Case Report

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# Self-healing Lesion of Bisphosphonate Induced Osteonecrosis of Maxilla in an Osteoporotic Patient: A Case Report

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## Abstract

Bisphosphonates (BP) are used as anti-osteoclastic and anti-resorptive agents for the management of osteoporosis, multiple myeloma, Paget's disease and hypercalcemia of malignancy. Their function is to improve bone morphology, prevent bone destruction and pathologic fractures while decelerating bone resorption. However, BP-induced osteonecrosis of the jaw (BRONJ) is one of the complications of BP intake. The aim of this paper is to report a case of BRONJ in a patient on oral BP for osteoporosis, which healed spontaneously on cessation of offending drug.

**Key words:** Bisphosphonate, Osteonecrosis, Osteoporosis

## INTRODUCTION

Bisphosphonate (BP) related osteonecrosis of the jaw (BRONJ) is one of the complications of BP intake for management of osteoporosis, multiple myeloma, Paget's disease and hypercalcemia of malignancy.[1] The reported incidence is significantly higher with the Intravenous preparation while the risk appears to be minimal for patients receiving oral BPs, where the prevalence approximates 0.1%.[2] Based on retrospective studies, estimates of cumulative incidence range from 0.8% to 12%. The mandible is more commonly affected than the maxilla and 60-70% cases are preceded by a dental surgical procedure.[2] The association of long-term application of bisphosponates and exposed bone has been first described by Marx in 2003. Since then, about 5000 cases have been documented.[1,3]

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The American Society for Bone and Mineral Research defines BRONJ as "an area of exposed bone in the maxillofacial region that has not healed within 8 weeks after identification by a healthcare provider in a patient who is receiving or has been exposed to a BP and has not had radiation therapy to the craniofacial region."[4,5] The American Association of Oral and Maxillofacial Surgeons (AAOMS) suggested a staging system based on four stages of BRONJ.[2,6,7]

Although antibiotics and chlorhexidine mouth rinses have been advocated in the literature in order to manage lesions of BRONJ, but no case have been reported in the literature till date. Here, we are reporting a case of Stage I BP induced osteonecrosis of maxilla in a patient who was on a low dose oral BP for osteoporosis and the lesion healed spontaneously on stoppage of the offending drug.

## CASE REPORT

A 52-year-old male patient reported to the department of oral medicine and radiology at Maulana Azad Institute of Dental Sciences with the complaint of ulceration on the left side of the palate for past 3 months. The patient had a previous history of extraction of upper left maxillary first

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molar followed by placement of fixed prosthesis in relation to upper left maxillary second premolar, first, second and third molar about 1 month before the appearance of lesion. There was no associated history of fever, trauma, and pus discharge, but there was mild, dull, intermittent pain, which relieved on taking analgesics. He was a diagnosed case of osteoporosis and was under treatment with oral BP alendronate 200 mg daily for the past 6 months. Personal history including habits was non-contributory.

On intraoral examination, there was sloughing of the alveolar mucosa of the palate with exposed bone in relation to upper left maxillary second and third molar approximately 1 cm away from the gingival margin. The surrounding mucosa was erythematous. Lesion was approximately 1 cm × 1 cm in size (Figure 1) and was bony hard and tender on palpation. The associated teeth were tender on percussion. Gingival and periodontal examination did not reveal any pathological finding. Orthopantomogram was advised, which did not reveal any pathological changes (Figure 2). Based on the positive history of intake of oral BP, previous history of dental treatment and clinical presentation, diagnosis of BRONJ was made.

In consultation with the treating physician, the patient was asked to stop the drug and was advised chlorhexidine mouth rinses. The patient was kept on regular follow-up and on subsequent visits, it was seen that there was covering of exposed bone with normal mucosa and healing was evident in about 1 month (Figure 3). Complete healing of the site was evident on subsequent follow-ups (Figures 4 and 5).

