***Case study***

# BISPHOSPHONATE INDUCED OSTEONECROSIS OF THE JAW IN RENAL SARCIODOSIS – A CASE REPORT


## Abstract

The therapeutic use of Bisphosphonates has increased in the last decade. The long-term use of bisphosphonates has led to a challenging complication related to jaws knows as Bisphosphonate-induced osteoradionecrosis of the jaw (BIONJ).In this paper we report a case of BIONJ in a renal sarcoidosis patient with clinical implications and management.



**Key words;** Bisphosphonates, sarcoidosis, osteonecrosis, jaws.




## Introduction

Bisphosphonates are widely used in the treatment of malignant tumors, bone metastasis, primary bony pathogenesis like multiple myeloma, Paget's disease, Rheumatoid arthritis, Fibrous dysplasia, Osteogenesis imperfect, hypercalcemia of malignancy and osteoporosis [1-4].

Bisphosphonates primary mechanism of action is inhibition of osteoclastic resorption of bone. Therapeutic action of Bisphosphonates as an antiresorptive agent is used in the treatment of metastatic disease and osteoporosis. They also have antiangiogenic property through which it decreases circulating vascular endothelial growth factor (VEGF). Thus, bone metabolism, which involves bone resorption and deposition is jeopardized [2].

The Bisphosphonates in clinical use are Alendronate, Pamidronate as intraveneous drugs and Zolendronate, Risedronate, Zolendronate, Ibandronate, Etiodronate, Tiludronate as oral drugs. [4]. The intravenously administered bisphosphonates show highest prevalence of BIONJ it is about 1-10% whereas, in oral route 0.00007%-0.04%[2]. The half-life of Bisphosphonates is 10 years [2]. The average duration of incidence of BIONJ is 9-14months [4].

Incidence of BIONJ in mandible compared to maxilla is in the ratio of 2:1. Maxilla accounts for 28% and mandible 68% and 4% occur in both jaws. It is reported that 31 % of cases, present with asymptomatic bone exposure and 69% with bone exposure, pain, intra oral or extra oral draining sinuses. Spontaneous bone exposure can occur in the patients who have optimal dental health and this particularly occurs in the lingual cortex of mandible [2]. The two main risk factors for BIONJ are IV bisphosphonate and dentoalveolar surgery.

Marx and Stern in 2003 first described, long term use of Bisphosphontes leads to a potential complication known as Bisphosphonate induced osteonecrosis of the jaw [2,3]. American association of Oral & Maxillofacial Surgeons(AAOMS) in 2007 defined BRONJ with three characteristic features as current/previous treatment with Bisphosphonates and exposed bone in maxillofacial region that has presented for more than 8weeks and with no history of radiotherapy to the jaws [4].

**Case report-**

A 68-year-old male patient presented to Department of Oral and Maxillofacial Surgery with a chief complaint of pain and pus discharge in the left upper jaw since three months. His medical history revealed diabetes, hypertension and sarcoidosis of kidneys 8 year back, during which he developed hypercalcemia and renal calculi. To regulate serum calcium level, four IV doses of Zoledronic acid was administered and to maintain same, sodium Alendronate 70mg Tab orally one per week with Methyl prednisolone 10mg Tab was advised.

The patient visited local dentist, where his medical history was not evaluated and extractions in all the four quadrants was performed. Six months following extraction he noticed greyish black area in the upper left extraction area with pus discharge. Patient was referred from the nephrologist to us for further management.

On examination in the left upper posterior region there was 1cm * 1cm exposed necrotic bone, and obliteration of the buccal vestibule with multiple draining sinus [figure 1]. In the right upper jaw, the alveolar mucosa was erythematous. In left lower jaw there was exposed bone on the lingual surface in extracted region. The panoramic radiograph showed necrotic bone measuring 1x1 cm in left upper quadrant, necrotic bone measuring 0.5x0.5 cm in right upper quadrant and osteolytic area in left lower extracted region [figure2].

CBCT showed fragments of detached alveolar bone in the region of 24-26, continuity of the sinus floor was lost. There was irregular radiolucency involving the alveolar bone in relation to 45,46,47 and 14,15 regions [figure 3]. A provisional diagnosis of BIONJ was made based on history, clinical and radiographic features.

Under local anesthesia with antibiotic coverage, necrotic bone in the left upper quadrant was removed. Healing was uneventful [figure4]. The other areas are under regular checkup once in three months with one year of follow up the other areas are asymptomatic.

Discussion:

Sarcoidosis is an immune mediated disease with multiorgan association. It affects mainly pulmonary system up to 90% [6]. The medical management in sarcoidosis is glucocorticoids to reduce inflammation. In this case bisphosphonate was used to treat hypercalcemia induced due to sarcoidosis of kidney.

Dixon et al demonstrated alveolar crest remodels at 10 times the rate of tibia, 5 times the rate of mandible at the inferior border and 3 to 5 times the rate of mandible at the level of canal. Bisphosphonates readily accumulates at higher concentration in the alveolar bone and hence predisposes to BIONJ. On axial loading of mandibular molars, stress concentration is on the lingual cortex and not the inferior borders of mandible. This occurs in the Bisphosphonate induced avascular bone and the overlying thin mucosa easily gives away exposing the underlying bone [2,4].

