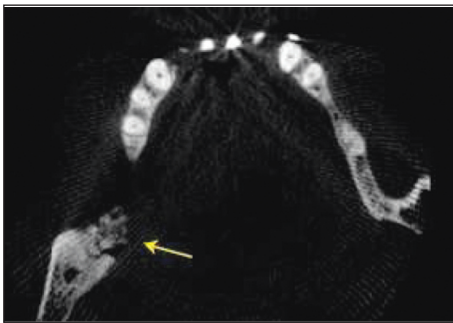


FIGURE 3: Axial computed tomography imaging showing the necrotic bone.



FIGURE 4: Four months later, a fistula was observed in same region.



FIGURE 5: Removal of the necrotic bone.



FIGURE 6: After 3 months, affected area is completely healed.

5). During the surgical operation, necrotic bone was removed and low-level laser (light) therapy (LLLT) (diode laser irrigation, 100 mW, 4 points of 4 J, 40 s/point, 142 J/cm²) was applied to the deep cavitation area.

After the patient's 3-month follow-up, the exposed bone covered with new epithelium and no signs of fistula were observed (Figure 6). Informed consent was obtained from the patient for the case report.

DISCUSSION

Despite different pathogenesis, it has been observed that osteomyelitis and MRONJ present in the jaws give the same clinical and pathological findings. However, the pathogenesis of MRONJ was associated with bone metabolism defects, whereas in osteomyelitis is not affected, but infectious pathogens were present.³

In this case, the patient used IV BP (zoledronic acid) management for osteoporosis. By considering the AAOMS criteria, osteonecrosis in the right lower molar region was associated with MRONJ.

Surgical treatment for MRONJ Stage 2 has been shown to improve early symptoms, high success and low complication rates.⁴ Removal of completely necrotic bone, but not excessive, is an important factor affecting surgical treatment. Treatment results may vary depending on the hand skill level of the surgeon, the correct detection of the surgeon between the normal and necrotic bone line.⁵

The beneficial effects of HBO treatment in BRONJ are increased wound healing, edema and inflammation reduction, stem cell mobilization and moderation of the suppression of bone turnover by BPs and also HBO therapy may improve inflammation and infection in necrotic tissues, increase blood vessels, oxygen concentration and antibiotic levels in patients.⁶

In this case, the treatment of the patient was planned as antibiotic therapy, antibacterial mouthwash, surgical treatment and 40 session HBO treatment.

Kang et al. showed that, the rate of impaired wound healing after the first surgical treatment was higher in the Stage 2 (19.1%, 14 patients) MRONJ than the osteomyelitis group (2.2%, 2 patients). Based on these results, it is recommended that the Stage 2 MRONJ patients should be monitored closely after the first surgical treatment and the recovery process be evaluated by clinicians every week after the first operation. In both groups, no patients had impaired wound healing after the second surgery in either group, suggesting that full recovery can be achieved when a reoperation is performed after detecting impaired wound healing from the first surgical treatment. This finding also suggested that surgical therapy can be used as a treatment strategy for Stage 2 MRONJ.⁷ Also in this study, patients in the MRONJ group were reoperated on average 14 weeks after their initial operation due to impaired wound healing was indicated. It has been noted that long-term patient follow-up is important to monitor wound healing.

In this case, after the first surgery and 32 sessions of HBO treatment, the patient had to go out of the city and was followed up in this period. HBO sessions were planned for daily and the patient could be followed up for 1 month on average. Three months later, the patient complained of pain and swelling in the operated area and it was determined that the infected tissue was repeated. The patient was operated for the second time. Hereby, which can be seen in MRONJ 2 patients, strengthens the association of the patient with MRONJ 2 rather than osteomyelitis.

The use of laser therapy for MRONJ alone or in combination with other treatments has increased due to its positive effects on tissue healing.⁸

In the systematic review study, it was stated that combined treatment with antibiotics, minimally invasive treatment (including Er: YAG laser surgery) and LLLT should be the gold standard in the early Stages of the MRONJ.⁹

As a result of the recurrence of the infection, drug treatment+surgical treatment+LLLT was applied as the second treatment planning. There were no radiological and clinical symptoms at the 1-year follow-up of the patient, and complete healing was observed.

