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CASE REPORT

CT imaging in bisphosphonate-associated mandibular osteonecrosis: case report, pathological correlates, and review of literature

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Abstract Osteonecrosis of the jaw is a severe bone disease that occurs as a result of reduced local blood supply. Bisphosphonate-associated osteonecrosis of the jaw usually occurs following dental procedures. We report clinical and radiological findings in a case of mandibular osteonecrosis associated with the use of bisphosphonate; the mandibular osteonecrosis was undiagnosed prior to cross-sectional imaging with computed tomography. The radiological correlation to the underlying pathological process and a correlative assessment of history, clinical, and imaging findings enabled the diagnosis. A discussion of differential diagnoses is provided to alert the oral radiologist to the presence of this condition in cases with typical imaging findings. The literature on indications for advanced imaging is reviewed to simplify the selection of the appropriate imaging modality for mandibular osteonecrosis.

Keywords Mandible · Osteonecrosis · Bisphosphonates · Computed tomography · Imaging

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Introduction

Osteonecrosis of the jaw (ONJ) is characterized by clinically exposed necrotic bone in the maxillomandibular region. ONJ has been reported in patients with cancer and hematological malignancies [1]. Rarely, it has been seen in patients with postmenopausal osteoporosis or Paget's disease receiving bisphosphonate therapy [1] to alleviate pain and reduce skeletal complications. The condition is characterized by ischemic or avascular osteonecrosis due to an inhibitory effect on circulating levels of vascular endothelial growth factor that affect the local blood supply to the bone.

An association between mandibular osteonecrosis and trauma or surgical procedures of the involved bone has been reported previously. However, there is a lack of evidence to support this correlation, and postsurgical exposure of bone that was already necrotic cannot be excluded [2]. Predisposing factors for osteonecrosis in patients on bisphosphonates include recent oral surgery, tooth extraction, denture use, and poor oral hygiene. Other proposed risk factors may include diabetes, comorbid conditions, and steroid use [3].

We report a case of bisphosphonate-associated mandibular osteonecrosis in which an inadequate diagnostic workup and incisional biopsy delayed the diagnosis and aggravated the lesion. The computed tomography (CT) imaging findings prompted a retrograde correlative assessment with history and clinical data to arrive at the diagnosis, which was reaffirmed by imaging correlates of the underlying pathological process.

Case report

A 68-year-old male patient reported to the DCA Imaging Research Center, New Delhi, for panoramic radiography of

the mandible for evaluation of a lower jaw swelling. The history revealed that the patient had been treated for multiple myeloma with 12 cycles of chemotherapy (melphalan in conjunction with bisphosphonates) 5–6 years previously. During treatment, the patient developed a painless swelling in the left lower jaw for which medical consultation was pursued. An incisional biopsy was attempted from the left lower jaw about 2 months previously, which had been inconclusive.

Gross clinical examination revealed minimal extraoral swelling of the left lower face. Intraorally, there was a large area of exposed and seemingly nonvital (black discoloration) bone in the left parasymphysis and body of the mandible. The adjoining left lateral border of the oral tongue appeared indurated and ulcerated with a fetid odor. No obvious fluid or purulent discharge from the lesional site was noted (Fig. 1). There was no evidence of extra- or intraoral sinus openings. No structural or functional dysfunction of the tongue was noted.

A digital panoramic radiograph (Fig. 2) was taken using a Kodak 8000C Digital Panoramic and Cephalometric System (Kodak Dental Systems, Carestream Health Inc., Rochester, NY) at 73 kV and 12 mA for 13.9 s, and the image was observed with a GE Centricity PACS-IW (GE Healthcare, UK).

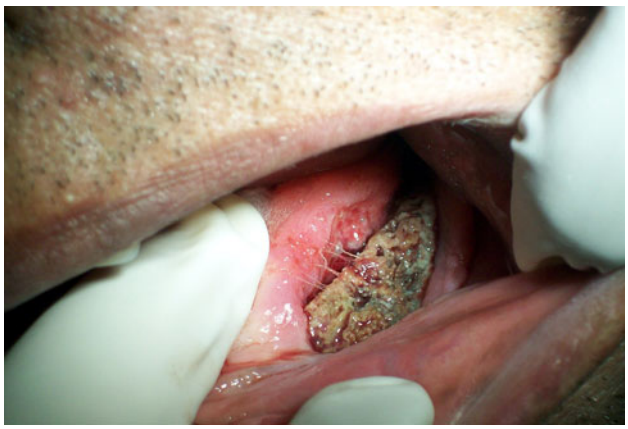

Fig. 1 Intraoral photograph demonstrating the large area of exposed necrotic bone in the left mandibular parasymphysis and body