Dental evaluation should be done before starting Bisphosphonate therapy, the unsalvageable teeth, local anatomic structures like tori, mylohyoid ridge, which are covered by thin mucosa, impacted teeth exposed to oral cavity should be removed at least 4-6 weeks before starting bisphosphonates to allow complete healing, Periodontal therapy, root canal therapy, Oral prophylaxis, fluoride application should be considered. In denture wearers regular examination and soft relining is considered [3].

The radiographic signs of bisphosphonate toxicity include generalized sclerosis in the alveolar bone and lamina dura, widening of PDL space, tooth mobility unrelated to alveolar bone loss and dry bone pain without an appropriate dental etiology.

During IV bisphosphonate therapy invasive dental procedures are contraindicated. The goal is to keep optimum dental and oral health.

According to Scooletta et al extraction of teeth in intravenous bisphosphonate treated patients, with antibiotic coverage, atraumatic luxation and removal, followed by piezo assisted minimal alveoloplasty with autologous platelet rich factors and primary closure had a favorable outcome [8]. In case of BIONJ after superficial curettage, the exposed bone covered with two layers of platelet rich growth factors, showed optimum healing. [9].

BIONJ revised staging system -–

Stage I: one quadrant or less of exposed bone

Stage II: Two or more quadrants of exposed bone without evidence of osteolysis beyond the alveolus or sinus involvement.

Stage III: osteolysis beyond the alveolus or pathologic fracture or cutaneous fistula or sinus involvement [1,2,5].

In stage I and II - chlorhexidine 0.12% mouth wash three times a day, Penicillin VK 500mg, who are allergic or who resist Levofloxacin 500mg / Azithromycin 500mg [2] along with vasodilator Pentoxyfyline, Vitamin E and Teriparatide [10].

In stage III - debridement, marginal resection, enbloc resection, resection with continuity defect is advocated [2]. Attempts of debriding and extensive osseous surgeries should be avoided, as it only increases defect size and chances of pathologic fracture.

## CONCLUSION

BIONJ is a potential complication in patients receiving bisphosphonates. Thorough dental and medical history evaluation is mandatory before dentoalveolar surgery.

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Figure1 : Intraoral photograph showing exposed bone in the left upper posterior quadrant with multiple draining sinuses.

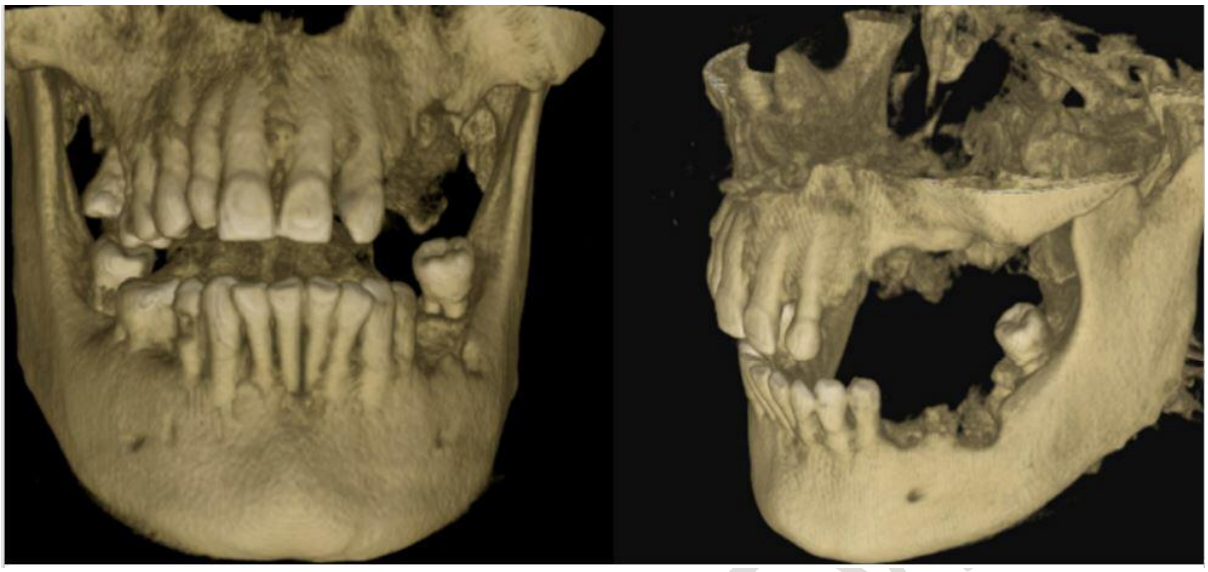

Figure2 :Orthopantamogram showing necrotic bone in the left upper posterior quadrant, necrotic bone in right upper posterior quadrant, osteolytic area in left lower posterior quadrant (extraction site).

Figure3 : CBCT shows detached alveolar bone measuring 22mm*11mm*11mm in left upper posterior quadrant, necrotic bone measuring 5mm*5mm in the right upper posterior quadrant, irregular radiolucency involving the alveolar bone in the left lower posterior quadrant.

Figure 4 : Intraoral photograph showing satisfactory healing.