


## Oral metastasis intraosseous mimicking periapical lesion: a case report

### Metástase oral intraóssea mimetizando lesão periapical: um relato de caso

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#### ABSTRACT

Jaw metastasis can be mistaken for inflammatory or infectious diseases. Then, they should be considered in the differential diagnosis of unknown jaw lesions. Study reported here involved metastasis of breast cancer in the mandible of a 45-year-old woman. The most important differential diagnostic was a reactive lesion in an unusual periapical location associated with a nonvital tooth. However, given patient's medical history and because paresthesia and pain were observed a few days after pulpectomy, metastasis of breast cancer could not be ruled out. When bone scintigraphy suggested the metastasis of a malignant bone tumor, incisional biopsy was performed. Histopathologic examination and immunohistochemical reaction confirmed the diagnosis of metastasis of breast cancer, and chemotherapy was thus performed as well. Unfortunately, patient died 2 years after diagnosis. Dentists as well as general physicians should therefore consider presence of oral metastasis in cases involving atypical symptoms, especially in patients with known malignant disease.

**Keywords:** Breast cancer, Oral metastasis, Periapical lesion.

#### RESUMO

*As metástases mandibulares podem ser confundidas com doenças inflamatórias ou infecciosas. Sendo assim, elas devem ser consideradas no diagnóstico diferencial de lesões desconhecidas na mandíbula. Esse relato de caso envolveu metástase de câncer de mama na mandíbula de uma mulher de 45 anos. O diagnóstico diferencial mais importante foi uma lesão reacional, em uma localização periapical incomum, associada a um dente não vital. No entanto, dado o histórico médico da paciente e uma vez que parestesia e*

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*dor foram observadas alguns dias após a realização da pulpectomia, a metástase de câncer de mama não foi descartada. Quando a cintilografia óssea sugeriu a metástase de um tumor ósseo maligno, uma biópsia incisional foi realizada. O exame histopatológico e a reação imunohistoquímica confirmaram o diagnóstico de metástase do câncer de mama, e a quimioterapia foi então realizada. Infelizmente, a paciente morreu 2 anos após o diagnóstico. Portanto, dentistas e médicos generalistas devem considerar a presença de metástases oral em casos que envolvam sintomas atípicos, principalmente em pacientes com doença maligna conhecida.*

**Termos de indexação:** Câncer de mama. Lesão periapical. Metástase oral.

## INTRODUCTION

A rare condition, metastasis in the oral cavity represents only approximately 1.5% of diagnosed oral cancer [1]. However, as a first sign of malignant disease, oral metastasis occurs among 20.4% [2] to 27.5% [3] of patients. Oral metastasis appears more often in the jaws than in soft tissues; indeed, its most common site is the mandible [1,3]. Van der wall et al. [1] have reported metastasis in the mandible in 62.5% of all cases of metastasis evaluated of 1537 patients with diagnosed oral cancers. Metastasis generally occurs in the posterior region of the mandible, ramus, and condyle, all of which are rich in red bone marrow [3]. In most cases (90%), the early clinical manifestation of metastasis resembles a hyperplastic or reactive lesion [1].

Patients with metastatic jaw disease can be entirely asymptomatic or present a few clinical signs and symptoms, including pain, swelling, paresthesia of the lip, loose or extruded teeth, regional lymphadenopathy, mandibular nerve involvement, the cortical expansion of the jawbones, ulceration, and exophytic growth [4]. At times, metastatic lesions in the jaw can be mistaken for inflammatory or infectious diseases of the jaw and adjacent structures as a result of their clinical and radiographic similarities [4-7]. Despite their rarity, metastatic diseases of the jaw should be considered in the differential diagnosis of unknown jaw lesions, especially among patients with a history of cancer [5].

The study reported here involved the metastasis of breast cancer in the mandible of a 45-year-old woman. The most important differential diagnostic was a reactive lesion with an unusual periapical location.

## CASE PRESENTATION

A 45-year-old white woman, lawyer, was referred to the Endodontical Services of the Military Police of Minas Gerais, Brazil, due to complaints of intense pain in the right mandibular region and lip paresthesia. Medical

history revealed heart disease and breast cancer, the latter of which had been treated 2 years prior with complete mastectomy, followed by chemotherapy and radiotherapy. The patient reported a smoking habit of 20 cigarettes per day during the previous 20 years.