Follow-up by dentists is important for patients who have removable dentures and who have been treated with BPs. Dentists should investigate the use of BPs in patient anamnesis and should carefully evaluate ulceration caused by the use of removable prosthesis.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions**Idea/Concept:** Meryem Şahin, Sirmahan Çakarer, Fatma Ünalın;**Design:** Meryem Şahin, Sirmahan Çakarer; **Control/Supervision:**Meryem Şahin, Sirmahan Çakarer, Fatma Ünalın; **Data Collec-****tion and/or Processing:** Meryem Şahin, Sirmahan Çakarer;**Analysis and/or Interpretation:** Meryem Şahin, SirmahanÇakarer, Fatma Ünalın; **Literature Review:** Meryem Şahin,Sirmahan Çakarer; **Writing the Article:** Meryem Şahin, SirmahanÇakarer; **Critical Review:** Meryem Şahin, Sirmahan Çakarer,Fatma Ünalın; **References and Findings:** Meryem Şahin,Sirmahan Çakarer, Fatma Ünalın; **Materials:** Sirmahan Çakarer,

Meryem Şahin.

REFERENCES

1. Ruggiero SL, Dodson TB, Fantasia J, Goodday R, Aghaloo T, Mehrotra B, et al. American Association of Oral and Maxillofacial Surgeons position paper on medication-related osteonecrosis of the jaw--2014 update. *J Oral Maxillofac Surg.* 2014;72(10):1938-56. [[Crossref](#)] [[PubMed](#)]
2. Ruggiero SL, Dodson TB, Assael LA, Landesberg R, Marx RE, Mehrotra B, et al. American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate-related osteonecrosis of the jaws--2009 update. *J Oral Maxillofac Surg.* 2009;67(5 Suppl):2-12. [[Crossref](#)] [[PubMed](#)]
3. Theologie-Lygidakis N, Schoinohoriti O, Iatrou I. Surgical management of primary chronic osteomyelitis of the jaws in children: a prospective analysis of five cases and review of the literature. *Oral Maxillofac Surg.* 2011;15(1):41-50. [[Crossref](#)] [[PubMed](#)]
4. Lopes RN, Rabelo GD, Rocha AC, Carvalho PAG, Alves FA. Surgical Therapy for bisphosphonate-related osteonecrosis of the jaw: six-year experience of a single institution. *J Oral Maxillofac Surg.* 2015;73(7):1288-95. [[Crossref](#)] [[PubMed](#)]
5. Ristow O, Otto S, Troeltzsch M, Hohlweg-Majert B, Pautke C. Treatment perspectives for medication-related osteonecrosis of the jaw (MRONJ). *J Craniomaxillofac Surg.* 2015;43(2):290-3. [[Crossref](#)] [[PubMed](#)]
6. Freiburger JJ, Padilla-Burgos R, Chhoeu AH, Kraft KH, Boneta O, Moon RE, et al. Hyperbaric oxygen treatment and bisphosphonate-induced osteonecrosis of the jaw: a case series. *J Oral Maxillofac Surg.* 2007;65(7):1321-7. [[Crossref](#)] [[PubMed](#)]
7. Kang SH, Won YJ, Kim MK. Surgical treatment of stage 2 medication-related osteonecrosis of the jaw compared to osteomyelitis. *Cranio.* 2018;36(6):373-80. [[PubMed](#)]
8. Goker F, Grecchi E, Grecchi F, Francetti L, del Fabbro M. Treatment of medication-related osteonecrosis of the jaw (MRONJ). A systematic review. *Eur Rev Med Pharmacol Sci.* 2021;25(6):2662-73. [[PubMed](#)]
9. Weber JBB, Camilotti RS, Ponte ME. Efficacy of laser therapy in the management of bisphosphonate-related osteonecrosis of the jaw (BRONJ): a systematic review. *Lasers Med Sci.* 2016;31(6):1261-72. [[Crossref](#)] [[PubMed](#)]