Bisphosphonate Related Osteonecrosis of Jaw in Female Patient: An Enigma

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Bisphosphonates are used in cases of osteoporosis, multiple myeloma, metastatic carcinoma to the skeleton, etc. The patients with nitrogen-containing bisphosphonates are a greater risk for osteonecrosis of the jaws. Osteonecrosis is considered to be one of the side effects of the bisphosphonate the most common affected jaw is mandible. The primary reason for the osteonecrosis of the jaw is basically due to the over suppression of bone turnover rate. Trauma, tooth extractions, and poor oral hygiene is also considered to be another co-factor which precedes the osteonecrosis of the jaw in the patients of bisphosphonate therapy. So, preventive measure as a reduction of oral microbial load and reduction foci of infection is mandatory step before the treatment of bisphosphonate therapy.

Keywords: Alendronate, Bisphosphonate- related osteonecrosis of jaw, Bone turnover, Osteonecrosis

INTRODUCTION

Osteonecrosis is a disorder of the bone which is due to the reduced blood flow to bones. Other names of osteonecrosis are avascular necrosis, aseptic necrosis, and ischemic necrosis.¹ Bisphosphonates are used in treatment of osteoporosis, Paget disease of bone, Heterotopic ossification, hypercalcemia, multiple myeloma, and skeletal events associated with metabolic neoplasms.² In bisphosphonate-related osteonecrosis of jaw (BRONJ) exposure of bone with pain will be present in the mandible and maxilla of patients receiving the bisphosphonates, such as pamidronate and zoledronate. It was first reported by Marx in 2003.³ Previously bone necrosis which happened because of bisphosphonates was called as BRONJ, bisphosphonate-associated ONJ, osteochemonecrosis, and avascular necrosis of the jaws. Now, it has been replaced with bisphosphonate-induced ONJ or drug-induced ONJ. Bisphosphonates inhibit bone resorption by suppressing the recruitment and activity of osteoclasts thus shortening their life span. Recently three bisphosphonates, pamidronate, zoledronate, and alendronate are more prone to induce painful refractory bone exposures in the jaws.³ Some of the other serious side effects of bisphosphonates are renal failure on intravenous bisphosphonate therapy and esophagitis when used oral bisphosphonate therapy.⁴ Here, we report a case of osteonecrosis, diagnosis, and management for BRONJ.

CASE REPORT

A 60-year-old female patient reported to the Department of Oral Medicine and Radiology with a chief complaint of discomfort while swallowing food. The patient gave a history of osteomyelitis of frontal bone for which she underwent treatment 2 years back. The patient also gives a history of leg fracture due to osteoporosis for which she has undergone surgery and was under medication Alendronate since 2 years. The patient noticed a foul smell from the mouth 2 months back and later exfoliation of upper anterior teeth.

Extraoral examination there was a depression in the forehead that is because of craniotomy procedure that she has undergone for osteomyelitis of frontal bone (Figure 1). Intraoral examination revealed oronasal communication. The border surrounding the communication was non-tender on palpation. Teeth 12, 11, 21, were Grade III mobile. Root stumps with 15, 16, and 26 were present, and speck of exposed bone was present in relation to 26 as shown in (Figure 2). The patient had poor oral hygiene with stains

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and calculus. Based on the history and clinical findings a provisional diagnosis of BRONJ was given. Later the patient was subjected to radiographs. Waters view (Figure 3) revealed radiolucency of maxillary sinus with the floor was observed and suspected that there is communication between oral and maxillary antrum. Later the patient was advised magnetic resonance imaging scan where axial view (Figure 4) shows hyperdense in the area of an anterior portion of the hard palate and the soft tissue destruction from 14 to 28 region.

**DISCUSSION**

This case report describes the problems associated with poor oral hygiene, adverse effects of bisphosphonates. BRONJ defined as an area of exposed bone in the maxillofacial region for more than 8 weeks in a patient who was receiving a bisphosphonate and had not underwent radiation therapy to the craniofacial region. The diagnosis of BRONJ is currently done by based on the patient’s medical history of bisphosphonate therapy and clinical findings. Clinical findings such as pain, bone exposure, purulent secretion or swelling will be present. The initial appearance of the disease is variable. That is why the clinical assessment of the disorder by the clinician is late. Exposure of the bone either occurs spontaneously, due to trauma, or tooth extractions that progresses into the formation of sequestration with purulent discharge and in some cases fistula formation can occur. Most reported cases of necrosis of the jaws associated with bisphosphonate use involve the recent nitrogen-containing injectable bisphosphonates such as pamidronate and zoledronate.2-6

