

The importance of Cone-Beam computed tomography in diagnosis of associated mandibular osteonecrosis: case report

A importância da TCFC no diagnóstico e prognóstico da osteonecrose mandibular associada aos bisfosfonatos: relato de caso clínico

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ABSTRACT

The Cone-Beam Computed Tomography (CBCT) is very useful in diagnosis and treatment planning, as well as in the prognosis of osteonecrosis of the jaws. This study reports a clinical case of Bisphosphonate-Associated Mandibular Osteonecrosis from the perspective of CBCT. The patient, female, 83 years old, presented painful symptoms in the posterior region of the right mandible and reported Bisphosphonate medication for more than five years to treat osteoporosis and osteopenia. Based on clinical and CBCT imaging characteristics, the patient was diagnosed with Bisphosphonate-Associated Mandibular Osteonecrosis. Initially, the treatment consisted of oral antibiotic therapy, pain control, hyperbaric oxygenation and oral hygiene (mouthwashes). After 11 months of clinical therapy, CBCT revealed bone reconstruction of the buccal cortex, but also a hypodense imaging in the lingual cortex compatible with bone lysis and bone sequestration. The patient was referred for bone debridement and sequestrectomy. The histopathological diagnosis consisted of osteonecrosis with secondary acute osteomyelitis. After 60 days of the surgical procedure and hyperbaric sessions/systemic antibiotic therapy, an oral healthy mucosa in the region of the right mandibular body was evidenced in the intraoral examination. Cortical bone regeneration was observed on CBCT. Concluded that the use of CBCT, in this case report, makes it possible to estimate the extent of the lesion and the post-treatment outcome, assessing bone density, the presence of bone sequestration and the involvement of the involved areas. In fact, early diagnosis is essential for the success of the therapeutic approach.

Keywords: bisphosphonate, cone-beam computed tomography, mandible, osteonecrosis.

RESUMO

A tomografia computadorizada de feixe cônico (TCFC) é uma importante ferramenta no auxílio do diagnóstico e do plano de tratamento assim como na avaliação do prognóstico da osteonecrose nos maxilares. O presente estudo relata um caso clínico de osteonecrose mandibular associado ao uso de bifosfonatos (BFS) sob a ótica da TCFC. A paciente, 83 anos de idade, apresentava sintomatologia dolorosa na região posterior da mandíbula direita e relatava uso de BFS há mais de cinco anos para tratamento de osteopenia e osteoporose. Com base nos exames clínico e imagiológico da TCFC, foi estabelecido o diagnóstico de osteonecrose mandibular induzida por BFS. Inicialmente o tratamento consistiu em

antibioticoterapia via oral, controle da dor, oxigenação hiperbárica e higienização bucal com uso de colutórios. Após 11 meses de terapêutica clínica, a TCFC revelou a reconstrução óssea da cortical vestibular, mas também uma imagem hipodensa na cortical lingual compatível com lise óssea, bem como a presença de sequestros ósseos. A paciente foi encaminhada para a realização do debridamento ósseo e sequestrectomia. O diagnóstico histopatológico consistiu em osteonecrose com osteomielite aguda secundária. Após 60 dias do procedimento cirúrgico, finalização das sessões hiperbáricas e antibioticoterapia sistêmica, foi evidenciado no exame clínico, uma mucosa oral íntegra na região do corpo mandibular direito. Observou-se nas imagens tomográficas regeneração óssea das corticais. Conclui-se que a utilização da TCFC neste caso clínico revelou o grau de implicação, extensão da lesão, e o desfecho pós-tratamento, avaliando a densidade óssea, a presença de sequestro ósseo e o comprometimento das áreas envolvidas. Diante disto, o diagnóstico precoce é fundamental para o sucesso da conduta terapêutica.

Palavras-chave: bisfosfonato, mandíbula, osteonecrose, tomografia computadorizada de feixe cônico.

