Sclerosis in bisphosphonate-related osteonecrosis of the jaws and its correlation with the clinical stages: study of 43 cases

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Abstract

We analysed the degree of sclerosis in the different stages of bisphosphonate-related osteonecrosis of the jaws (BRONJ) and studied the relation between the grade of sclerosis, the clinical symptoms, and the depth of lucency. We compared 43 patients with mandibular BRONJ with a control group of 40 cases with no bony lesions. The presence of sclerotic bone, cortical irregularities, radiolucency, fragmentation or sequestration, periostitis, and narrowing of the mandibular canal were studied from computed tomographic (CT) scans using the program ImageJ 1.47v (National Institute of Health, Bethesda, USA) to measure the radiolucency, width of the cortices, and degree of sclerosis. Patients with BRONJ had more severe sclerosis than controls ($p < 0.01$). There was also a significant difference among the different stages of BRONJ, with the highest values found in stage III ($p = 0.02$). The degree of sclerosis differed according to sex, type of bisphosphonate, and the clinical characteristics such as pain, or suppuration, but not significantly so ($p > 0.05$). We conclude that the degree of sclerosis increases with the clinical stage of BRONJ, and is correlated with the depth of lucency.

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Introduction

In 2003 Marx presented what are to our knowledge the first reported cases of bisphosphonate-related osteonecrosis of the jaws (BRONJ) in patients treated with intravenous bisphosphonates.[1] Since then many papers have described

the clinical aspects, the classification established by Ruggiero et al. being the most widely used.[2]

Initially, three stages of BRONJ were described with exposed bone, but later cases were reported with no exposure[3] and included as stage 0.[4] They were characterised by the presence of pain in the jaw bone (88/96; 92%) and sinus tract (51%), bony enlargement (36%), and gingival swelling (18%). No radiological abnormalities were identified in 28 of these patients (29%).[4]

The typical radiographic findings in BRONJ include trabecular alteration with changes in thickening and mineral

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Fig. 1. Coronal view in a patient with a large sequestrum as a result of bisphosphonate-related osteonecrosis of the jaw with widening (c) and erosion (b) of cortical bone, and deep radiolucency (a).

content, sclerosis, formation of sequestra, erosion of cortical bone, periosteal new bone,[5–7] lucency, and persistent sockets.[7] Sclerosis and changes in alveolar bone density are among the most commonly described changes in BRONJ[7–11] but few studies have measured the degree of sclerosis[8,12] or made measurements in panoramic studies.[8] Recently, Hamada et al.,[12] reported a controlled study using computed tomography (CT) in 20 patients with BRONJ and compared the degree of sclerosis in stage 0 with that in other stages, but they did not distinguish among stages I, II, and III.[12]

We therefore studied the degree of sclerosis at the different stages of BRONJ and examined the relations between the degree of sclerosis, the clinical characteristics, and other radiographic findings.

Patients and methods

The study was approved by the Ethics Committee of Valencia University and the patients gave their informed consent. We studied 43 cases of mandibular BRONJ with sagittal, axial, and coronal CT views. The diagnosis of osteonecrosis was established according to established criteria and the cases were classified into the four stages reported.[2,13]

The control group comprised 43 patients with lesions of the jaw bone who had not been treated with any drug, who had had a CT scan for other reasons (mainly cysts in the maxilla), and who had no obvious radiographic alterations to the mandible. There were no significant differences between the groups in age or sex.

CT scans were done using Helicoidal (VCT model, General Electrics, Health Care, Wakesha, Wisconsin, USA). The details of window and levels were the same in every CT. We used the three views of the area of the osteonecrosis to assess the presence of sclerotic bone, cortical irregularities, lucency, fragmentation or formation of sequestra, periostitis, and changes in (or narrowing of) the mandibular canal.[6,7,14] In addition, we measured the length of the lucency (mm) with a real scale in every coronal view (Fig. 1). Finally, to analyse
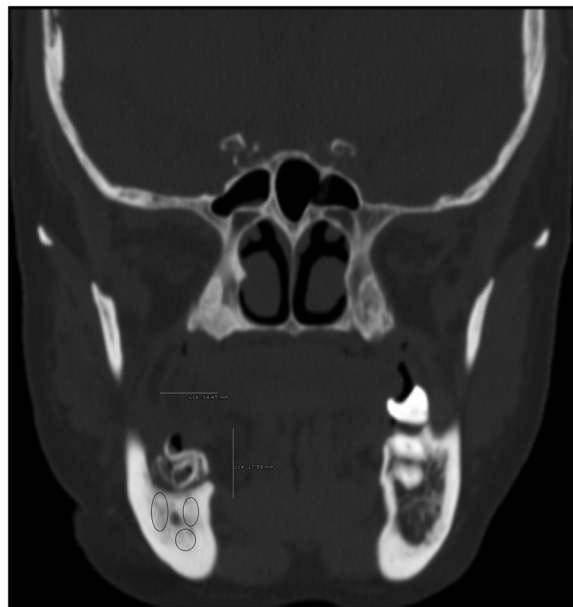

Fig. 2. Coronal view to measure the mean grey value of the three selected areas with circles in the Image J programme.

the sclerosis of the bone beneath the area of osteonecrosis, we used the program ImageJ 1.47v of the National Institute of Health, USA,[15] a public domain that is widely known for its reliability and validity.[16,17]

To analyse the sclerotic area we selected three zones in the coronal CT to obtain three measurements (Fig. 2). We first established a set scale (mm) from measurements on the CT scan, and every selected view of the coronal CT was loaded into ImageJ. These images were converted to grey-scale, 8-bit images. To set measurements we selected the mean (SD) grey value and range.

In the ImageJ program the first step in calibrating the image is to measure the mean grey value of the background and then compare it with the selected areas. The method has been used successfully in the analysis of the texture of various medical digital images, such as CT, dental radiographs, or positron emission tomography (PET) images.[15,16] This gives us the mean grey value of every area selected.

We used the Mann–Whitney *U* test to compare the means between the two groups and the Kruskal–Wallis test to calculate the differences among several groups. The Levene test and the Shapiro–Wilk test were used to assess the significance of differences between groups that came from populations with the same variance. The relations between the length of the lucency and the degree of sclerosis were analysed using Spearman's correlation coefficient. Finally we used a multiple regression analysis with the degree of sclerosis as the dependent variable and the age, duration on bisphosphonate treatment, the width of the cortex and the length of the lucency as independent variables. Probabilities of less than 0.05 were accepted as significant.