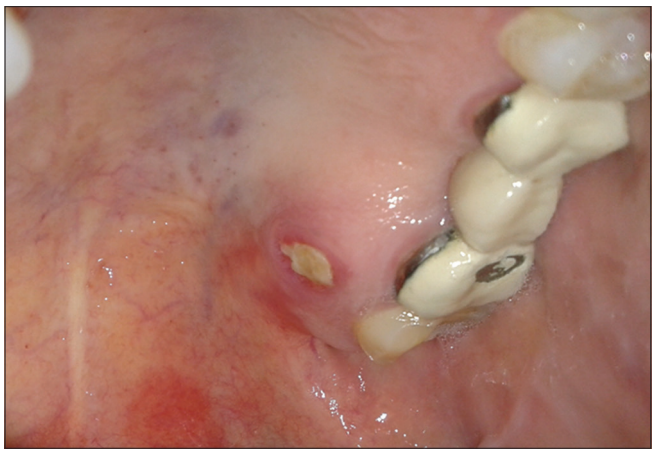

**Figure 1: Intraoral photograph of the patient at first visit showing exposed necrotic bone of left alveolar mucosa of palate in relation to 27, 28 diagnosed as bisphosphonate-induced osteonecrosis of the jaw**

## DISCUSSION

Osteoporosis is a major public health problem because of its high cumulative fracture risk and the potentially disastrous consequences. Oral BPs are synthetic drugs used primarily in the treatment of osteoporosis. Being strong

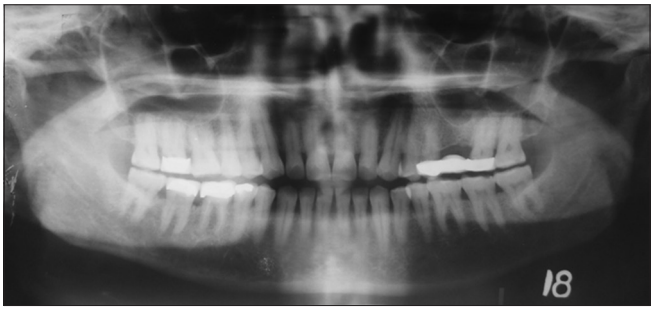

**Figure 2: Orthopantomograph of the same patient with no pathological finding with respect to the site of lesion (left posterior maxilla)**

