

## Osteosarcoma of the jaw: diagnosis and treatment challenges

### *Osteossarcoma de mandíbula: desafios do diagnóstico e tratamento*

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#### ABSTRACT

**Introduction:** Osteosarcoma is a primary malignant bone tumor most commonly found in long bones. However, in the oral cavity it mainly affects the ramus and angle of the mandible.

**Objective:** To present a case of osteolytic osteosarcoma of the mandible and discuss the difficulties of diagnosis and treatment.

**Case Report:** A 22-year-old white female patient, non-smoker and non-drinker attended the stomatology service with complaints of increased volume on the right side of the mandible, exhibiting premolar and molar mobility in that area. Periapical and occlusal radiographs were performed and showed presence of radiolucent area and floating teeth, confirmed by a panoramic radiography showing involvement of the mandibular ramus. Two biopsies were performed in the region with inconclusive results for malignancy. The diagnostic hypothesis was osteosarcoma. A CT scan showed bone loss, floating teeth and involvement of areas adjacent to the tumor lesion and lymph nodes. The patient was referred to the oncology hospital and a frozen section biopsy was conclusive for osteosarcoma, with removal of the base and most of the right and left mandible ramus, followed by reconstruction with titanium plate. The tumor recurred and a new surgery, radiotherapy and chemotherapy were performed in an attempt to improve the clinical condition, with failure and death after four years of initial diagnosis and tumor mutation for rhabdomyosarcoma.

**Conclusion:** Imaging and even histopathological outpatient exams were not able to promote the final diagnosis of osteosarcoma, impairing treatment and favoring recurrence and patient death.

**Keywords:** Osteosarcoma. Bone tumor. Diagnostic imaging.

#### RESUMO

**Introdução:** O osteossarcoma é a neoplasia óssea maligna primária mais encontrada em ossos longos, porém na cavidade bucal atinge mais o ramo e ângulo da mandíbula.

**Objetivo:** O objetivo deste trabalho é apresentar um caso clínico de osteossarcoma osteolítico de mandíbula e discutir as dificuldades de seu diagnóstico e tratamento.

**Caso clínico:** Paciente do sexo feminino, 22 anos de idade, leucoderma, não fumante e não etilista compareceu ao serviço de Estomatologia com queixa de aumento de volume na mandíbula, do lado direito e mobilidade dos dentes pré-molares e molares na região. Foram realizadas radiografias periapicais e oclusal que demonstraram presença de área radiolúcida e dentes flutuantes, confirmada no exame radiográfico panorâmico com envolvimento de ramo da mandíbula. Foram feitas duas biopsias na região, inconclusivas para malignidade. A hipótese diagnóstica foi de osteossarcoma. A tomografia computadorizada demonstrou perda óssea, dentes flutuantes e envolvimento de áreas adjacentes à lesão tumoral e linfonodos. A paciente foi encaminhada ao hospital oncológico e a biopsia por congelação foi conclusiva de osteossarcoma, com remoção da base e grande parte do ramo da mandíbula do lado direito e esquerdo e reconstrução com placa de titânio. Houve recidiva e nova cirurgia, radioterapia e quimioterapia na tentativa de melhorar o quadro clínico, com insucesso e óbito após quatro anos do diagnóstico inicial e mutação tumoral para rhabdomyosarcoma.

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**Conclusão:** Conclui-se que os exames imaginológicos e mesmo histopatológico ambulatoriais não foram capazes de promover o diagnóstico final do osteossarcoma, comprometendo o tratamento, favorecendo a recidiva e óbito da paciente.