**Why Bisphosphonates Causes ONJ?**

One theory suggests that osteonecrosis in patients with bisphosphonates is due to cessation of bone remodeling and bone turnover. That is due to osteoclast inhibiting effect of Bisphosphonates. It is seen that more potent bisphosphonates such as alendronate, pamidronate, and zoledronate inhibit osteoclasts activity by interruption of the mevalonate pathway. Jaws have the greater blood supply, and faster bone turnover rate that is due to the presence of teeth which makes daily bone

![Figure 1: Facial profile picture showing depression on the forehead](image1)

![Figure 2: Exposed bone in relation to 26](image2)

![Figure 3: Water’s view](image3)

![Figure 4: Magnetic Resonance Imaging showing hypointense area in the anterior part of hard palate region](image4)
remodeling and replenishment causes the concentration of bisphosphonates. Osteoblasts and osteoclasts live for 150 days. After the death of osteoblasts and osteoclasts the mineral matrix which was deposited by them has to be resorbed by osteoclasts which release the cytokines of bone morphogenetic protein and insulin growth factors which induce new osteoblasts from the stem cell population. As the osteon becomes a cellular and necrotic and the small capillaries within the bone become inviolated, causing avascular of the bone. As the some trauma or injury to the overlying mucosa causing the necrotic bone exposure of bone which then there will be a failure to heal.7

Local factors such as tooth extractions, periodontal disease, dental implant procedures, exostoses, and ill-fitting dentures, were also reported as preceding ONJ. Delayed epithelialization (wound healing) may result in exposed bone with the presence of oral bacteria, increases the risk of infection. A number of systemic diseases like diabetes, human immunodeficiency virus infection also predispose patients to becoming immunocompromised, which results in delayed healing and reduced ability to combat opportunistic infections. The combination of compromised immunity and medications that can affect wound healing suggests that a multifactorial model is required to explain the pathogenesis of ONJ.23,9

The American Association of Oral and Maxillofacial Surgeons position paper provides the following staging system for the stratification of patients with, or at risk of BRONJ.58

**At Risk Category**

No apparent necrotic bone in patients who have been treated with either oral or intravenous bisphosphonates.

Stage 0: No clinical evidence of necrotic bone, but non-specific clinical findings and symptoms.

Stage 1: Exposed and necrotic bone in patients who are asymptomatic and have no evidence of infection.

Stage 2: Exposed and necrotic bone associated with the infection as evidenced by pain and erythema in the region of the exposed bone with or without purulent drainage.

Stage 3: Exposed and necrotic bone in patients with pain, infection, and one or more of the following: exposed and necrotic bone extending beyond the region of alveolar bone, (i.e., inferior border and ramus in the mandible, maxillary sinus and zygoma in the maxilla) resulting in pathologic fracture, extraoral fistula, oral antral/oral nasal communication, or osteolysis extending to the inferior border of the mandible of sinus floor.5

**Therapeutic Management of Disease**10

As there is no any established treatment regimen, conservative management has to be considered first. After the confirmation of osteonecrosis that presents as a non-healing wound in patients with bisphosphonate conservative therapy has to be started as soon as possible. The patient was asked to stop the medication with physician consent. Antibiotics such as amoxicillin with the clavulanic acid combination of 625 mg were started. Extraction of Grade III mobile teeth was done. Antiseptic mouthwashes such as betadine mouthwash were given. Gentle, with the aseptic precaution of exposed bony spicule was done. Prosthetic rehabilitation was done with obturator. The patient was advised to keep oral hygiene maintenance.

**CONCLUSION**

This case report shows the importance of maintenance of oral hygiene in patients with bisphosphonate treatment. There is increased risk associated with poor oral hygiene. Here comes the importance of dentist too. Therefore, to avoid ONJ, it is recommended that patients who are about to start bisphosphonate therapy have a complete dental exam to identify possible existing infections, compromised teeth and dentures that do not fit properly the risk of developing ONJ in osteoporosis patients treated with bisphosphonates is low, with estimates suggesting an incidence of 1 event per 20,000-110,000 patient/years. It has to be made compulsory to regular follow-up to the dentist.

**REFERENCES**


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