

CASE REPORT

Olgu Sunumu

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Biphosphonate Related Osteonecrosis of the Jaw: A Case Report

Bifosfonat Kullanımına Bağlı Maksillada Osteonekroz: Bir Olgu Sunumu

ABSTRACT

Medication-related osteonecrosis of the jaw (MRONJ) is a condition that occurs in the presence of exposed and necrotic bone in the maxillofacial region for more than 8 weeks in patients treated with antiangiogenic or antiresorptive drugs without a history of radiotherapy. This case report aims to present the management of maxillary jaw osteonecrosis caused by tooth extraction in a patient using IV (intravenous) bisphosphonates following surgical removal of the necrotic lesion supported with the use of oral pentoxifylline and alpha tocopherol. An 80-year-old female patient has been using IV bisphosphonates (zoledronic acid, ibandronic acid, alendronate sodium) regularly for osteoporosis diagnosed in 2011. The patient applied to the Oral and Maxillofacial Surgery Clinic of Akdeniz University Faculty of Dentistry in 2021 due to osteonecrosis in the left maxilla, which developed after extraction of tooth number 23 at a different center. Pentoxifylline and alpha tocopherol treatment was started and continued for 2 months preoperatively. Following the use of the drug, extensive resection including areas of necrosis was performed and improvement together with resolution of symptoms were observed. Medical treatment with Pentoxifylline and alpha tocopherol is an effective supportive option for the management of maxillary MRONJ.

Key Words:

Pentoxifylline, Alpha-tocopherol, MRONJ

ÖZ

Medikasyon ile ilişkili çene osteonekrozu (MRONJ); radyoterapi hikayesi olmayan, antiangiogenik veya antirezorptif ilaç kullanan hastalarda maksillofasial bölgede 8 haftadan uzun süre var olan ekspoze ve nekrotik kemik varlığında ortaya çıkan durumdur. Bu vaka raporunda; IV (intravenöz) bifosfonat kullanan hastada diş çekimine bağlı oluşan maksiller çene osteonekrozunun oral pentoksifilin ve alfa tokoferol kullanımını takiben nekroz alanının cerrahi olarak çıkartılması sonrası oluşan iyileşmeyi göstermek amaçlanmaktadır. 80 yaşındaki kadın hasta 2011 yılında tanısı konulan osteoporozdan dolayı aynı yıldan itibaren düzenli olarak IV bifosfonat (zoledronik asit, ibandronik asit, alendronat sodyum) kullanmaktadır. 2021 yılında diş merkezde çektiği 23 numaralı dişe bağlı olarak gelişen sol üst çenedeki osteonekroz nedeniyle 2021 yılında Akdeniz Üniversitesi Diş Hekimliği Fakültesi Ağız Diş ve Çene Cerrahisi kliniğine başvurmuştur. Hastaya 2 ay süre boyunca pentoksifilin ve alfa tokoferol medikal tedavisi uygulandı. İlaç kullanımını takiben nekroz alanları içeren geniş rezeksiyon yapıp iyileşme sağlandı. Pentoksifilin ve alfa tokoferol medikal tedavisi, MRONJ tedavisinde etkin bir destek yaklaşımıdır.

Anahtar Sözcükler:

Pentoksifilin, Alfa Tokoferol, MRONJ

INTRODUCTION

Medication-related osteonecrosis of the jaw (MRONJ) is a condition that occurs in the presence of exposed and necrotic bone in the maxillofacial region for more than 2 months in patients without a history of radiotherapy and using antiangiogenic or antiresorptive drugs (1). Antiangiogenic drugs are used in oncology to prevent vascularization of malignant tumors and act by suppressing vascular endothelial growth factors (2,3). Antiresorptive drugs, on the other hand, act by strengthening the bone structure by providing adequate bone remodeling and repair of micro-damages in the bone (4). Antiangiogenic drugs include sunitinib, sorafenib, bevacizumab, axitinib, cabozantinib, and pazopanib. Among antiresorptive drugs, bisphosphonates and denosumab are proven agents to cause MRONJ (5).

In this case report, we aim to present management of a maxillary jaw osteonecrosis in a patient under IV (intravenous) bisphosphonates using oral pentoxifylline and alpha-tocopherol and surgical removal of the necrosis area.

