

Challenge in Diagnosis and Management of Simultaneous Multiple Myeloma Bone Lesion and Medication-Related Osteonecrosis of the Jaw

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Abstract

Case Report

Medication-related osteonecrosis of the jaw (MRONJ) is a well-known complication of antiresorptive treatments and was first described with bisphosphonate treatment and recently with denosumab, and other anti-angiogenic drugs. It has been reported that MM patients have the highest risk of MRONJ mainly in patients who received combination of pamidronate and zoledronate. Neither clinical nor radiologic features are pathognomonic for MRONJ, in fact bone metastasis may have overlapping characteristics and must be excluded in histologic examination. We report a case of a multiple myeloma patient treated with zoledronic acid and whose initial clinical presentation was challenging to distinguish between bone metastasis and MRONJ.

Keywords: multiple myeloma, bone metastasis, Medication-related osteonecrosis, antiresorptive treatments.

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INTRODUCTION

Anti-resorptive therapy such as BPs or denosumab are widely used to treat bone metastasis of malignant condition such as multiple myeloma by inhibition of osteoclastic bone resorption and angiogenesis [1, 2]. Medication-related osteonecrosis of the jaw (MRONJ) is a well-known complication of antiresorptive treatments and was first described with bisphosphonate treatment then denosumab, and other anti-angiogenic drugs [3].

Although the etiology remained unclear (2), the prevalence of MRONJ in patients treated with intravenous BPs ranges from 0.8 to 12% [4]. It's reported that MM patients have the highest risk of MRONJ mainly in patients who received combination of pamidronate and zoledronate range 5 to 51% [3, 4].

Occurrence of Medication related osteonecrosis of the jaw and myeloma osteolytic jaw lesions within the same jaw site has been reported in the literature with overlapping clinical and radiographic presentations leading to confusion and challenge for earlier diagnosis and precise treatment [5, 6].

CLINICAL CASE

A 63-year-old patient consulted the oral surgery department, Farhat Hached Teaching Hospital

Sousse Tunisia with a chief complaint of pain and swelling in the right mandibular area.

Medical history revealed antecedent of multiple myeloma diagnosed 7 years ago and managed by chemotherapy (Melphalan, Dexamethasone, thalidomide and 24 zoledronate injections) in addition to autogenic bone marrow stem cells transplantation. 5 years after the initial treatment, the patient relapses and have received 3 additional zoledronate injections.

Extraoral examination was unremarkable. Intra oral examination revealed: pain on palpation; buccal productive fistula in the posterior right mandible (regarding the teeth 44,45) and productive fistula of the lingual cortex (regarding molar 46)

The CBCT scan revealed osteolytic bone lesion extending from distal aspect of 46 till mesial aspect of 44 (figure 1). The oblique coronal reconstructions showed moth-eaten appearance of the bone trabeculae and lytic bone destruction extending beyond the region of alveolar bone and lingual area of the right hemi-mandible (Figure 2).

Based on clinical, radiological data and the medical history, the diagnosis of spontaneous stage II MRONJ was established. To manage infection, 10 days

antibiotics were prescribed based on 2g (amoxicillin+clavulanic acid: Augmentin) and 750 mg metronidazole daily. Paracetamol and antiseptic mouth rinse were also prescribed.

One month later surgical management under local anesthesia was performed; 3g amoxicillin and 1.5g metronidazole daily was taken 3 days prior to the surgery.

Surgical steps consisted of

- Extraction of the mobile teeth totally involved in the osteolytic bone lesion The molar (44,45 and 46) associated with the lesion were extracted
- Reflection of full-thickness mucoperiosteal flap
- Autofluorescence guided bone curettage to visualize and remove the necrotic bone.
- Necrotic bone curettage using piezo inserts with an integrated saline spray to maintain a low temperature and good vision of the surgical site and to avoid the use of an excessive force.
- Sharp bony edges smoothing.
- Use of autologous Platelet rich fibrin (PRF) clots over the bone to promote healing (figure 3)
- Tension-free flap fixation with both periosteal and transmucosal sutures to prevent post-operative bone exposure (figure 5)

The patient was instructed to continue 1.5g metronidazole daily one week after surgery and 2g amoxicillin until complete mucosal healing.