**Palavras-chave:** Osteossarcoma. Neoplasias ósseas. Diagnóstico por imagem.

## INTRODUCTION

Osteosarcoma (OS) is the primary malignant bone tumor. It is commonly found in long bones. However, maxilla and mandible lesions are rare, comprising 6–9% of cases and 23% of total head and neck tumors.<sup>1</sup> OS affects 0.7 people per million and most often affects the ramus and/or condyle of the mandible.<sup>2</sup>

Among the suggested causes, about 10% are caused by radiation. Other risk factors include hereditary retinoblastoma, Paget's disease of bone, fibrous dysplasia or local trauma. The age range of commitment of OS of mandible is 10–20 years later than of long bones. In addition, there are geographic differences in OS prevalence, for example, younger patients (mean age of 27.2 years) have the osteogenic type of OS in the mandible in Africa and Shanghai.<sup>2,3</sup>

The most frequent clinical manifestations are pain, edema in the compromised bone area and surrounding tissues, mobile teeth, trismus, paresthesia, face asymmetry, absence of scarring and abrupt swelling after tooth extraction and dental treatments.<sup>1,2,3,4,5,6,7</sup> Osteosarcomas of the mandible have a different biological reaction from other sites, with less metastases, despite frequent recurrence.<sup>1</sup>

Diagnosis based on panoramic radiographs is insufficient and inconclusive, since they only allow the observation of benign or malignant aspects of bone lesions. Bone remodeling patterns, cortical bone resorption and floating teeth in the radiolucent mass are parameters that can provide diagnostic hypotheses of malignancy, along with the development time. Effectively, the radiographic aspect of the osteosarcoma of the mandible can be identified

by bone formation and mineralization or destruction or even by the periosteal response. ACT scan is of great importance in the diagnosis of distant metastases. Additionally, an MRI shows the extent of lesions and infiltration in adjacent soft tissues.<sup>1,5</sup> The final diagnosis must be histopathological and is often impaired in an ambulatory basis, due to presence of large areas of tissue necrosis; thus, requiring the collection of material in a surgical center (frozen section biopsy procedure).<sup>1,5</sup>

The treatment of choice of these tumors is surgical, since they do not respond positively to chemotherapy and radiotherapy, and their metastases are rare and late. Early recurrence is likely at the same site, reaching surrounding tissues with rapid and highly destructive development.<sup>4,6,7</sup> Prognosis depends largely on the total excision of the lesion and negative limits in radical surgery.<sup>7</sup> These tumors are difficult to treat due to the aggressive growth of the lesion and late diagnosis (4–6 months of development).<sup>8</sup> Knowledge and early diagnosis are essential for better conditions of the surgical treatment and patient survival.<sup>4,8</sup>

Based on previous data, this study presents a case of osteosarcoma of the mandible with an osteolytic pattern and discusses the diagnostic difficulties and recommended treatments concerning patient survival.

## CLINICAL CASE

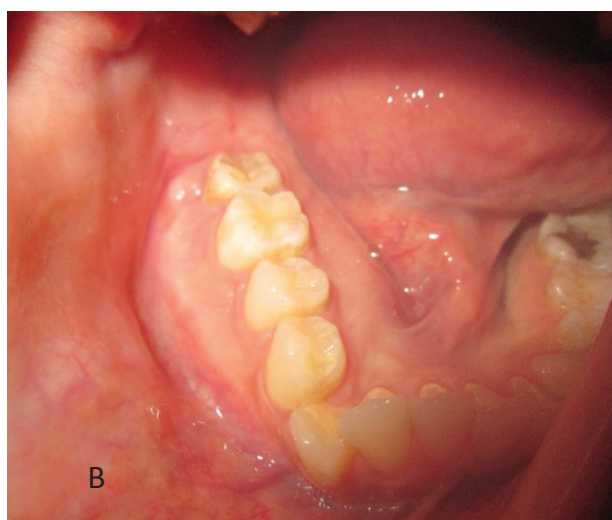
In agreement with resolution 466/2012 of the National Council of the Ministry of Health and Declaration of Helsinki, the patient signed a Statement of Informed Consent.

