Case Report

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Medication-Related Osteonecrosis of the Jaw Associated with Palatal Bone and Soft Tissue Trauma: A Case Report

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The aim of this case report is to present a case of 68-year-old male with a history of multiple myeloma and the intravenous use of Zometa (zoledronic acid) who had developed medication-related osteonecrosis of the jaw (MRONJ) following a hot pizza burn to the palate. Clinical and radiographic findings revealed grade 1 MRONJ of the right side of the hard palate. Soft tissue trauma and delayed epithelialization may be associated with some cases of MRONJ. Patients on anti-resorptive medications or anti-angiogenic drugs should be informed of the risk of bone exposure and subsequent MRONJ secondary to physical/chemical insults to the bone and soft tissue in the oral cavity.

Key Words: Bisphosphonates; Medication related osteonecrosis of the jaw; Osteonecrosis; Zoledronic acid

INTRODUCTION

According to the 2014 criteria set by the American Association of Oral and Maxillofacial Surgeons (AAOMSs), the definition of medication-related osteonecrosis of the jaw (MRONJ) requires the following characteristics: 1) Ongoing or antecedent treatment with anti-resorptive or anti-angiogenic drugs. 2) No patient history of radiation therapy or manifestation of metastasis to the jaw. 3) Exposed bone or presence of an intraoral or extra oral fistulae in the maxillofacial region persisting for longer than 8 weeks [1].

The AAOMSs changed the nomenclature from bisphosphonate-related osteonecrosis of the jaw (BRONJ) to MRONJ in 2014 to accommodate the increasing number of cases presenting the osteonecrosis of jaws associated with various drugs other than bisphosphonates. Initially, only bisphosphonate and other anti-resorptive drugs were associated with MRONJ. However, in recent years anti-angiogenic drugs and other immunomodulatory drugs have been added to the list of drugs causing MRONJ [1]. Various theories have been postulated for the initiation of MRONJ, with the main theory associated with the irreversible inhibition of osteoclasts in the process of bone resorption [2]. However, with the addition of new drugs that are not involved in bone metabolism but still induce osteonecrosis of the jaw, other mechanisms, such as angiogenesis inhibition, immunity dysfunction, inflammation, infection, and soft tissue toxicity, have been suggested to play a role in the underlying mechanism of MRONJ [3]. Some investigators propose an "outside-in process" wherein MRONJ can be initiated from soft tissue rather than the bone itself [4]. This theory can explain the role of trauma from oral prosthetic appliances, such as dentures inducing MRONJ. The purpose of the present case report is to describe an unusual occurrence of MRONJ in a multiple myeloma (MM) patient, which resulted from a burn to the soft tissue of the palate caused by hot food.

CASE REPORT

The patient was referred to the Oral Medicine Clinic at the University of Florida, College of Dentistry with a chief complaint of a fetid odor in the oral cavity. On presentation, the patient stated that he acquired a lesion on his palate after eating a very hot pizza followed by the development of unpleasant smell in his mouth. The medical history was significant for stage III IgA Kappa MM treated by autologous hematopoietic stem cell transplantation eight years ago. The patient had taken zoledronic acid 4 mg by an intravenous infusion for a total of 7 years, but had stopped the medication 2 years ago. Current medications included Acyclovir 400 mg one tablet once daily, Bystolic 5 mg one tablet once daily, Gabapentin 100 mg 2 capsules twice daily, Ibuprofen 400 mg 2 tablets twice daily, Methylprednisolone sodium succinate (Solu-medrol; Pfizer, New York, NY, USA) 500 mg intravenous every 30 days, Simvastatin 40 mg one tablet once daily, Temazepam 15 mg one capsule daily at bedtime and Bortezomib in IV 0.9% NaCl injection 1.6 mg/m^2 into the skin every 30 days. Intraoral examination revealed an area of exposed bone, which was about 5 mm in diameter, on the right side of the posterior palate (Fig. 1). The margins of the lesion were not inflamed but tender. A cytologic smear taken to rule out bacterial and fungal infection, which was negative for all. A cone beam computed tomography (CBCT) revealed an irregular lytic lesion on the posterior right area of the palate (Fig. 2) suggestive of osteonecrosis, possibly with sequestra, with no bony changes in the left side (Fig. 3). A diagnosis of MRONJ stage 1 was rendered with a differential diagnosis of palate necrosis. Since the lesion did not heal within a month from inception, the patient had a history of bisphosphonate IV injections, and the clinical and radiological presentation indicated bone exposure with the lytic lesion. The patient was advised to use chlorhexidine gluconate 0.12% rinse twice a day. In subsequent follow-up sessions, the lesion progressed to the size of 1.2 cm in diameter without epithelialization. At this time the lesion is stable and asymptomatic. In as much as the patient is still on chemotherapy for his MM,