1 INTRODUCTION

Osteonecrosis of the jaw (OM) is a rare, severe, difficult-to-treat disease associated with the chronic use of antiresorptive (Bisphosphonates and Denosumab) or antiangiogenic drugs (Bevacizumab) capable of altering bone metabolism and angiogenesis¹. The drug-related OM was defined by the American Association of Oral and Maxillofacial Surgeons (AAOMS) as necrotic bone in the maxillofacial region that persists for more than eight weeks in patients with current or previous treatment for the chronic use of medicines such as Bisphosphonates (BFS) and who do not present a history of head and neck radiotherapy^{2,3}. Its incidence is higher in the mandible compared to the maxilla and in women, since they are more affected by pathologies with bone loss⁴.

Bisphosphonates (BFS) are synthetic and antiresorptive medicines frequently used in the treatment of bone disorders and metastatic malignant disease. They are able to adhere to the bone matrix and cause changes in its remodeling⁴. These drugs have a half-life that can vary from months to years. In this way, they act and accumulate in areas that have a great function in bone formation and resorption, which is the case of the jaws and still have an affinity for hydroxyapatite⁵. According to the AAOMS, Bisphosphonate-Related Osteonecrosis of the Jaw (BRONJ) is classified based on its clinical and radiographic characteristics in stages 0 to 3, which have specific treatment strategies⁶ (Table 1). The objectives of the adopted therapy are to control pain and infection of soft and hard tissues, as well as attenuate their progression and avoid the occurrence of bone necrosis³. Treatment is limited and difficult to resolve, but can be targeted according to each stage of the disease⁵.

In order to obtain a precise surgical planning and evaluate the clinical evolution of the patient diagnosed with BRONJ in relation to the therapeutic strategies used, three-dimensional images obtained by Cone Beam Computed Tomography (CBCT) permits the dental surgeon to measure with relative precision the extension and severity of this bone lesion⁷. The AAOMS states that mandibular osteonecrosis associated with bisphosphonates exhibits signs marked by the presence of alveolar bone resorption and changes in the morphology and density of the trabecular bone⁸. A clinical case of an elderly patient with a diagnosis of mandibular osteonecrosis associated with the use of bisphosphonates from the perspective of CBCT will be described below.

Table 1 - Classification of bisphosphonate-related mandibular osteonecrosis according to the AAOMS

Stages	Clinical and radiographic features	Treatment
Stage 0	No clinical evidence of necrotic bone; Pain (mandibular body, may radiate in the temporomandibular joint region); Presence of periapical fistula without association with pulp necrosis. Radiographic findings: bone loss, trabecular alteration with persistence of unremodeled bone in the sockets of extracted teeth, areas of osteosclerosis involving alveolar bone.	Systemic medication: analgesic and antibiotic therapy; Careful mechanical oral hygiene and chlorhexidine care; Quarterly clinical follow-up; Oral hygiene education and medical review of the indication for continued bisphosphonate therapy. Antibiotic therapy and pain control; Careful mechanical oral hygiene and chlorhexidine care; Superficial debridement.
Stage 1	Exposure of necrotic bone or fistulas in asymptomatic patients with no evidence of infection. Radiographic findings similar to stage 0, located in the region of the alveolar bone. Pain and erythema in the region of exposed necrotic bone, with or without purulent drainage; Fistulas that penetrate the bone structure. Radiographic findings are similar to stage 0. Necrotic bone exposure beyond the alveolar region (inferior border and ramus of mandible, maxillary sinus, and zygoma) which may result in pathological fracture; Intra and extra-oral fistula; oronasal communication; Evidence of infection. Radiographic	Systemic medication: analgesic and antibiotic therapy. Careful mechanical oral hygiene and chlorhexidine care; Quarterly clinical follow-up; Oral hygiene education and medical review of the indication for continued bisphosphonate therapy. Antibiotic therapy and pain control; Careful mechanical oral hygiene and chlorhexidine care; Superficial debridement.