A 22-year-old single white female, non-smoker and non-drinker patient attended the

Stomatology Service – Lins – São Paulo – Brazil complaining of persistent swelling in the region of the right lower gum and teeth mobility in the affected area. The incident occurred after extraction of tooth 48, two months earlier. The patient had undergone treatment with antibiotics; but no improvement was noticed. The patient showed no systemic disease. Hypertension, heart disease and diabetes mellitus were reported in the family history; however, no cases of carcinoma were identified.

Clinical examination was normal, with a slight overweight and swelling in the right

mandibular, submandibular and submental area. Intrabuccally, a discreet reddish color and slight swelling were observed in the alveolar ridge from the canine to the lower right second molar teeth, with sharp and irregular edges, painless and no exuding or bleeding gums. Mobility of teeth 44 to 47 were observed with crepitus at palpation. The patient complained of pain in the upstream region of the right mandible (Figure 1A and B). Right submandibular lymphadenopathy with chronic aspect was noticed. Blood pressure and blood glucose were within normal parameters.



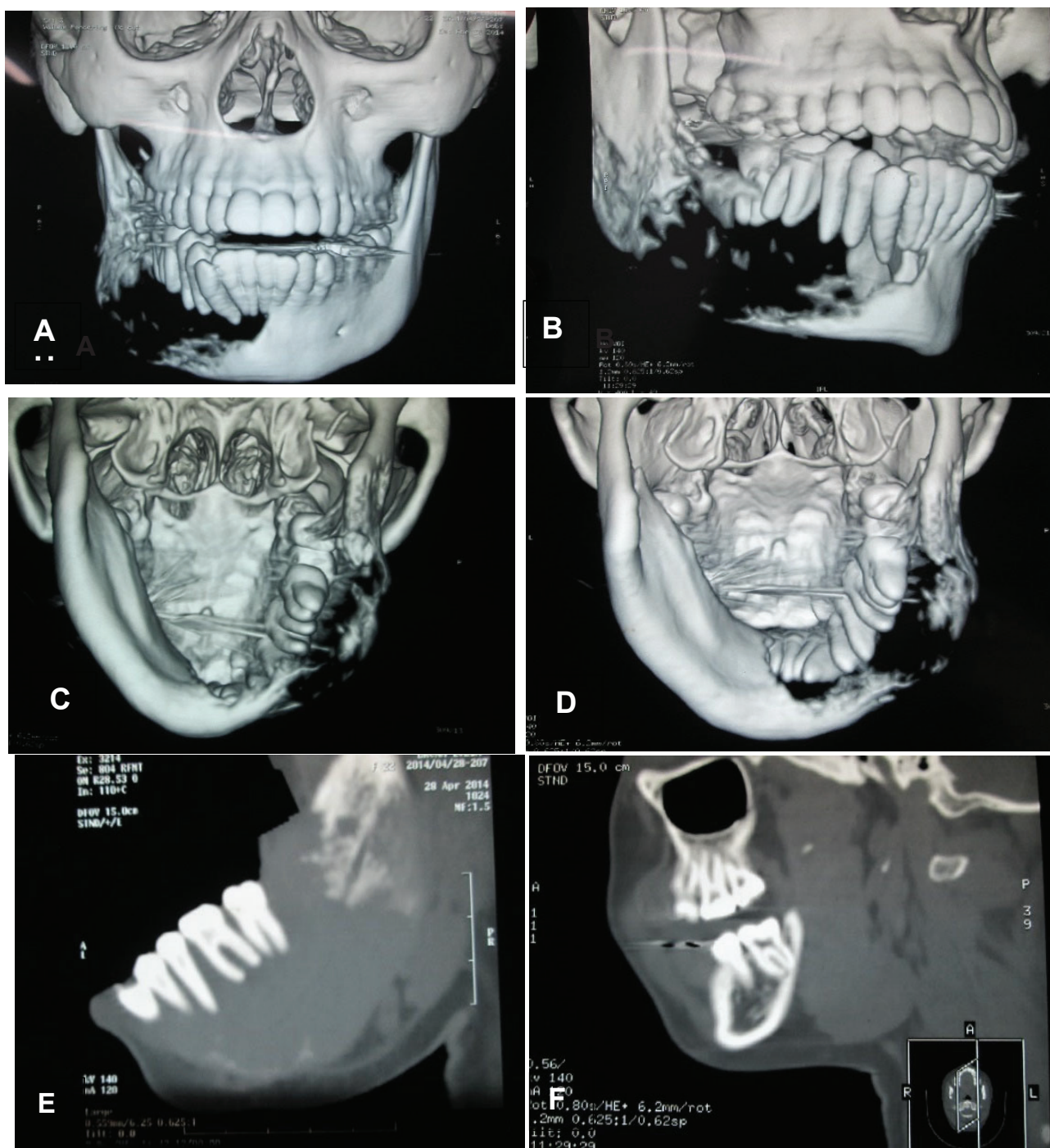
**Figure 1A** – Swelling of right mandible, submandibular and submental region. **B** – Clinical intraoral aspect of lingual-vestibular expansion of alveolar bone with no exuding or bleeding.

