



Medication-Related Osteonecrosis of the Jaw – A Case Report

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Received: October 12, 2017; Published: October 30, 2017

Abstract

Aim: Bisphosphonates are synthetic analogs of pyrophosphates, which are used for malignancy-related hypercalcemia, multiple myeloma, bone metastases and osteoporosis. After the realization of the similarities between the effects of some chemotherapeutic agents and bisphosphonates, a new term emerged in 2014: Medication-Related Osteonecrosis of the Jaw (MRONJ). In this case, we present a MRONJ in the mandible.

Method: 65 years old female patient referred to Istanbul University, Faculty of Dentistry, Department of Oral and Maxillofacial Surgery with a pain at the both retromandibular areas and halitosis. After getting anamnesis, It was understood that the patient had a pancreas cancer and due to the metastases on her liver, she was taking sunitinib malate (Sutent® 37.5 mg capsule, Pfizer, Istanbul, Turkey) for 3 years. 0.7 x 0.7 x 2,5 cm³ necrotic regions were seen on the right, 0.5 x 0.5 x 0.3 cm³ necrotic areas were seen on the left side of the mandibular alveolar process. For the detection of the necrotic borders of MRONJ, Cone Beam Computed Tomography (CBCT) images were interpreted.

Results: Amoxicillin/clavulanic acid tablet and chlorhexidine mouthwash were prescribed and necrotic areas were cleansed with the physiological saline solution once a week. On our recommendation, sunitinib malate was reduced to 25 mg per day by oncologists. Sunitinib malate taking was not quit since It may increase the occurrence chance of a metastasis. Pain and halitosis were removed however borders of necrotic tissue hasn't changed. The patient is under control for 1 year in our clinic.

Conclusion: Osteonecrosis is characterized by irregularity at the cortical bony margins and the destruction of cortical bone in CBCT images. Sunitinib malate is an antiangiogenic agent which was first used in 2006 hence the long-term effects are yet to know. Although the most common reason of MRONJ is tooth extraction, It can be seen in regions/patients which/who have no surgical procedure history. In order to avoid complications dentists need to take a thorough anamnesis and should be aware of the side effects of intaking drugs. Patients who had anti-resorptive medication treatments should have a regular follow up even no surgical operation was performed.

Keywords: MRONJ; Sunitinib Malate; Cone Beam Computed Tomography; Bisphosphonate; Osteonecrosis; Jaws

Introduction

Bisphosphonates are synthetic analogs of pyrophosphates, which are used for malignancy-related hypercalcemia, Paget disease of bone, heterotopic ossification, multiple myeloma, bone metastases and osteoporosis [1,2]. Long-term use of these medications may cause a clinical condition called "Bisphosphonate-Induced Osteonecrosis of Jaw (BRONJ)" and described by Marx in 2003 [3]. After the realization of the similarities between the effects of some chemotherapeutic agents, denosumab and other antiangiogenic medications, and bisphosphonates (IV and oral), a new term emerged in 2014 by American Association of Oral and Maxillofacial Surgeons (AAOMS): Medication-Related Osteonecrosis of the Jaw (MRONJ) [4,5]. Patients who; has any treatment history

with antiangiogenic or antiresorptive agents, has exposed bone in the maxillofacial region for longer than 8 weeks, has no radiation therapy history or metastatic jaw disease may be diagnosed with MRONJ if all three features exist [6]. Both the prevalence and pathogenesis of the MRONJ are not well understood and further investigation is required. In this case, we present a MRONJ, which takes place on both sides of the mandible after a tooth extraction.

Case

65 years old female patient referred to Istanbul University, Faculty of Dentistry, Department of Oral and Maxillofacial Surgery with a pain at the both retromandibular areas, halitosis and exposed bone regions both at left and right molar site of the man-

dible. After getting anamnesis, It was understood that the patient had a pancreas cancer and due to the metastases on her liver she was taking sunitinib malate (Sutent® 37.5 mg capsule, Pfizer, Istanbul, Turkey) for 3 years and while taking medications the patient had her right lower molar extracted. During the intraoral examination, necrotic bone regions were seen both on the left and the right molar site of the mandible. Ortopantomographic image revealed bone destruction regions (Figure 1) and for the exact detection of the necrotic borders of MRONJ, Cone Beam Computed Tomography (CBCT) was applied and the images were interpreted. 0.7 x 0.7 x 2,5 cm³ necrotic region was seen on the right, 0.5 x 0.5 x 0.3 cm³ necrotic region was seen on the left side of the mandibular alveolar process (Figure 2, 3A, 3B, 4A, 4B). The condition was diagnosed as MRONJ.



Figure 1: Ortopantomographic radiography of the patient. Note the defect areas on the both left and right posterior mandible.