	<p>Findings: Areas of bone lysis may extend to the lower border of the mandible or sinus floor.</p>
<p>Stage 2</p>	<p>Exposure of necrotic bone or fistulas in asymptomatic patients with no evidence of infection. Radiographic findings similar to stage 0, located in the region of the alveolar bone. Pain and erythema in the region of exposed necrotic bone, with or without purulent drainage; Fistulas that penetrate the bone structure. Radiographic findings are similar to stage 0. Necrotic bone exposure beyond the alveolar region (inferior border and ramus of mandible, maxillary sinus, and zygoma) which may result in pathological fracture; Intra and extra-oral fistula; oronasal communication; Evidence of infection. Radiographic Findings: Areas of bone lysis may extend to the lower border of the mandible or sinus floor.</p> <p>Systemic medication: analgesic and antibiotic therapy. Careful mechanical oral hygiene and chlorhexidine care; Quarterly clinical follow-up; Oral hygiene education and medical review of the indication for continued bisphosphonate therapy. Antibiotic therapy and pain control; Careful mechanical oral hygiene and chlorhexidine care; Superficial debridement.</p>
<p>Stage 3</p>	<p>Exposure of necrotic bone or fistulas in asymptomatic patients with no evidence of infection. Radiographic findings similar to stage 0, located in the region of the alveolar bone. Pain and erythema in the region of exposed necrotic bone, with or without purulent drainage; Fistulas that penetrate the bone structure. Radiographic findings are similar to stage 0. Necrotic bone exposure beyond the alveolar region (inferior border and ramus of mandible, maxillary sinus, and zygoma) which may result in pathological fracture; Intra and extra-oral fistula; Oronasal communication; Evidence of infection. Radiographic Findings: Areas of bone lysis may extend to the lower border of the mandible or sinus floor.</p> <p>Antibiotic therapy and pain control; Careful mechanical oral hygiene and chlorhexidine care; Debridement and/or surgical resection.</p>

Source: CORDEIRO; GOTTARDO, 2018⁵; VETTORI et al, 2021⁶.

2 CLINICAL CASE DESCRIPTION

Diagnosis

A 71-year-old female patient with leukoderma sought dental service complaining of pain and a wound in the region of the right mandibular body that persisted for more than ten weeks with gradual evolution, however the patient does not know the time of evolution precisely. The medical history revealed renal failure, mild anemia and use of oral drug therapy of Bisphosphonates (BFS) for the treatment of osteopenia and osteoporosis for more than five years. In the intraoral examination, the patient was completely edentulous in the upper arch and with free ends in the lower arch. It was also verified that the patient used upper removable complete dentures and lower removable partial dentures. It was observed that the prosthesis was old and poorly adapted in the lower right hemiarch, showing an extensive erythematous area with mucosal ulceration and exposure of necrotic bone. There was drainage of spontaneous purulent secretion and pain in this region.

On panoramic radiography, periosteal hyperplasia of the alveolar bone crest was observed with a poorly defined radiolucent image in the right posteroinferior region, with central radiopaque sequestration (Figure 1). In the CBCT scan, the axial section revealed an image of bone lysis on the lingual and buccal aspect of the right mandibular body with cortical involvement and the presence of bone sequestration. There were areas of gaseous content suggestive of an active infectious process (Figure 2).

Based on clinical, imaging and histopathological examinations, the diagnosis of osteonecrosis induced by prolonged use of BFS was established.

Treatment Plan. Treatment Progress/Outcome.

The patient was referred for 40 sessions of hyperbaric oxygen, this procedure being daily. For three months, she used oral antibiotic Bactrim F800mg / 160mg every 8 hours associated with a mouthwash with 250mg metronidazole oral solution twice a day, in addition to monitoring of oral hygiene, and use of 0.12% chlorhexidine-based mouthwash twice a day for 15 days. The follow-up, through tomographic images visualized in the axial, sagittal and 3D reconstruction cuts, proved that after six months of clinical treatment there was a process of bone regeneration of the vestibular cortical bone. In the axial cuts, irregular and discontinuous areas were also observed in the lingual cortex of the right mandibular arch (Figure 3).

Eleven months after the beginning of treatment, a new CBCT was performed showing images in the axial cut of a hyperdense area compatible with the reconstruction of the buccal cortex, but showing a loss of bone periosteum in the lingual cortex. In the sagittal view, an

important loss of bone mass with the presence of bone sequestration can be observed (Figure 4). In view of these imaginological findings, there was a suspicion of diagnosis of osteomyelitis resulting from osteonecrosis. Debridement of necrotic bone tissue and surgical removal of areas of bone sequestration were performed until the visualization of healthy bone. There were no reports of pain or postoperative complications. After the surgical procedure, the patient was instructed on oral hygiene protocols as well as the use of Cephalexin 500 mg every 6 hours and metronidazole 250 mg orally every 8 hours for fifteen days, and she was also referred for another 40 sessions of hyperbaric oxygenation.