CASE REPORT

An 80-year-old female patient had been using IV bisphosphonates regularly since due to osteoporosis diagnosed in 2011. The patient started with IV ibandronic acid every 3 months between 2011 and 2012. She continued with oral alendronate sodium once a week between 2012-2013, 2014-2015, and 2016-2017 and then used IV ibandronic acid in 2017 and lastly IV zoledronic acids in 2019. She applied to our clinic in 2021 due to osteonecrosis in the left maxilla, which developed after the extraction of tooth number 23 in 2021.

After the clinical examination, inflamed gingiva and exposed bone areas were observed in the left maxilla. Radiographic evaluation revealed an empty extraction socket of tooth number 23. For the treatment of osteonecrosis, pentoxifylline 400 mg (Trentilin Retard 400 mg tablet), and Alpha tocopherol 400 IU (Evicap 400 IU capsule) were used for 2 months. During this period, the extraction site was irrigated 2 times a week with rifampicin (125 mg/1 ampoule). Surgery was planned for the resection of the necrotic bone after the tomography was obtained. Following the PENTO (pentoxifylline- alpha-tocopherol) protocol, the patient was started on pre-operative antibiotics and underwent surgery. Areas of necrosis in the maxilla were resected until living bone was observed. After resection, the exposed areas of bone in the mesial and distal parts of the lesion were closed primarily. The soft tissue aspects with no bony foundation were stabilized with sutures and left for secondary healing. The patient was followed up for 6 weeks with an interval of 1 week. Complete healing was observed in follow-up controls.

DISCUSSION

The onset of MRONJ is associated with direct cytotoxicity to osteoblasts, osteoclasts, BMSCs, bacterial infection, microcirculatory dysfunction immune dysfunction, and the TGF- β 1 pathway (6).

In this case, the development of MRONJ occurred immediately after tooth extraction. Invasive dental treatments are trigger factors for developing MRONJ. Long-term use of IV bisphosphonates and the combination of ibandronic acid, alendronate sodium, and zoledronic acid over many years may also have played a role in the development of MRONJ. Although oral ones are prescribed more frequently than IV bisphosphonates, more than 90% of MRONJ cases are in cancer patients, and long-term use in monthly IV bisphosphonate treatments over some time has been reported (7). The incidence of MRONJ may depend on the type and duration of administration of the bisphosphonate, as well as on comorbidities such as underlying systemic disease, concomitant drug therapy, and local injury.

Pentoxifylline is used in the treatment of vascular diseases such as ischemic heart disease and intermittent claudication. It increases erythrocyte elasticity and vasodilation which cause improvement in peripheral blood flow. Pentoxifylline can inhibit inflammatory reactions and reduce fibrosis due to its antitumor necrosis factor effect. It probably accelerates healing in soft tissue necrosis caused by radiation and reduces pain (8,9).

Alpha-tocopherol is very effective in eliminating radicals related to oxygen by inhibiting platelet aggregation. It also disrupts tissue fibrosis. The combination of these 2 molecules (PENTO) has shown some efficacy in the treatment of osteoradionecrosis and the combination is well tolerated (8,9). Delanian et al. suggested that PENTO may stimulate defective osteoblastic healing (8,9). Insomnia, nausea, asthenia, epigastralgia, headache, and diarrhea are the side effects that are associated with pentoxifylline.

The treatment modality presented was previously reported by Epstein et al. in association with antimicrobial therapy in 6 patients. All patients (2 with osteoporosis and 4 with cancer) presented with MRONJ after IV bisphosphonate treatment. The lesions healed in all patients (10).

Numerous studies show potentially modifiable factors for reducing the risk of MRONJ, including performing high-risk surgical procedures before initiating therapy using pre and post-surgical antibiotics and mouthwashes that reduce microorganisms, maintaining efficient oral hygiene, and primarily closing extraction regions. Practices such as quitting smoking and optimizing diabetes, which will increase the patient's general health, are indicated. While no individual practice and enforcement strategies can eliminate all MRONJ risks, there are recommended preventive procedures.



Figure 1. Clinical examination.

