THE USE OF CONE BEAM COMPUTED TOMOGRAPHY IN THE DIAGNOSIS AND TREATMENT OF MEDICATION-RELATED OSTEONECROSIS OF THE JAW

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ABSTRACT

In the diagnosis of osteonecrosis of the jaw (ONJ), imaging may have an important role in determining the extent of the disease, diagnosing early stages of osteonecrosis, identifying a potential association between metastasis of the jaw and ONJ lesions, excluding other diseases or complications of the jaws, such as fractures, and evaluating the jaw before surgical orofacial procedures. Since the appearance of ONJ at imaging is variable and very often nonspecific, imaging findings should always be related to the clinical context. The panoramic radiography is the most often used imaging technique in cases of ONJ, whereas CBCT is an adequate tool in evaluating bone involvement, in addition to offering the advantage that destructive processes can be seen at high resolution.

Keywords: osteonecrosis of the jaw, antiresorptive agents, cone-beam computed tomography

INTRODUCTION

Medication-related osteonecrosis of the jaw (MRONJ) is the new nomenclature of bisphosphonate-related osteonecrosis of the jaw because of the growing number of osteonecrosis cases involving the maxilla and the mandible associated with other antiresorptive (denosumab) and antiangiogenic therapies [1].

Patients may be considered to have MRONJ if one of the following characteristics are present: curernt or previous treatment with antiresorptive and/or antiangiogenic agents; exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region that has persisted for longer than 8 weeks; no history of radiation therapy to the jaws or obvious metastatic disease of the jaws [1].

Although initially periapical x-rays, panoramic x-ray or computed tomography were used in the diagnosis of MRONJ, in recent years CBCT scanners have become increasingly popular in oral and maxillofacial surgery. The great advantage of CBCT is its easy and inexpensive access to 3-dimensional images of bone structures of high resolution. Exposure to radiations is higher than for panoramic radiographs, but lower than multislice computed tomography [2].

Certain radiological alterations of the jaws, including thickening of the lamina dura and of the cortical borders, diffuse sclerosis an narrowing of the mandibular canal, have been reported after bisphosphonate therapy.

The CBCT images have been studied as a tool for the measurement of trabecular bone...
in patients with MRONJ. Therefore, cortical bone measurements on CBCT of the jaws might also help understand bone changes in patients with MRONJ.

**MATERIAL AND METHODS**

8 patients out of 42 diagnosed with MRONJ underwent cone-beam computed tomography in order to evaluate the bone lesions.

The CBCT scanner used was PlanmecaPromax 3D Mid (Planmeca OY, Helsinki, Finland). Images were obtained at 90kV, 12mA, with a 0.4 voxel size. The selected field of view was 40mm x 40mm.

The initial and final reconstructions of the panoramic and cross-sectional images were made using the Romexis 3.0.1 software, at a preestablished width of 1 mm.

The measurements were made by a radiologist under standardized viewing conditions: 40cm viewing distance, diagnostic screen, dimmed room.

Every CBCT scan was assessed for the typical radiological findings of MRONJ, which have been described by several authors (3,4,5,6,7): destruction of the trabecular structure of the cancellous bone, erosion of the cortical bone, sequestration, osteosclerosis and formation of new periostal bone.