The pathological examination consisted of a fragment, 0.7x0.4x0.2, hardened, irregular and brownish. It presented sections composed of irregular bone masses with empty osteoplasts and medullary canals also empty or filled with bacterial colonies. A mild to moderate acute inflammatory infiltrate was also noted. Bacterial colonies surrounded the bone mass, which showed frequent surface bone resorptions. No fungi were observed (GROCOTT with positive control). The histopathological diagnosis consisted of osteonecrosis with secondary acute osteomyelitis.

After 60 days of the surgical intervention and after the hyperbaric sessions and systemic antibiotic therapy, an intact oral mucus in the region of the right mandibular body was evidenced in the clinical examination. In the panoramic view, the absence of all areas of radiopacity with extension to the areas of radiolucency was observed (Figure 5).

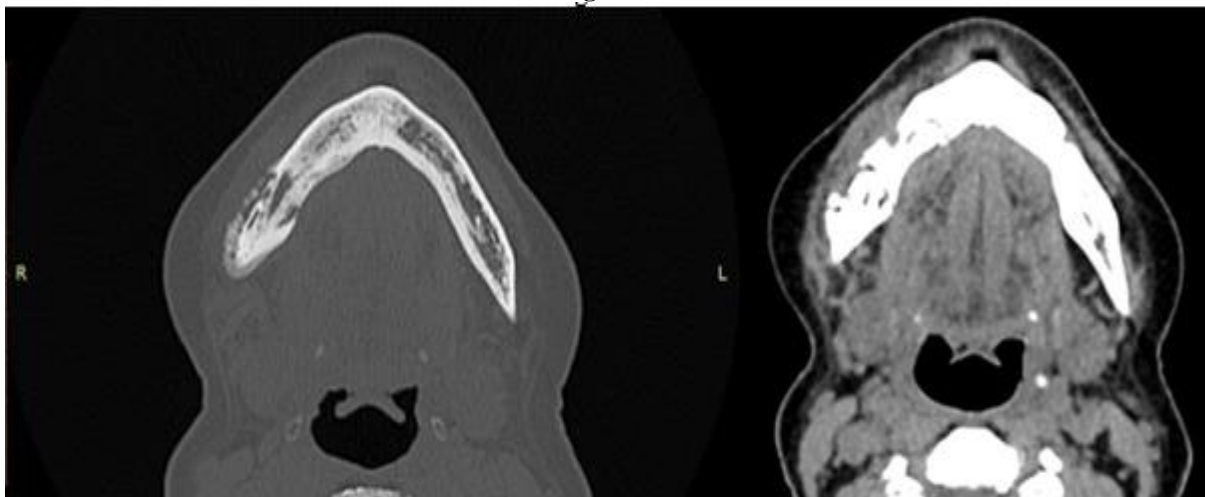
Figure 1





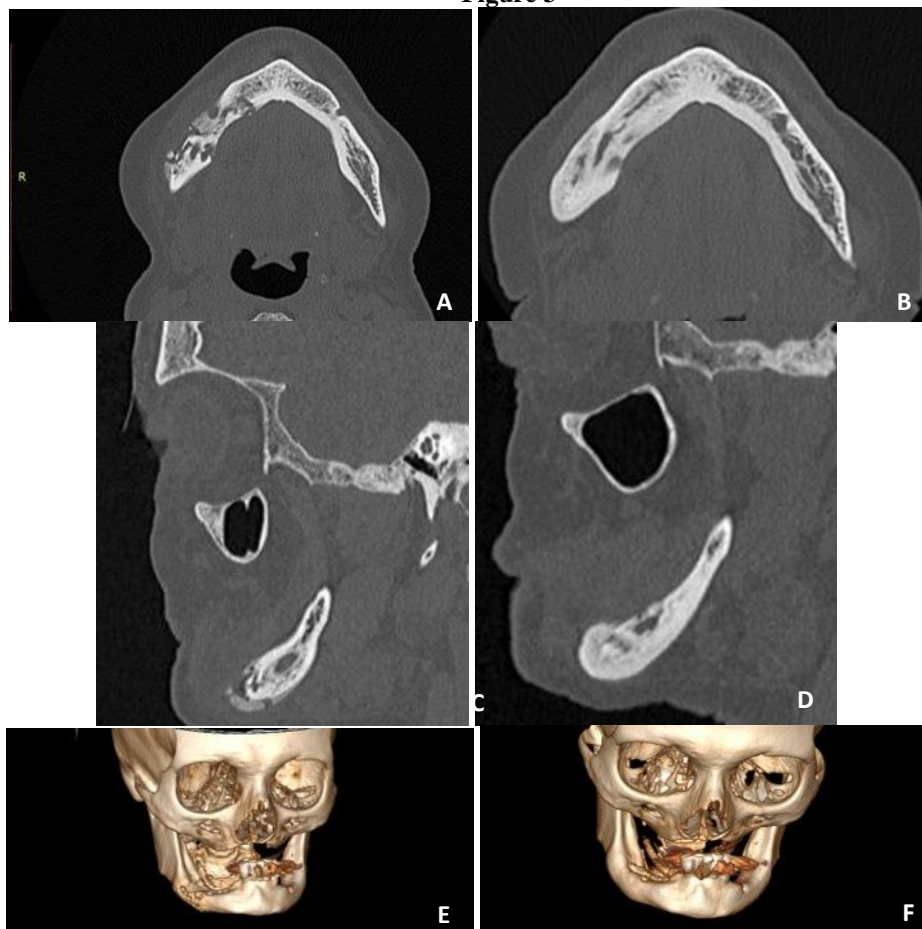
The initial intraoral photographs of the 71-year-old patient revealed a lesion with an ulcerated appearance, with exposure of necrotic bone in the right postero-inferior region. The initial panoramic radiograph showed the total absence of the upper and postero-inferior dental units. Periosteal hyperplasia of the alveolar bone crest is observed with a poorly defined radiolucent image and central radiopaque sequestrums in the region of the right mandibular body.

Figure 2



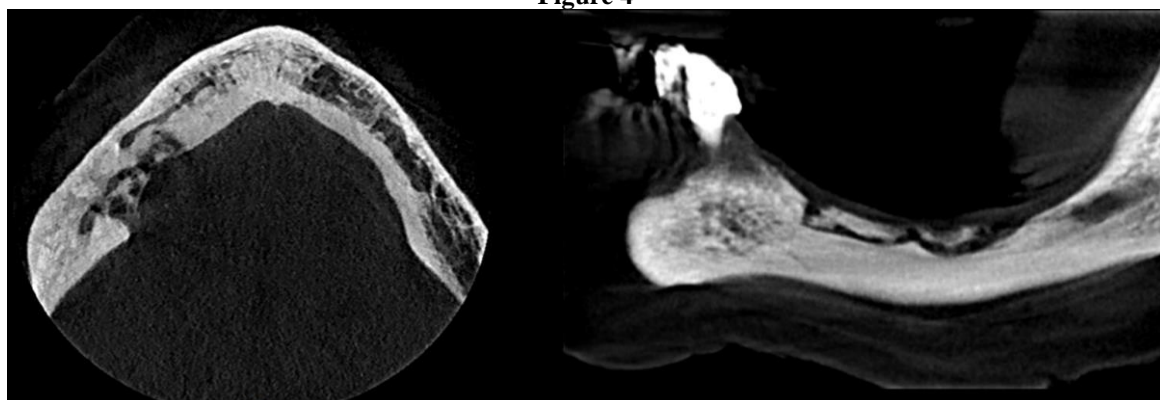
Initial tomographic images of the same patient. Axial sections reveal the presence of an ill-defined area of bone lysis on the buccal and lingual surface of the right posteroinferior region, with small bone sequestrum and cortical bone involvement. Areas of gaseous content are noted, indicating an active infectious lesion.