After 2 weeks routine control, incomplete wound healing with exposed PRF was noticed. Infection and inflammation resolution were achieved, without any bone exposure (Figure 6).

On 30-day post-operative, complete wound healing without any bone exposure or infection signs were achieved. The histopathologic examination revealed necrotic bone with signs of inflammation, but also A plasmacytoma of densely packed plasma cells was observed with increased vascularization in the soft tissues surrounding the area of osteonecrosis of the jaw. Neoplastic cells were immunoreactive to kappa light chain restriction and CD 138 during immunohistochemical study and the patient was referred to his hemathologist for further treatment.

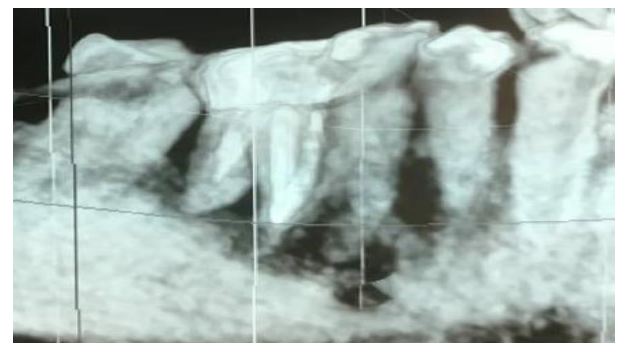


Fig-1: CBCT scan, panoramic reconstruction showing large osteolysis extending from distal aspect of 46 till mesial aspect of 44

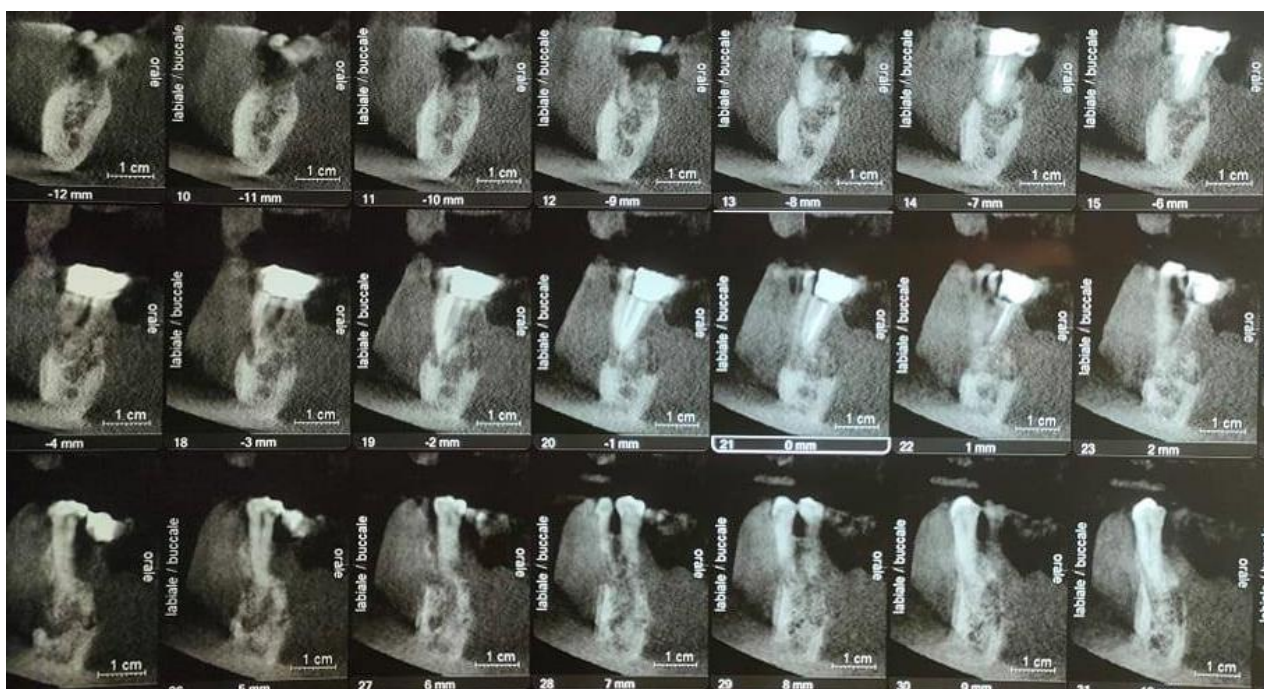


Fig-2: CBCT scan showing oblique-coronal sections: lytic bone destruction extending beyond the region of alveolar bone and lingual area of the right hemi-mandible