**RESULTS**

There were 8 cases selected for the study. The characteristics of the MRONJ cases are shown in table 1. Most of them were treated with acidum zoledronicum.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Primary disease</th>
<th>Location of RONJ</th>
<th>Onset of disease</th>
<th>Signs and symptoms</th>
<th>Type of bisphosphonate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>46</td>
<td>M</td>
<td>KCa, BM</td>
<td>Mandible</td>
<td>TE</td>
<td>Exposed bone</td>
<td>Zoledronate</td>
</tr>
<tr>
<td>2</td>
<td>52</td>
<td>F</td>
<td>BCa, BM</td>
<td>Mandible</td>
<td>TE</td>
<td>Non healing socket</td>
<td>Zoledronate</td>
</tr>
<tr>
<td>3</td>
<td>71</td>
<td>F</td>
<td>Bca,BM</td>
<td>Mandible</td>
<td>S</td>
<td>Exposed bone</td>
<td>Zoledronate</td>
</tr>
<tr>
<td>4</td>
<td>64</td>
<td>F</td>
<td>O</td>
<td>Maxilla</td>
<td>TE</td>
<td>Oro-antral fistula</td>
<td>Alendronate</td>
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<tr>
<td>5</td>
<td>66</td>
<td>F</td>
<td>BCa</td>
<td>mandible</td>
<td>TE</td>
<td>Non-healing socket</td>
<td>Zoledronate</td>
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<td>6</td>
<td>66</td>
<td>M</td>
<td>Pca</td>
<td>Mandible</td>
<td>TE</td>
<td>Non-healing socket</td>
<td>Zoledronate</td>
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<td>7</td>
<td>71</td>
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<td>Pca</td>
<td>mandible</td>
<td>TE</td>
<td>Exposed bone</td>
<td>Zoledronate</td>
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<tr>
<td>8</td>
<td>57</td>
<td>M</td>
<td>Pca</td>
<td>maxilla</td>
<td>TE</td>
<td>Oro-nasal fistula</td>
<td>zoledronate</td>
</tr>
</tbody>
</table>

Kca, kidney cancer; BM, bone metastasis; Bca, breast cancer; O, osteoporosis; Pca, prostate cancer; TE, tooth extraction; S, spontaneous

### Case 1

A 63-year-old male was hospitalized in our clinic with stage 3 osteonecrosis (according to AAOMFS) of the right maxilla. He had been diagnosed with lung cancer and bone metastasis 6 years before for which he had undergone local radiotherapy, chemotherapy (cisplatin and etopside) and bisphosphonates (zoledronat). He had undergone extraction of first and second right upper molars three months prior to the mentioned therapy.

CBCT examination of the patient was conducted for the maxilla and highlights: alveolar bone destruction of the right maxilla, oro-antral fistula, partial osteonecrosis of anterior and lateral wall of the right maxilary sinus, chronic inflammation of the Schneiderian membrane which blocks the maxillary ostium.

Osteosclerosis of the right maxillary sinus walls extends towards greater and lesser wings of the sphenoid bone, with peripheral thickening of sphenoid sinus mucosa. An
inflammatory process of the soft palate can be observed near the oral cortical osteonecrosis area.

![Figure 1. CBCT images of MRONJ (coronal section, cross-section, axial section and 3D reconstruction)](image)

The patient underwent exploration of his right maxilla with debridement of bone sequestrum and closing of the oroantral fistula using vestibular flap. One month after surgery he had made a satisfactory postoperative recovery.

**Case 2**

We present a 72-year-old patient with stage 2 osteonecrosis (according to AAOMFS) of the anterior mandible. His past medical history was significant for prostate cancer diagnosed in 2007 and bone metastasis diagnosed in 2011. After three years of intravenous bisphosphonates (zoledronat) he underwent tooth extractions of the inferior incisors. Clinical examination revealed exposed bone in the anterior mandible and congestion of the surrounding mucosa.

The CBCT analysis highlights the osteosclerosis area located in the mandibular anterior area (41-43), with multiple bone lesions with sequestra and erosion of both oral and bucal cortical bone.

The patient underwent debridement of the bone sequestrum and wound closure with mucoperiosteal flap. After one year there are good postoperative results, with no bone exposure.
Case 3
We present a case of a 73-year-old patient, previously diagnosed with prostate cancer and bone metastasis in 2012. The patient has been submitted for chemotherapy and bisphosphonates (zoledronat). He gave a history of extraction 36 under local anaesthesia four months before. He presented a non-healing extraction socket (stage 1 of MRONJ according to AAOMFS staging system). We initiated long-term oral systemic antibiotic therapy (penicillin in association with oral antimicrobial rinses).

A 73-year-old patient was diagnosed with prostate cancer and bone metastasis in 2012 for which he was treated with chemotherapy and bisphosphonates (zoledronat).