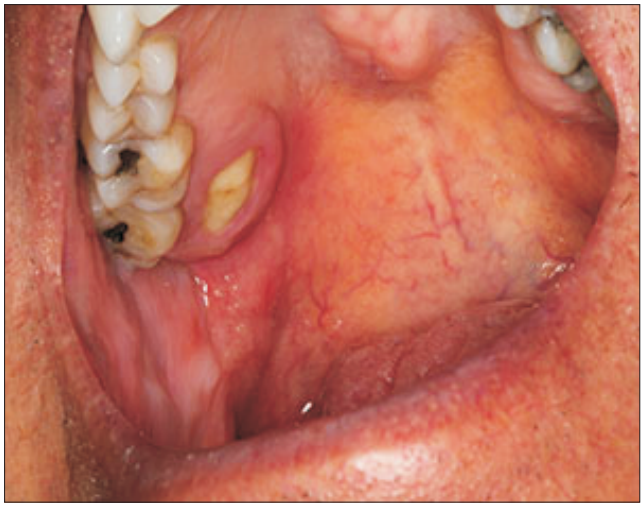

Fig. 1. Clinical photograph showing the exposed bone on the right palatal area with minor inflammation.

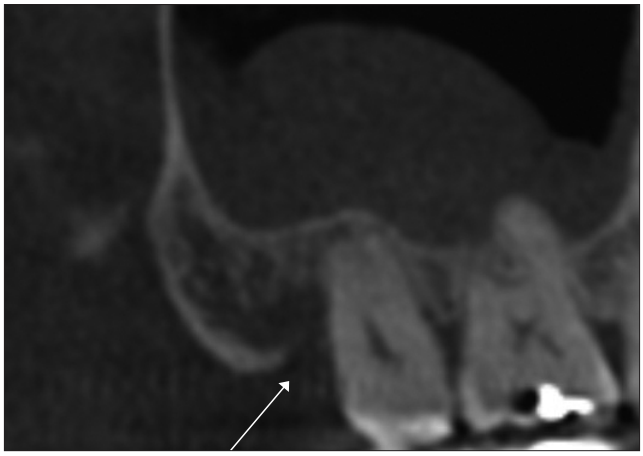

Fig. 2. Medication-related osteonecrosis of the jaw of the maxilla. The cone beam computed tomography scan shows an irregular lytic lesion with bony sequestrum on the posterior right area of the palate (arrow).

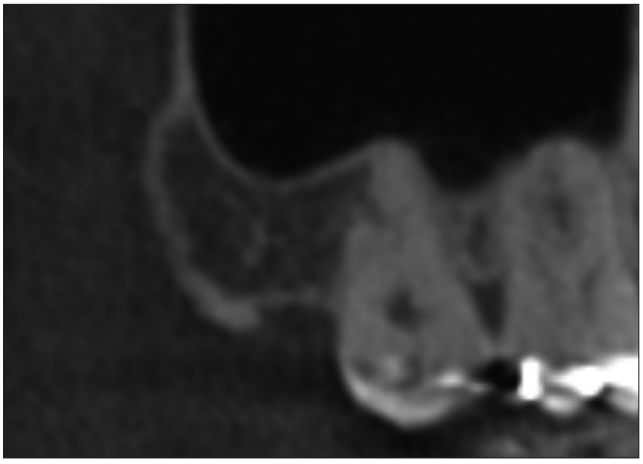

Fig. 3. Medication-related osteonecrosis of the jaw of the maxilla. The left side was visualized for comparison.

his lesion in the palate did not heal properly. However, as the patient is currently asymptomatic and shows no sign of infection, a surgical intervention procedure is not considered at present time. Surgical debridement can be one of the options if MRONJ progresses further.