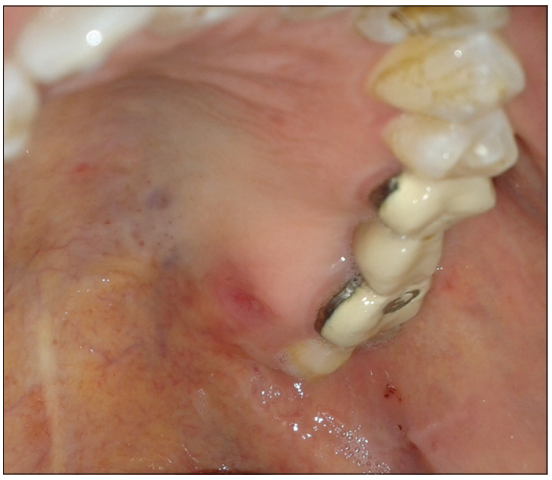

**Figure 3: Intraoral photograph of the patient at follow-up visit after 1 month with the healing of lesion evident**

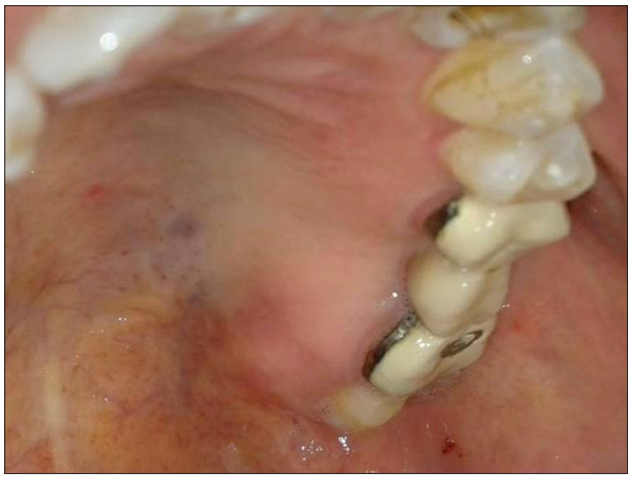

**Figure 4: Intraoral photograph of the patient at follow-up visit after 3 months**

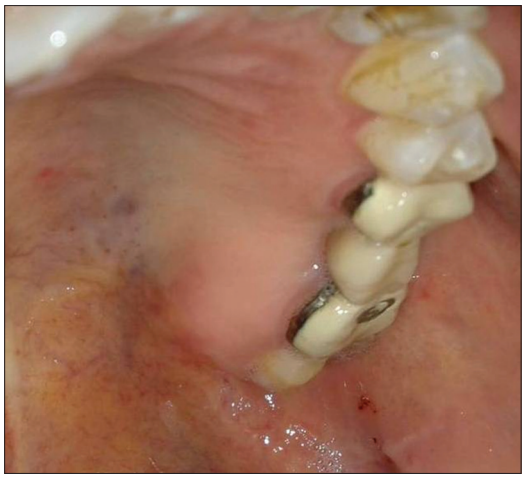

**Figure 5: Intraoral photograph of the patient at follow up visit after 6 months**

suppressors of osteoclasts, they slow down the remodeling process and thus increase bone mineral density. Despite the benefits of these drugs, BRONJ, which was first published in the literature in 2003, is a severe side-effect of BP therapy.[3]

A clear causal relationship between oral BP and osteonecrosis of the jaw has yet to be established. Two theories have been put forward. First, that BPs induce compromised vascularity of the jaws by decreasing vascular endothelial growth factor, inducing apoptosis of the endothelial cells and inhibiting capillary neoangiogenesis.[2,3,8] These events lead to avascular necrosis of the jaws.[2,3] The second hypothesis is that the ischemia is thought to be induced through dense, poorly formed bone via the anticlastic mechanism of BPs as they alter the cytoskeletal morphology of osteoclasts inducing integrin signaling, trafficking of endosomes and disruption of the ruffled border.[2,9] Microstress and microfractures of jaw bones signal the osteoclastic and osteoblastic resorption and mineralization of the damaged bone, respectively. As a result, there is no release of bone morphogenic protein with no induction of osteoblastic differentiation resulting in an avascular and acellular osteon.[2,9]

BRONJ may remain asymptomatic for many weeks or months and is usually identified by its unique clinical presentation of exposed bone in the oral cavity. These lesions typically become symptomatic when sites become secondarily infected or if there is trauma to adjacent or opposing healthy soft tissues.[10] Radiographic changes in early stages are very subtle and difficult to detect but over time, as the surface bone breaks down, changes such as osteolysis consistent with bone loss may be evident.[10] Preventive measures should always be taken to subvert the risk of developing this severe ailment. These include careful dental examination and extraction of candidate's

**Table 1: Treatment guidelines for BRONJ devised by AAOMS[2]**

| Stages | Treatment guidelines |
|---|---|
| Stage zero or risk category | No treatment indicated<br>Patient education |
| Stage I | Antibacterial mouth rinse<br>Clinical follow up every 4 months |
| Stage II | Treatment with broad spectrum oral Antibiotics<br>Antibacterial mouth rinse<br>Superficial debridement to relieve soft tissue irritation |
| Stage III | Antibacterial mouth rinse<br>Antibiotic therapy and pain control<br>Surgical debridement or resection for larger palliation of infection and pain |

BRONJ: Bisphosphonate related osteonecrosis of jaw, AAOMS: American Association of Oral and Maxillofacial Surgeons

teeth with enough time allowed for healing in advance of the start of BP treatment, control of dental caries and periodontal disease, avoiding implant placement.[2,8,11] Non-restorable teeth should be treated by removal of the crown and endodontic treatment of the root remnants.[2] Other risk factors including diabetes, smoking, alcohol abuse, poor oral hygiene and corticosteroid therapy should be taken care of. Patient should be adequately informed of the potential risk of defective bone healing.[2,12]

Currently, there is no effective treatment for BRONJ. The AAOMS has proposed a staging system and based on it, treatment strategy (Table 1) has been devised with the goal of preventing progression of lesions and limiting complications related to chronic infection.[2]

The literature, until date, does not document any case in which there was spontaneous healing of the lesion of BRONJ solely on cessation of the drug. Although the exact mechanism of this phenomenon is not known, but it can be hypothesized that the self-healing ability might be due to the fact that the bone renews itself and discontinuation of therapy might have a beneficial effect as the newly formed bone is unable to absorb BP.

## CONCLUSION

In view of the present case, it may be advised to stop the BP therapy for the management of osteoporosis in patients who manifest with BRONJ since alternative therapies for osteoporosis are available. However, the treatment should be based on individual's systemic conditions.

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