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Grade of sclerosis in the contralateral mandibular area in osteonecrosis of the jaws

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Abstract. The objective of this study was to compare the grade of radiographic sclerosis between the area of osteonecrosis and the at-risk contralateral mandibular area without osteonecrosis. Three groups were studied: group 1 comprised 30 cases of medication-related osteonecrosis of the jaws (MRONJ); group 2 was the healthy contralateral area without osteonecrosis of the group 1 cases; group 3 comprised 30 healthy controls. ImageJ software was used to analyze the computed tomography images, and the grade of bone sclerosis was compared between the three groups. The grade of sclerosis was significantly higher in group 1 than in the other groups ($P < 0.05$); the difference between groups 2 and 3 was not significant. Sclerosis was significantly greater in the area of bone necrosis than in the contralateral mandibular area in patients with MRONJ. No significant differences were found in the grade of sclerosis between the contralateral non-affected mandibular area of patients with MRONJ and the control patients.

Key words: medication-related osteonecrosis of the jaws; bisphosphonates; bone sclerosis.

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In 2003, Marx described an adverse reaction to bisphosphonates (BPs) and coined the term 'osteonecrosis of the jaws' (ONJ) to describe a severe complication in patients with cancer treated with BPs. This initial report described 36 cases, mainly in patients with metastatic breast cancer and multiple myeloma.[1] Subsequently, many authors have reported series of cases of medication-related osteonecrosis of the jaws (MRONJ), and several societies have developed protocols for the staging, management, and prevention of MRONJ.[2–7]

The incidence of ONJ is greater in patients with cancer treated with intravenous BPs (1–15%). This incidence is much lower in patients with osteoporosis, ranging from 0.001% to 0.01%.[8,9]

The diagnosis of MRONJ is based mainly on clinical criteria and is easy to make due to the typical presence of necrotic and exposed areas. Nevertheless, the performance of panoramic radiography or, even better, computed tomography (CT), is advisable in every case to look for the characteristic radiographic findings and to determine the extent of the necrosis for surgical planning when necessary.

Some authors have described the radiographic changes in patients with MRONJ.[10–16] The most common findings are altered trabeculae, with changes in thickness and mineral content, sclerosis, sequestrum formation, cortical bone erosion, periosteal new bone, lucency, and persistent sockets. Arce et al. described the radiographic findings in patients with bisphosphonate-related osteonecrosis of the jaws (BRONJ), including osteosclerosis,

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osteolysis, dense woven bone, a thickened lamina dura, subperiosteal bone deposition, and failure of postsurgical remodelling.[17] One of the most common radiographic findings is the presence of bone sclerosis.[18]

The present study group recently analyzed the grade of sclerosis in 43 patients with BP-related mandibular osteonecrosis in comparison with a control group of 40 patients without bony lesions. Bone sclerosis was measured from CT images using ImageJ version 1.47 software (National Institutes of Health, Bethesda, MD, USA). Patients with MRONJ had more severe sclerosis than did controls ($P < 0.01$).[19]

According to the most widely accepted classification of MRONJ worldwide, there is a stage known as 'patient at risk'. In 2007, Ruggiero and Drew reported that patients can be categorized into those at risk and those with established disease.[20] Patients who are considered to be 'at risk' according to the criteria of the American Association of Oral and Maxillofacial Surgeons (AAOMS) have no evidence of exposed or necrotic bone, but have been exposed to either intravenous or oral BPs. In 2009, Ruggiero et al. retained these patients at risk in their classification,[21] and again in the last classification update of 2014.[22]

The aim of this study was to analyze the degree of sclerosis at those sites 'at risk in the contralateral area', where the bone has also been exposed to BPs.

Materials and methods

The study included a total of 30 cases of mandibular MRONJ, identified on sagittal, axial, and coronal CT views (group 1). The diagnosis of osteonecrosis was made according to established criteria and the cases were staged.[22] The study was approved by the necessary ethics committee.

For group 1, the presence of lucency and persistent sockets (Fig. 1), narrowing of the mandibular canal (Fig. 2), sequestrum formation (Fig. 3), the existence of cortical bone erosion and thickening (Fig. 4), and possible mandibular fractures was registered.

The main objective of the study was to compare the degree of bone sclerosis in MRONJ due to BPs with each patient's at-risk contralateral mandibular area without osteonecrosis (group 2) and with a healthy control group of 30 patients (group 3). None of these subjects were included in the previous report by this study group[19]; they were selected randomly from a series of cases with MRONJ.

Fig. 1. Presence of lucency in the area of osteonecrosis.

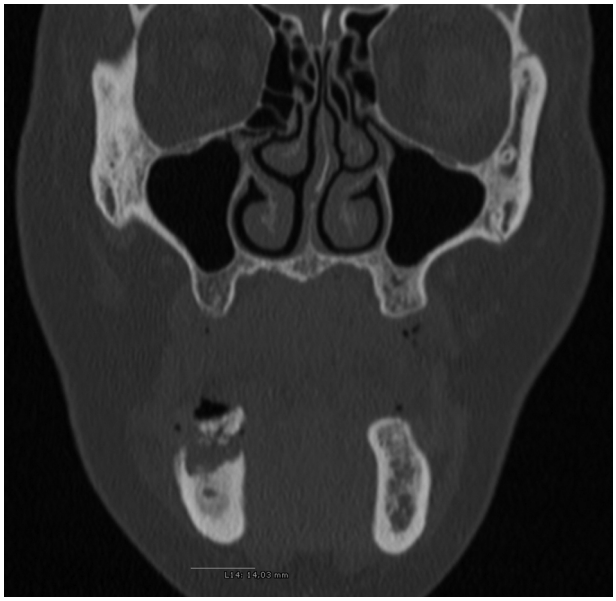

Fig. 2. Presence of mandibular canal narrowing.

The inclusion criteria for the different groups were as follows: (1) group 1 included patients with MRONJ due to intravenous BP treatment for metastatic cancer and multiple myeloma or oral BP treatment for osteoporosis; (2) group 2 included the contralateral mandibular areas of the group 1 cases, where there was no osteonecrosis or other lesion; (3) group 3 included patients without MRONJ who had not been treated with any drug and who had undergone CT for other reasons, mostly cysts in the maxilla, and who had no mandibular radiographic alterations on CT. Age and sex did not differ significantly between the patients in groups 1 and 3.

CT was performed with a helical scanner (VCT model; General Electric Healthcare, Waukesha, WI, USA). For group 1, three views of the area of osteonecrosis were used to assess the presence of lucency and persistent sockets, narrowing of the mandibular canal, sequestrum formation, the existence of cortical bone erosion, thickening of the cortical bone, and possible mandibular fractures.

ImageJ version 1.47 (National Institutes of Health, Bethesda, MD, USA; http://imagej.nih.gov.ij), a public domain programme with demonstrated reliability and validity, was used to compare the grade of bone sclerosis beneath the area of osteonecrosis in the three groups.[23–26] The method described in the previous study by the present authors was used to analyze the dense woven bone area (Fig. 5).[19]

The Kruskal–Wallis test was used to compare means among the three groups.

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