Periapical radiographs showed disappearance of the cortical of teeth 44 to 47, floating amid the radiolucent area advancing to the missing tooth area with irregular and invasive edges. The occlusal radiograph showed destruction of the outer and inner cortical of mandible and alveolar ridge. The initial hypothetic diagnosis was osteosarcoma.

The patient underwent a biopsy of the alveolar ridge region, which showed negative for malignancy. Subsequently, a CT scan was performed (Figures 2 to 4).

A new biopsy was performed in order to determine the final diagnosis, also inconclusive. The patient was referred for cancer treatment. However, she was treated for four months only, due to administrative health insurance issues. The histopathological frozen section diagnosis was osteolytic osteosarcoma. Tumor removal and reconstitution with titanium plate were performed in an oncology hospital.

Other recurrences of the lesion and subsequent metastases in the mandible, maxillary sinus, retromandibular region occurred, affecting facial tissues and lungs. The patient underwent radiotherapy and



**Figure 2.** A–F, CT scan of different sections with and without contrast, showing tumor mass with destruction of ramus and base of mandible. D shows floating teeth.

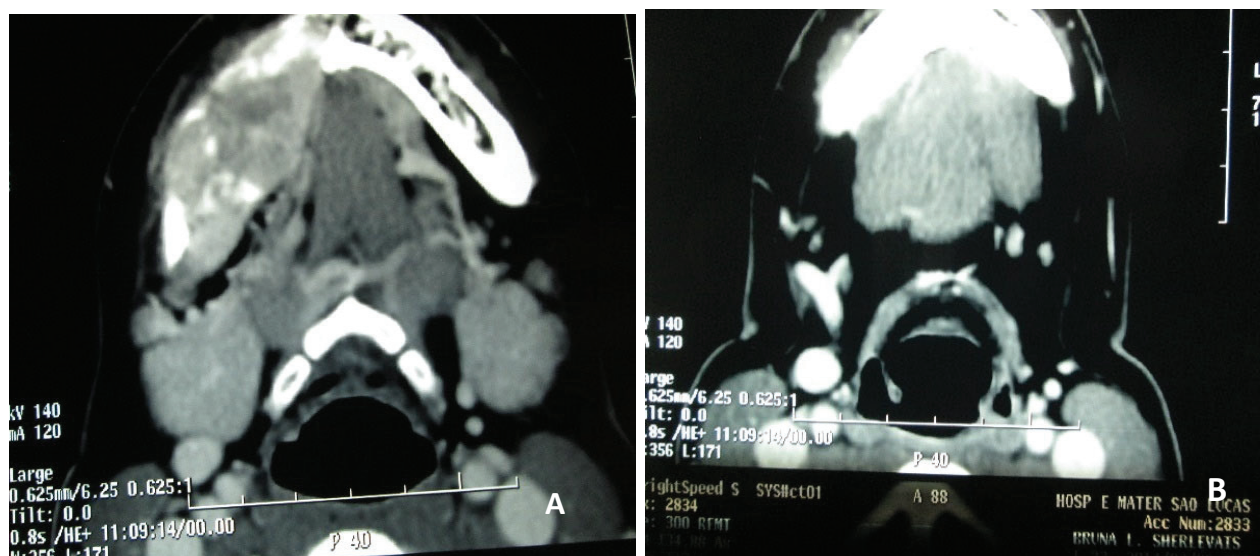


Figure 3. A–B – Metastatic lymphadenopathy.