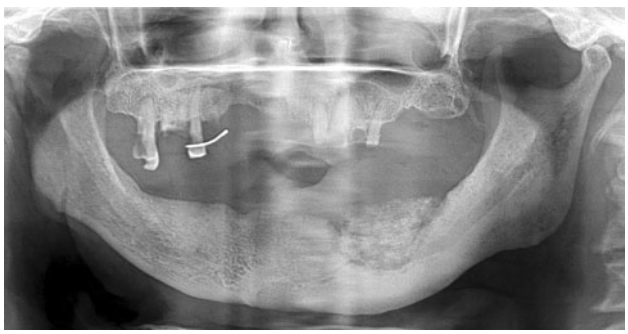

Fig. 2 Digital panoramic radiograph showing a large bony sequestrum with a peripheral radiolucent rim and sclerosis surrounding the rim

A large area of bone destruction, corresponding with the region of clinical involvement, was noted. A large radiopaque sequestrum was seen centrally in the lesion with a wide radiolucent band separating it from the peripheral sclerotic bone. No subperiosteal new bone formation was noted. A CT scan of the mandible (Fig. 3) was performed for better definition of the features and extent of the lesion. CT images were obtained using a SOMATOM Sensation 64-Slice Scanner (Siemens Ltd., Erlangen, Germany) at 120 kVp and 100 mAs, with a slice thickness of 0.75 mm at 0.5-mm intervals; kernels H70 and H30 were selected. Image reconstruction and viewing were performed using the OnDemand3D imaging software (Cybermed Inc., Seoul).

There was expansion of the left parasymphysis and body of the mandible with diffuse trabecular sclerosis. An ovoid osteolytic lesion (approximately 2.5 cm in the long axis and 1.6 cm in the short axis) was noted in the left parasymphysis and body with a large central sequestrum measuring approximately 2.4 × 1.2 cm in the anteroposterior and transverse dimensions. The sequestrum was heterogeneous in appearance with dense peripheral sclerosis [>1,200 HU (Hounsfield units)], an amorphous internal structure (443–1,434 HU), and interspersed osteoporotic densities. The margins of the lesion were distinct, yet irregular and rough. The sequestrum was separated from the underlying basal bone and peripheral alveolus by a homogenous lucent (hypodense) band. There was erosion of the superior cortical outline of the left inferior alveolar canal from the left mental foramen to the mesial aspect of left lower second molar region. There was poor definition of the outline of left mental foramen. A diagnosis of bisphosphonate-associated mandibular osteonecrosis was made based on history and clinical and radiological findings.

The patient was subsequently referred to an oral surgeon for management of the lesion.

Discussion

Bisphosphonates play an important role in bone resorption, inhibit osteoclastic action, have an antiangiogenesis effect, and help to maintain calcium and phosphate equilibrium [1, 3–5]. Inhibition of osteoclast function can also inhibit normal bone turnover such that local microdamage from normal mechanical loading or injury (such as tooth extraction) is not repaired. This may explain the onset of osteonecrosis in our case following tooth exfoliation in the absence of clinically significant predisposing factors. Signs