The CBCT examination highlights nonhomogenous osteocondensation located in the left mandible, associated with both bucal and lingual cortical erosion, empty 36 extraction socket without bone sequestrum.

Case 4
A 46-year-old patient with stage 2 osteonecrosis (according to AAOMFS) of the right hemimandible was referred to our clinic. His medical history was significant for renal cancer (diagnosed in 2004) and bone metastasis. The CBCT examination highlights nonhomogenous osteocondensation located in the right hemimandible, associated with both bucal and lingual cortical erosion, empty 36 extraction socket without bone sequestrum.
metastasis in 2011. The patient was submitted to bisphosphonated for 18 months; during that period he underwent extraction 48.

CBCT analysis highlights osteolytic areas with central sequestrum, which includes the right horizontal ramus of the mandible starting from 45, the mandibular angle and half of the vertical ramus, ending near the inferior alveolar nerve foramen.

The treatment included systemic antibiotic therapy, debridement of bone sequestrum, PRP (platelet rich plasma) placing and wound closure. After 6 months the patient remained asymptomatic showing no exposed bone.

DISCUSSIONS
For the classification and description of the severity of MRONJ sites, different staging systems have been published, although there is still no worldwide consensus on a specific staging system. The clinical picture does not usually show the full extent and severity of MRON (8). There are few papers in literature that study the use of CBCT as a modality for imaging of MRONJ lesions.

CBCT can assess both cortical and trabecular bone characteristics and it can provide 3-dimensional information, while using lower doses and costing less than conventional CT.

It is important to add that the imaging appearance of ONJ is variable and very often nonspecific, and should always be related to the clinical context.

There is no standard protocol in quantifying dimensional changes of bone. CBCT is the best modality to provide information about cortical and trabecular bone as it allows estimations of the extent of the necrotic process and distinguishes ONJ from malignant diseases such as bone metastases [4,8,9,10]. Focal medullary sclerosis with disorganized microtrabeculae and poor corticomedullary differentiation in the suspected necrotic site has been described as a finding associated with early symptoms of tooth loosening. Persistent alveolar sockets related to delayed socket healing, especially after teeth extractions, are a typical panoramic radiographic feature of early ONJ [9,11] and may represent an early imaging finding associated with medication related ONJ.

Several authors have described bone sclerosis as the most common finding: its appearance can range between subtle thickening of the lamina dura and alveolar crest to attenuated osteopetrosis-like sclerosis [3,11,12]. In advanced stages, osteonecrosis is seen as an irregular area of osteosclerosis with “a cotton wool-like” appearance.
Osteolyses often show a central sequestrum; lytic areas may also indicate foci of bacterial infection [3,9,11]. Periosteal reaction and bone sequestrum may be predominant in advanced stages of the disease [10,11].

Narrowing of the marrow space and involvement of the inferior alveolar canal are also common findings at CT [3,9,11]. However, it was recently demonstrated that even if adjacent alveolar bone is altered by lytic or sclerotic changes, sparing of the mandibular canal may represent the diagnostic clue for malignancies.

CT is a useful imaging modality to demonstrate both the size and the type of alveolar involvement, to precisely assess the dimensions and locations of the lesions, and to define lesion margins during management [13,14].

If the maxilla is involved, there may be associated abnormalities in the adjacent maxillary sinus, from muco-periosteal thickening to air-fluid levels and purulent drainage [11,13,14].

CONCLUSIONS

Osteosclerosis of the jaw as a radiological sign of MRONJ in CBCT can be seen in all stages of the disease.

 Destruction of the trabecular structure of the cancellous bone and erosion of the cortical bone are the two most frequent findings for MRONJ in CBCT scans.

Although the changes associated with MRONJ are apparent with various imaging modalities, the findings are typically nonspecific. Currently, the primary role of imaging is to demonstrate the extent of disease before surgical intervention and complications such as pathologic fractures. The clinical implications of the imaging-based diagnosis of unexposed lesions that may be associated with bisphosphonate treatment are currently unknown. It is important for the radiologist to be aware of this entity and to include ONJ in the differential diagnosis in patients with a history of antiresorptive treatment.

REFERENCES


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