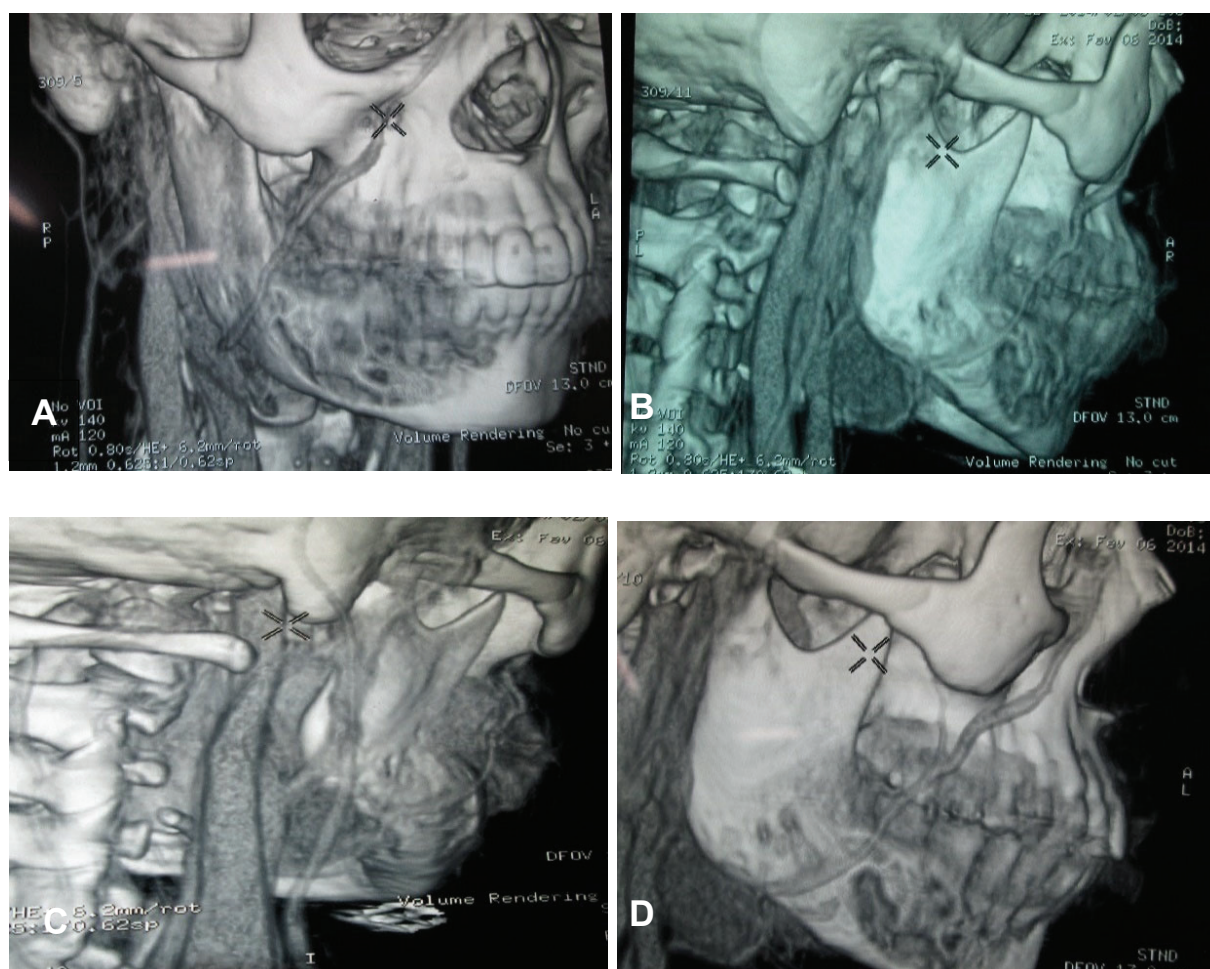