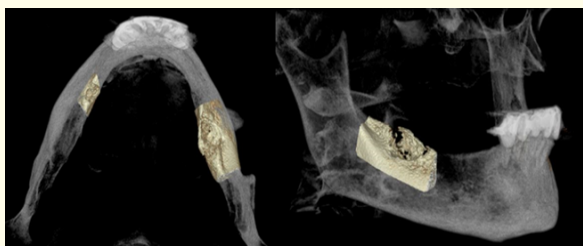


Figure 2: 3D - CBCT - Reconstruction images of the patient.

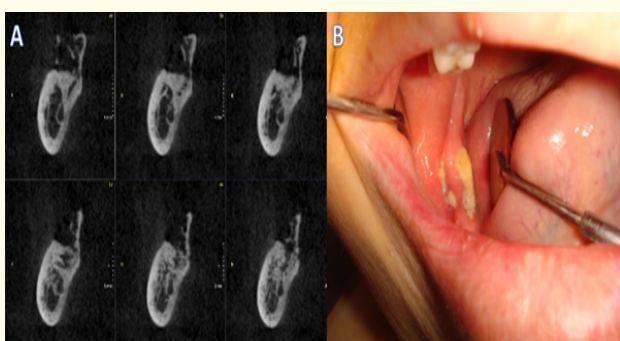


Figure 3A: CBCT-Cross section images of the patient's right molar site of the mandible. Note the destruction and osteosclerosis at the bone.

Figure 3B: Intraoral image of the patient's right molar site of the mandible. Note the exposed bone regions.

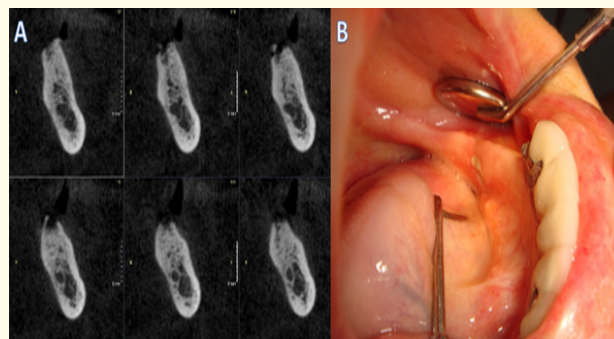


Figure 4A: CBCT-Cross section images of the patient's left molar site of the mandible. Note the destruction and osteosclerosis at the bone.

Figure 4B: Intraoral image of the patient's left molar site of the mandible. Note the exposed bone region.

Amoxicillin/clavulanic acid tablet and chlorhexidine mouthwash were prescribed and necrotic areas were cleansed with the physiological saline solution once a week. On our recommendation, sunitinib malate was reduced to 25 mg per day by oncologists. Sunitinib malate taking was not quit since It may increase the occurrence chance of metastases. Pain and halitosis were removed however borders of necrotic tissue hasn't changed. The patient is under control for 1 year in our clinic.

Discussion

MRONJ has been defined by the AAOMS as the existence of an exposed bone region in the maxillofacial area for over 8 weeks, no radiation therapy history and treatment history including bisphosphonates or other anti-resorptive medications. The most common initiator is tooth extraction, which is followed by odontogenic infections and implant surgery [7]. There are 4 stages of MRONJ which are; Stage 1: patients are asymptomatic, they have no soft tissue inflammation or infection but have exposed bone, Stage 2: patients have exposed bone and are symptomatic, they have soft tissue inflammation or swelling, infection and pain in the related region, Stage 3: patients have the features in stage 2 and more than that complicated situations like extra-oral fistula or pathologic fractures are seen [8,9]. MRONJ's clinical management is still controversial and surgery is not sufficient alone to recover the condition [10]. Treatment guidelines suggest conservative treatment for the stage 0-1-2 but following the conservative treatment, in order to eliminate acute inflammation and recurrences, sequestrectomy may be required [11]. After all, the main goal should be to prevent actions which may develop MRONJ. Ruggiero stated even some patients with spontaneously developed MRONJ, this condition occurs generally after maxillofacial surgical interventions. Herewith, the patients who will get/get/got should be informed about the outcomes of the anti-resorptive medications and should pay utmost attention to their oral hygiene in order to avoid interventions like tooth extraction [12].

Conclusion

Osteonecrosis is characterized by irregularity at the cortical bony margins and the destruction of cortical bone in CBCT imag-

es. Sunitinib malate is an antiangiogenic agent which was first used in 2006 hence the long-term effects are yet to know. Although the most common reason of MRONJ is tooth extraction, It can be seen in regions/patients which/who have no surgical procedure history. In order to avoid complications dentists need to take a thorough anamnesis and should be aware of the side effects of intaking drugs. Patients who had anti-resorptive medication treatments should have a regular follow up even no surgical operation was performed.

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Volume 1 Issue 5 October 2017

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