DISCUSSION

Anti-resorptive drugs are strong osteoclast inhibitors with anticancer and anti-angiogenic properties. These drugs decrease osteoporosis in MM and cancer patients. It has been reported that the prevalence of MRONJ is 5.2% for MM patients [5]. However, long-term use of such drugs results in suppression of bone turnover and delayed healing of even physiologically small injuries inside the skeletal system [6]. MRONJ is strongly related to the combination of the long-term use of bisphosphonates and mechanical trauma [7]. Furthermore, oral injuries such as mucosal inflammation and stomatitis along with the lack of patient's compliance with oral hygiene can increase the risk of developing MRONJ [8]. Some investigators have suggested that possible mechanisms of MRONJ caused by these drugs may be attributed by the combination of a vascular supply deficit, a remodeling and bone regeneration deficit [9], accumulation of micro cracks in desiccated bone with empty osteocyte lacunae [10], and infection of bone via osteoclast-independent bone resorption [11]. It has been reported that the simultaneous administration of chemotherapy drugs increases the severity of the disease, especially when soft tissue defects are present in combination with chemotherapy drugs and immunosuppressive agents [12]. The capacity of anti-cancer medications to speed up MRONJ is mainly due to their ability to intercept endothelial cell movement and proliferation [13].

Subclinical trauma caused by dentures can also lead to the onset of MRONJ due to soft tissue toxicity. Continuously irritating dentures can result in the inflammation of the underlying mucosa, which leads to the progression of infection of the bone, which ultimately leads to the development of MRONJ [14]. It has been reported that even a minor trauma or a small mucosal bruise increases the chances of MRONJ in patients who were on intravenous bisphosphonates for more than 3 years [15]. Reid et al. [14] and Walter et al. [16] have suggested that loss of epithelium resulting in exposed bone can be due to the toxic effect on the oral epithelium of high concentrations of bisphosphonates in underlying bone being released into the epithelium after trauma, thereby impairing the healing process. The hypothesis involves that trauma to overlying effected mucosa with high doses of bisphosphonates results in inflammation, infection, and finally bone involvment [4,17].

In the present case, the patient developed MRONJ on the hard palate where the attached mucosa is coarse and in the absence of palatal tori. In reviewing the literature, we have found only a few similar cases. de Souza and Stepavoi [18] published a report on "silver nitrate-induced, bisphosphonate-related osteonecrosis of the hard palate following a mucosal lesion biopsy in a MM patient receiving zoledronic acid". Rayan and Larson [19] reported MRONJ of the torus palatinus in which a hot pizza resulted in palate burn and within six months the patient was diagnosed with denuded bone resulting from bisphosphonates and soft tissue trauma. Due to thin and less vascularized mucosa on torus palatinus, which is formed of a dense cortical bone with a limited amount of bone marrow, the chances of being traumatized in this area in the oral cavity is relatively high [20].

In conclusion, we have described a case of MRONJ in a MM patient on a long-term treatment with zoledronic acid, which was initially triggered by a burn to the palate. Trauma to the soft tissue by chemical or mechanical stimuli should be avoided in patients at risk for MRONJ. The development of MRONJ may lead to delays or alterations in restorative or dental care, either of which may affect patient's general wellbeing. Providing patients with up-to-date information related to the risks/benefits of traumatic dental treatments should be a duty of oral health professionals at the onset of the anti-reorptive/anti-angiogenic therapy.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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