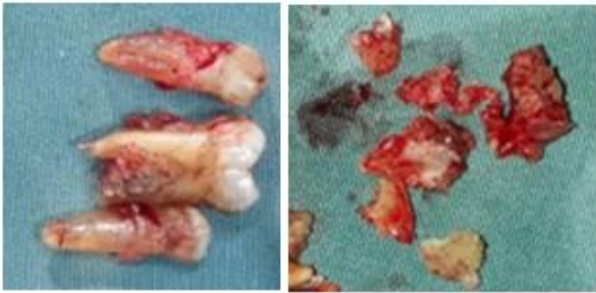


Fig-3, 4: Surgical piece including the extraction teeth and the removed necrotic bone and granulation tissue



Fig-5: Intraoral view after Tension-free flap fixation.



Fig-6: Two weeks routine control showing incomplete wound healing with exposed PRF



Fig-7: Complete wound healing was achieved on 30-day post-operative

DISCUSSION

Multiple myeloma is a hematologic malignancy characterized by neoplastic proliferation of plasma cell clones [7]. 20% to 30% of multiple myeloma patients developed osteolytic jaw lesions (8), the mandible is more commonly affected than the maxilla, with a predilection for the posterior region [9].

The oral presentations of MM, although rare, being mostly osteolytic jaw lesions, alveolar swelling, pain, paresthesia, dental displacement, root resorption, gum bleeding and gingival mass [7, 10].

MM jaw lesions are often missed in the radiological reports, The most common radiographic findings reveal punched-out or poorly margined osteolytic lesions and generalized osteoporotic changes, normal patterns with mild or undetectable bone resorption were also identified [9-11]. Up to now there is no standardized clinical and radiographic features of MM jaw lesions [12].

The prolonged duration of chemotherapy including as thalidomide, dexamethasone and especially bisphosphonate has been associated with frequent report of MRONJ in Multiple myeloma patients [12]. MRONJ is defined as oral bone exposure or fistula that probes to bone persisting for longer than eight weeks in a patient who has been previously treated with antiresorptive or antiangiogenic agents. Invasive dental procedures are the most common etiologic factors [9, 13].

Similar to multiple myeloma jaw lesions, MRONJ occur in the posterior mandible rather than in the maxilla [11]. But on the contrary MRONJ usually exhibits the typical signs and symptoms of bone pain, soft tissue swelling, recurrent abscess, draining fistula, and bone sequestration [12].

Neither clinical nor radiologic features are pathognomonic for MRONJ; both may show overlapping characteristics [10]. In up to 5% of patients with malignant cells within the jaw, no radiologic features can be detected and bone metastasis may clinically and radiographically mimic MRONJ and must be excluded by histopathologic examination [11, 12].

Junquera *et al.* reported that 9.09% of 22 MRONJ specimens in patient with multiple myeloma showed association of MRONJ and MM bone lesion on histopathologic examination. Likewise, in the Zürich study of 121 Multiple myeloma patients with MRONJ, they found underlying malignancy in 3 cases. Since multiple myeloma bone lesion may modify the treatment strategy, this finding should not be underestimated [3, 12]. In the reported case no further treatment was indicated since the patient was already under relapse treatment with many systemic complications.

The possibility that MRONJ and MM jaw lesion could occur within the same jaw site raises one the important role of Histologic analysis following surgical treatment of the assumed MRONJ area, avoiding 2 invasive interventions [3, 11].

Histological examination showed neoplastic cells within osteonecrosis peripheral margins [9]. Thus, the biopsy specimen must be carefully selected to involve marginal vital bone resulting in better highlighting of the neoplastic cells. [3, 12].

CONCLUSION

Medication-related osteonecrosis of the jaw (MRONJ) is a well-known complication in MM patients. Association of Zoledronate and pamidronate administration is a major risk factor. Multiple myeloma can be identified in jaw specimens firstly diagnosed as osteonecrosis in MM patients. histological exam is mandatory for all surgical removed bone in case of MRONJ.

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