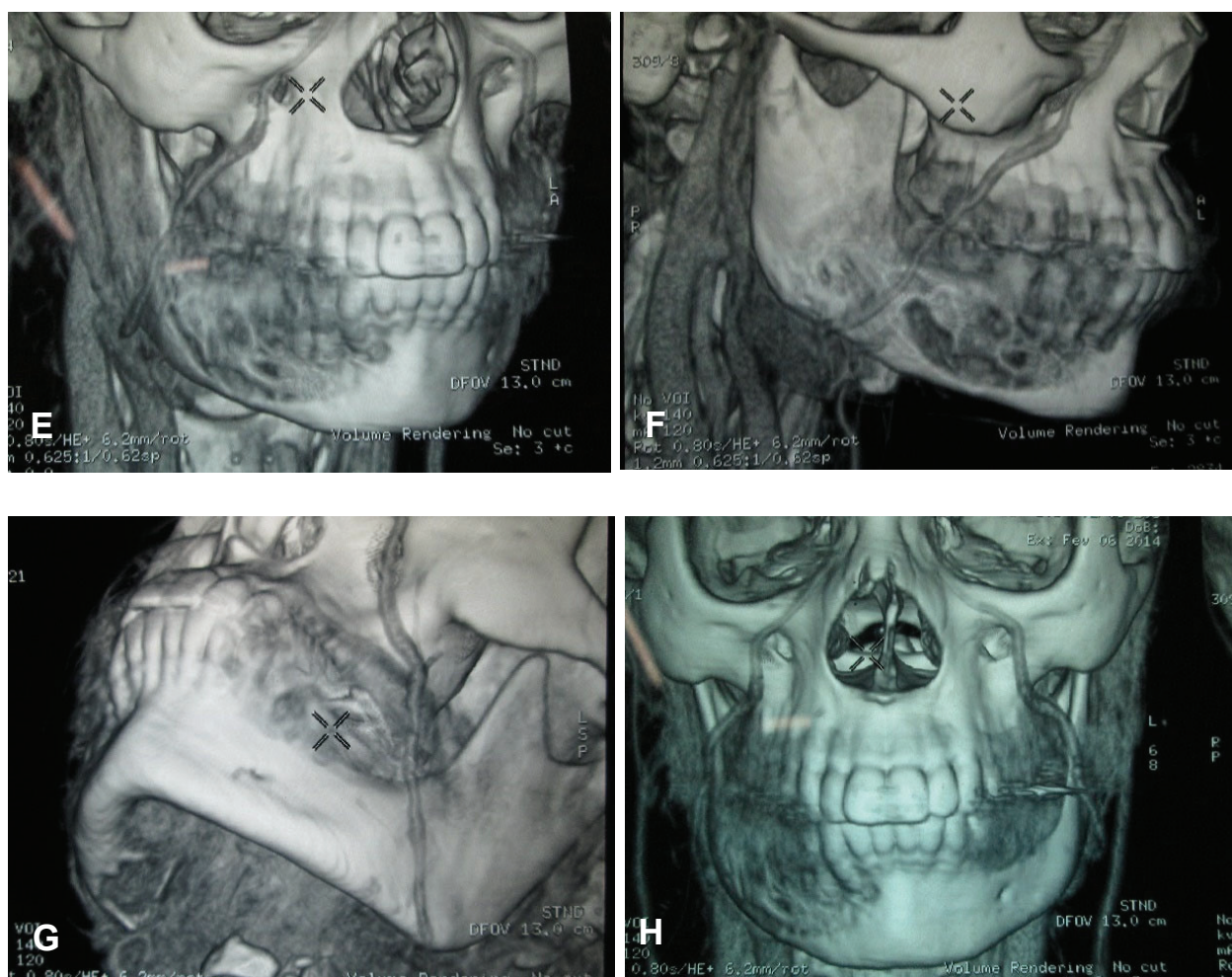