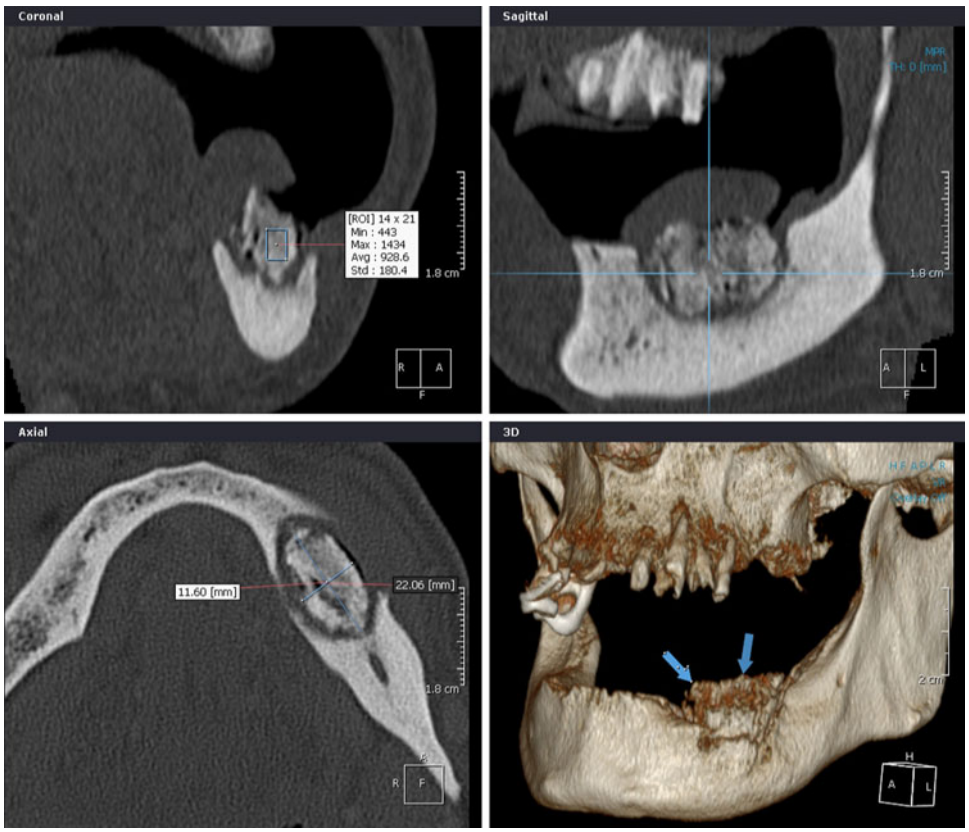

Fig. 3 Multiplanar reformatted and volume-rendered (VR) images show CT HU values of the sequestrum in coronal (*top left*) and sagittal (*top right*) sections. Axial image (*bottom left*) gives dimensions of the peripheral radiolucent rim (approximately 2.26 × 1.16 cm) of the sequestrum. VR image (*bottom right*) provides a 3D view of the sequestered bone in relation to the alveolus

of secondary infection, such as soft tissue induration and necrosis noted at the lesional periphery, may have represented perpetuating factors, resulting in the wide area of involvement noted in the left mandible. The CT HU values of the bony sequestrum were indicative of its poor vascularity; the heterogeneity of HU values noted centrally could suggest the presence of focal abscess pockets and soft tissue due to the secondary infection.

The clinical progression in this case from tooth exfoliation in the mandible to bone biopsy and multiple courses of antibiotics without resolution of exposed bone was similar to that reported by Carneiro et al. [1]. Development of jaw pain, numbness, and extensive mandibular involvement would have resulted with further progression of the lesion.

Clinically, the present case was categorized as stage 2, according to the staging system of Ruggiero et al. [6] and reports by other groups [7, 8], although there was an absence of pain in relation to the exposed bone and associated regional soft tissue inflammatory changes. The history of bisphosphonate use, presence of exposed necrotic bone for more than 8 weeks, and no previous history of radiotherapy of the jaw bones were consistent with typical characteristics of bisphosphonate-associated mandibular osteonecrosis [9].

On cross-sectional imaging (i.e., CT [10]), manifestations of ONJ include increased medullary bone density and thickening and sclerosis of trabeculae, indicating a chronically reduced local blood supply. These changes may be difficult to distinguish from bone changes due to chronic periodontitis or dentoalveolar abscessing. Bone sequestration and periosteal reactions are predominant in advanced stages of the disease. These are manifestations of ischemic or avascular osteonecrosis, which could also be observed with chronic mandibular osteomyelitis. Mucosal involvement in ONJ could be confused with gingivitis or mucositis in the absence of history and clinical radiological examination. The patient history will, in most cases, allow for the exclusion of osteoradionecrosis and even metastatic bone tumors; however, neuralgia-inducing cavitational osteonecrosis (NICO) should be ruled out with history and clinical examination [11]. Radiological features of NICO may show similarities to those of bisphosphonate-associated ONJ [3].

We agree with Chiandussi et al. [2] that CT permits a better corticomedullary differentiation, delineation of cortical involvement, and lesional extent when preceded by conventional (panoramic) radiography suggestive of osteonecrosis.

Advanced imaging with magnetic resonance imaging (MRI) reveals exposed areas of diseased bone as low signals on T1- and T2-weighted images (WI) and relatively lower signals on inversion recovery, suggesting low water content. Unexposed diseased bone appears hypointense on T1WI and hyperintense on T2WI inversion recovery sequences, indicating high water content. Combinations of these two MRI patterns with high water content peripherally and low water content centrally may also be seen [10]. MRI should be considered in cases with extensive soft tissue involvement or where clinical signs of nerve involvement are noted.

Significantly decreased or even absent radionuclide activity on scintigraphy [2] has been reported in the necrotic focus due to decreased metabolism, secondary to the reduced blood supply. Scintigraphy has been recommended as a screening tool to detect subclinical osteonecrosis in patients receiving bisphosphonates, primarily due to limitations of low resolution and the inability to distinguish inflammation from metastases (in late stages of disease).

Management of mandibular osteonecrosis includes systemic or oral antimicrobial use and close follow-up for asymptomatic oral lesions. Preoperative interruption of bisphosphonates for 3 months or longer with or without hyperbaric oxygen therapy has also been recommended [12].

In conclusion, recognition of the typical CT imaging findings presented here is important in considering the possibility of bisphosphonate-associated osteonecrosis when clinically exposed necrotic bone is seen in the mandible. Awareness of the condition among oral radiologists is vital during retrospective, collective assessment of patient history and clinical data to achieve a timely diagnosis when such imaging findings are noted. Additionally, selection of the appropriate imaging modality will be simplified after clinical evaluation.

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