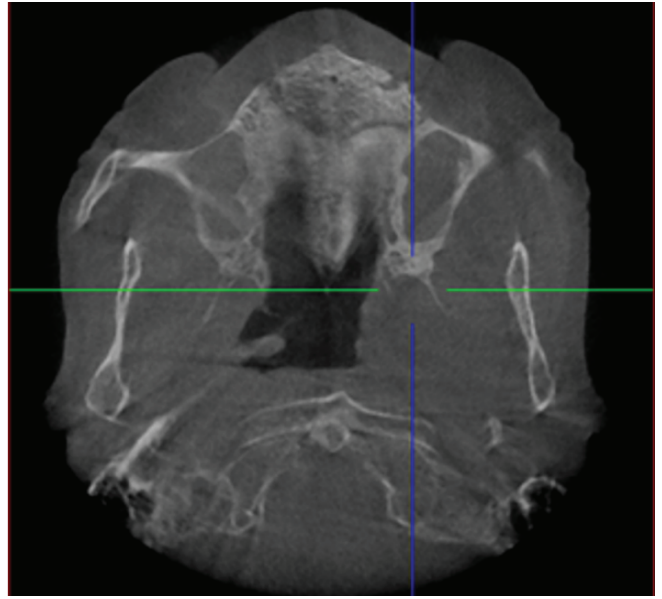


Figure 2. Preoperative CBCT image.

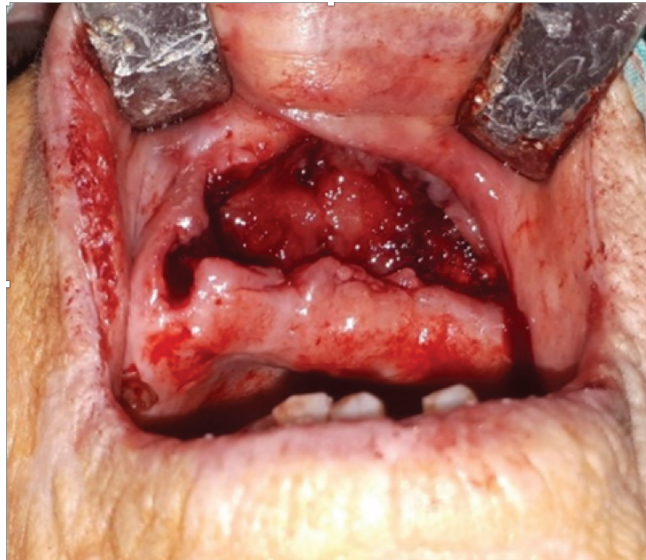


Figure 3. Areas of necrosis in the maxilla were resected until living bone was observed.



Figure 4. a) After surgery, b) 1 week follow-up.



Figure 5. a) 6 weeks follow, b) 6 months follow.

The realization that patients receiving antiresorptive therapies that can change osseous wound-healing capacity is very important for the prevention of MRONJ. Alterations wound healing capacity of the osseous tissues can be a risk for developing MRONJ. Healthcare providers need to recognize the importance of coordinated dental care and pretreatment management for reducing the risk of MRONJ. This approach requires education of dentists, patients, and medical professionals about the real risks associated with these therapies and clinical prevention strategies that can reduce MRONJ onset (11).

Looking at the treatment outcome obtained in the presented case, it can be suggested that the surgical management of MRONJ, if supported medically, provides favorable outcomes. Supportive use of pento protocol may aid clinicians in reaching these outcomes owing to its benefits in enhanced wound healing. With regards to the surgical extent; primary closure, which typically requires flap reflection and further periosteal stripping, is only essential in areas of exposed bone.

CONCLUSION

MRONJ lesions can be managed satisfactorily using appropriate medical/surgical treatment protocols. Medical treatment with Pentoxifylline and alpha-tocopherol is an effective supportive option for the surgical management of maxillary MRONJ. Final -primary- closure of the wound is solely indicated for exposed -living- bone surfaces.

Author Contribution Statement:

Case preliminary diagnosis and follow-up, article writing: A.Y., T.T., G.Ş.K. and M.A.A.

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Conflict of Interest:

None of the authors mentioned in this case report are or there is no conflict of interest with the organization.

Ethics Committee Approval:

Consent was obtained from the patient. Ethics Committee Approval Certificate was not required.

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