Figure 4. A–H. Tomographic sections showing involvement of areas adjacent to tumor area.



**Figure 4. A-H.** Tomographic sections showing involvement of areas adjacent to tumor area.

chemotherapy in an attempt to improve the clinical condition, with no success and death after four years of initial diagnosis. The tumor lesion mutated to a rhabdomyosarcoma, extending to all the right hemi-face.

## DISCUSSION

Osteosarcoma is a mesenchymal and malignant bone tumor, common in long bones, around the second decade of life. Nevertheless, it is rare in head and neck bones, affecting nearly 10% of malignant tumors with incidence in older age groups, that is, around the third to fifth decades of life.<sup>7</sup> Osteosarcomas occur predominantly in males;<sup>9</sup> however, they can

be found in the mandible in women.<sup>10</sup> The incidence peak is 29.7 years in facial bones, superior in the case presented.<sup>11</sup>

The causes and biological behaviors of osteosarcomas are inaccurate, since there is no experimental model to elucidate the development mechanism and tumor progression.<sup>4</sup> The reported causes have been genetic-related diseases,<sup>12</sup> trauma, periapical lesions,<sup>5</sup> radiation, or other diseases such as Paget's disease of bone or fibrous dysplasia.<sup>13</sup> OS has also been described after tooth avulsion,<sup>5</sup> as in the present case, which could possibly be the triggering stimulus for tumor growth, since other causes were not observed.

The clinical findings were swelling of the right mandibular bone, tooth mobility in the posterior region of the mandibular base, no complaint of paresthesia or pain after third molar avulsion, approximately 60 days after surgery. These findings allow questioning whether the malignant lesion was installed previously or occurred after the trauma. Other causes have been described, associated with periapical pathologies, odontogenic lesions, edema, pain, tooth mobility, poorly adapted prosthesis and paresthesia, however, they are not related to the tumor identified in the present study.<sup>5</sup>

Radiographic or imaging exams act as a valuable tool in the diagnosis of bone tumors, since clinical behaviors, as mentioned above, are not specific. The correlation between radiological and imaging findings along with histopathological analysis is of great importance to define the type of mesenchymal tumor and its extension<sup>11</sup> and to classify the type, i.e., with destruction named osteolytic or with bone formation named osteogenic (formation of sunrays, common in maxillary bones).<sup>11</sup> Lee et al (1988)<sup>14</sup> reported that the presence of osteolytic osteosarcomas in the craniofacial area, therefore in the mandible, often occur after irradiation. These authors reported four cases of the osteolytic type involving the mandible, all with involvement of adjacent soft tissues, swelling, usually painless and no lymphadenopathy. However, only imaging exams were inconclusive, but demonstrated destruction pattern compatible with the described pathology.<sup>8</sup> Similarly, these image exams suggested a mesenchymal tumor and sarcoma lineage, although the final diagnosis is necessarily done by histopathologic evaluation. In the present case study, two biopsies were inconclusive for malignancy because amid the tumor area there was a large amount of necrotic tissue.<sup>10</sup> Thus, it was difficult to collect material for the histopathological exam, as it is obtained by frozen section biopsy procedure, or even

after removal of the surgical piece, unlike the osteogenic type, which besides typical imaging aspects, also allows the performance of a biopsy enabling a final diagnosis.<sup>14</sup>