Figure 3



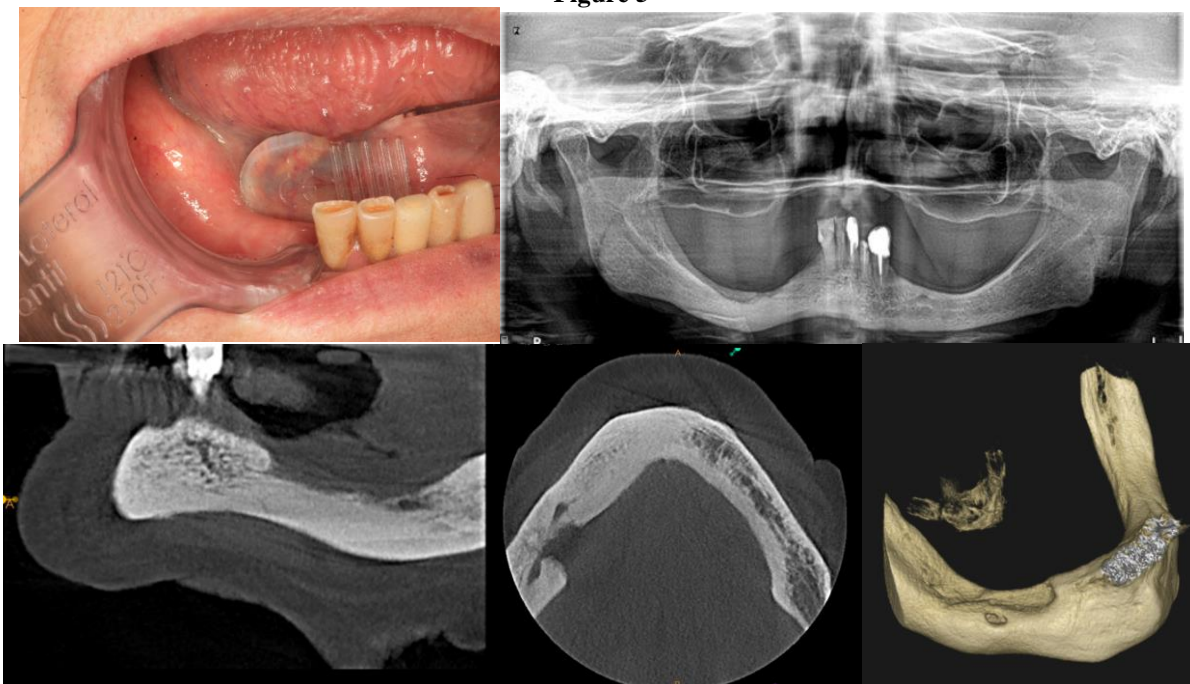
Comparison of tomographic images before and after six months of clinical treatment in axial (A and B), sagittal (C and D) and 3D reconstruction (E and F) sections, respectively, of the right mandibular body region.

Figure 4



Tomographic image after 11 months of clinical treatment of the same patient. In the axial section, it is noted that despite the bone reconstruction of the buccal cortex, the hypodense image in the lingual cortex is compatible with bone lysis. The sagittal section shows the presence of bone sequestration

Figure 5



Intraoral photograph of the patient 60 days after surgical treatment revealed intact oral mucosa of the right mandibular body. Panoramic radiography reveals the absence of areas of radiopacity extending to the radiolucent area in the right mandibular body. Tomographic images show a process of bone reconstruction of the lingual cortex in sagittal and axial sections and 3D reconstruction, respectively.

3 DISCUSSION

The Bisphosphonate-Associated Osteonecrosis of the Jaws (BRONJ) is a rare condition in patients with osteoporosis resulting from cumulative doses of bisphosphonate for a long period of oral use⁹. In the present clinical case, the patient had been using antiresorptive medication for more than five years as a treatment protocol for osteoporosis and osteopenia when she was diagnosed with BRONJ. In contrast to cancer patients who use this medication intravenously and are more susceptible for a shorter period of time for BRONJ to appear⁹. According to the American Association of Oral and Maxillofacial Surgeons¹⁰, the BRONJ classification can be defined in three stages: Stage I, asymptomatic necrotic bone exposure; Stage II, bone necrosis with exposure, pain, and infection; Stage III, bone necrosis with exposure, pain, infection, and pathologic fractures or skin fistulas. The patient in this report was diagnosed with BRONJ stage II due to painful symptoms, secondary infection and lesion with bone exposure in the region of the right mandibular body that persisted for more than eight weeks. It was found that it is in agreement with the scientific findings that point to the mandible as an area frequently affected, with females being the most affected.