The computed tomography (CT) scan allowed us to assess the degree of involvement of bone tissue and adjacent structures, but was not conclusive.<sup>16,17</sup> The need to perform the biopsy in the operating room became paramount in this case. A CT scan is able to contribute and simplify the final histopathological description. Furthermore, the CT scan is an effective resource in the definition of morphological changes caused by benign and malignant tumors, showing the relationship between the tumor and adjacent tissues. Unfortunately, bureaucratic and administrative medical-hospital agreement issues hindered the patient referral. It took four months for the service to be authorized, which favored tumor progression to adjacent areas and lymph nodes and decreased the patient's survival time.<sup>18</sup>

OS is considerably diverse in characteristics and histologic grades but has a better prognosis when diagnosed early.<sup>8</sup> In the early stage of the disease, a slight and less aggressive bone increase is clinically identified; however, it becomes more invasive and malignant in the second stage, when a precise diagnosis is a challenge.<sup>10</sup> Mistaken diagnoses often lead to delay in the recognition and treatment of this tumor.<sup>18</sup> Thus, prognosis is more satisfactory when combined with a more appropriate treatment, otherwise, there may be an advance in the affected area and an effective treatment is more difficult.<sup>16</sup>

Regarding the histopathologic aspects, it is observed that dealing with maxilla-mandibular osteosarcoma, most are of osteoblastic origin, with limited cytologic atypia in well-differentiated lesions and large osteoid matrix deposition.<sup>4</sup> In the present case, the histopathological findings were compromised by the lack of access to the

material removed in the hospital environment and a non-descriptive report, defining it only as osteolytic pattern. The histopathological aspects in this type of osteosarcoma were ineffective in the literature.<sup>4,14,15</sup>

Another challenge is the treatment of these bone tumors, since they tend to recur locally.<sup>4</sup> The initial treatment is surgical resection with clear margins, which was not possible in the present case study, in view of the involvement of adjacent and muscle tissues and even maxilla.<sup>19</sup> Positive or negative margins in hemi-mandibulectomy can determine variable prognosis and survival.<sup>19</sup> Subsequent radiation therapy, although recommended by some,<sup>20</sup> does not always produce the expected results positively, as happened in this case. Best survival is observed when radiation therapy is adopted in long bone tumors. Osteosarcomas are considered radio-resistant and application of radiation therapy should be limited to cases where the surgical margins are committed, justifying its use.<sup>7</sup>

Chemotherapy, following the poor response to radiotherapy, was an attempt to minimize the tumor development and prevent lung metastases.<sup>7</sup> As previously mentioned, the role of chemotherapy and radiation therapy is uncertain in gnathic osteosarcomas and chemotherapy has been associated with increased tumor, which may have happened in this case.<sup>7,14</sup> Thus, prognosis and survival are considered more favorable when treatment is surgical resection with clear margins in relation to radiotherapy or chemotherapy sessions adopted as part of the treatment.<sup>14,20</sup> Prognosis is poor in case of recurrences and metastases, which reduce patient's survival time. In the present case, radiotherapy and chemotherapy were not effective and promoted tumor mutation to a rhabdomyosarcoma, which involved all the hemi-face and along with pulmonary metastasis was the cause of death, after four years of diagnosis. Data show that the survival rate of

patients with osteosarcoma has not changed over the last 40 years; therefore, there is an imminent need for more effective therapeutic approaches.<sup>21,22</sup>

## CONCLUSION

Considering that the osteolytic osteosarcoma rarely manifests in the oral cavity, imaging and even histopathological outpatient exams were not able to promote the final diagnosis of osteosarcoma, compromising the surgical, radio and chemotherapy treatments, thus favoring recurrence and patient death.

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