Trujillo et al.¹¹, in a literature review, reported that imaging studies obtained by panoramic radiographs and Cone Beam Computed Tomography (CBCT) are important in the

evaluation of the initial signs of osteonecrosis of the jaws, with a focus on prevention. CBCT reveals in detail imaginological signs such as: change in thickness and mineral content of trabecular bone, formation of micro gaps, cortical bone erosion, osteosclerosis, small (less than 15 mm) or extensive (more than 15 mm) sequestration and presence of bone new periosteal^{8,11,12}. Corroborating with the literature, it was possible to assess the severity and extent of the bone lesion in the right mandibular body of the present case by the initial tomographic images that revealed the presence of poorly defined bone lysis on the buccal and lingual surface, with small bone sequestration and involvement of the bone corticals.

According to Ogura et al.⁷, the information obtained in the diagnosis aided by the CBCT exam, allow a better elaboration of the surgical planning. In consensus in the literature, the treatment of osteonecrosis depends on the stage of the pathology and can be performed conservatively or through surgical intervention, which group includes intact bone debridement¹³. Thus, in the present case, through the tomographic images visualized in the axial, sagittal and 3D reconstruction cuts, it was proved that after eleven months of clinical treatment there was a process of bone regeneration of the vestibular cortical bone, but an irregular hypodense suggestive image of bone lysis was also noted in the lingual cortex of the right mandibular body, as well as the presence of bone sequestration. In view of these imaginological findings, a surgical plan was adopted to remove the necrotic bone, through bone debridement, which favored healing and tissue re-epithelialization, ensuring a good prognosis. The importance of CBCT in the longitudinal follow-up after treatment of bone lesions has been highlighted in the literature. The observation of possible bone alterations such as: neof ormation, bone sequestration, bone density and the measurement of cortical thickness are elements for the prognosis of the adopted therapy^{8,14}. In this context, it can be observed in the tomographic images, 60 days after the surgical treatment of the present clinical case, the process of bone reconstruction of the right mandibular body.

According to a randomized clinical trial with 46 patients who used hyperbaric oxygenation (HBO) as a therapeutic alternative for BRONJ associated with antibiotic therapy and surgical intervention, stimulation of angiogenesis and bone tissue repair by means of reactive species of oxygen and nitrogen production were observed¹⁵. A similar effect was observed in the present clinical case, where after the use of HBO associated with antibiotic therapy and surgical intervention, there was regeneration of the alveolar bone cortical and absence of pain. Beth-Tasdogan et al.¹⁶, in a systematic review, shows that the trial by Freiburger et al. has low quality and high risk of bias, compromising the results. Another systematic review of 19 articles covering 400 patients highlights that treatments based on ozone,

Debridement/Biostimulation with laser therapy and laser surgery showed good results, different from those obtained with HBO therapy in 10 patients. However, in a cohort study, Watanabe et al.¹⁷ analyzed subgroups of patients diagnosed with stage 2 of the disease and visualized a positive therapeutic effect of hyperbaric oxygenation before and after surgery, as in the present clinical case. However, as it was performed in a single center and is retrospective in nature, this study has limitations that impact the quality of its evidence. Therefore, even with the good prognosis of the case where HBOT was used adjuvant to other therapeutic alternatives, further research is needed with a double-blind, randomized, multicenter, clinical trial design for a more accurate and unbiased analysis of the real therapeutic effect of HBO.

4 CONCLUSION

In view of the above, this case report suggests that the images obtained by means of CBCT allowed us to assess the severity and extent of the BRONJ and contributed to the choice of OHB therapy OHB therapy before and after surgery associated with antibiotic therapy and rigorous oral hygiene. Therefore, CBCT is an important tool in aiding treatment strategies, evolution and prognosis.

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