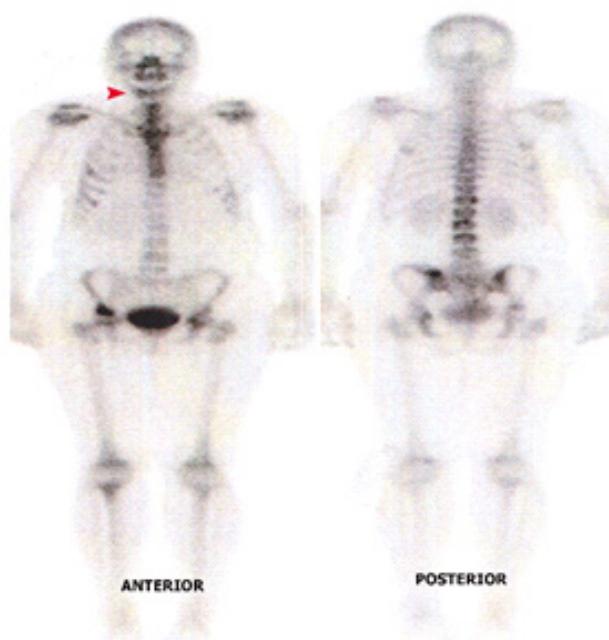
An extraoral clinical examination showed no facial swelling (figure 1A), and an intraoral clinical examination revealed normal oral mucosa and no expansion of the mandible (figure 1B). A radiographic examination revealed a unilocular radiolucency in the periapical region of the first lower right premolar (i.e., Tooth 44) and the slight widening of the periodontal ligament (figure 1C). Pulp vitality was tested, and the tooth was determined to be nonvital given pain during vertical percussion. The diagnosis was pulp necrosis and a periapical inflammatory process characteristic of chronic apical periodontitis [8]. Pulpectomy was performed, followed by the chemical-mechanical debridement of the root canal systems with



**Figure 1.** A) Extraoral examination showing lack of facial swelling. B) Intraoral examination showing normal oral mucosa and absence of expansion. C) Periapical x-ray demonstrates unilocular radiolucency involving periapical region of first premolar of right side in mandible. D) and E) cone-beam computed tomography scan in sagittal plane showing a hypodense image with destruction of cortical bone and root resorption of the first premolar of right side.

nickel-titanium rotary instruments and abundant irrigation with 5% sodium hypochlorite solution. Once calcium hydroxide paste was applied, the patient reported a reduction of pain. However, paresthesia and the pain returned a few days later.

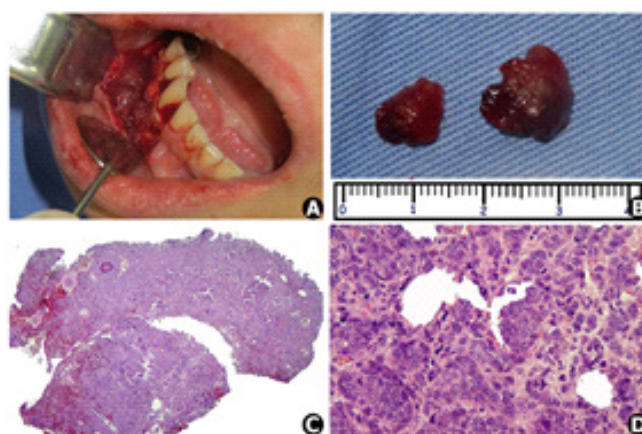
Given the presence of paresthesia and pain a few days after pulpectomy, other differential diagnoses, including a noninflammatory odontogenic lesion and central giant cell granuloma, were suggested. Another distant possibility was a benign or malignant epithelial or mesenchymal lesion. Given the patient's medical history, the metastasis of breast cancer could not be ruled out. Additional imaging was performed to facilitate surgical planning that would rule out malignancy. Cone beam computed tomography was performed, which revealed a hypodense image in a sagittal plane of the right mandibular region, with the destruction of the buccal and lingual cortical bone and the root resorption of the first lower right premolar, yet without expansion (figure 1D and E). Following the analysis of the radiographic and tomographic findings associated with lip paresthesia and the medical history of breast cancer treatment, a more aggressive process was suspected. Bone scintigraphy was thus requested, the results of which suggested the metastasis of a malignant bone tumor (figure 2).



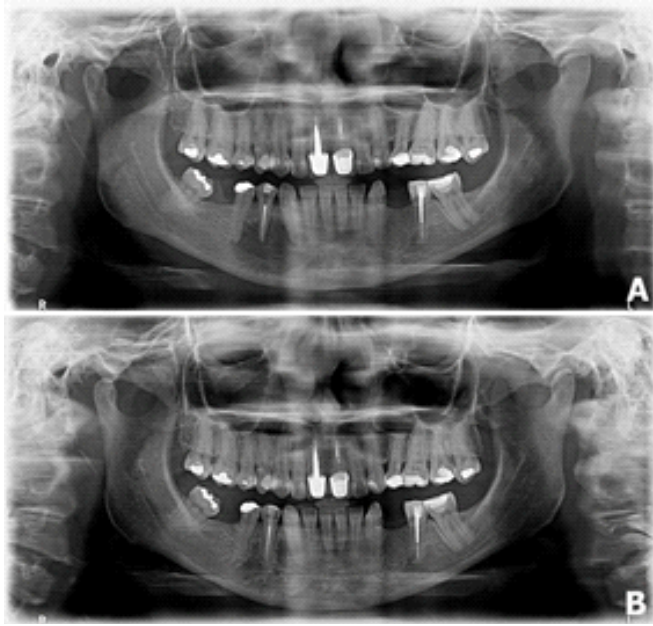
**Figure 2.** Bone scintigraphy exam demonstrated hyper uptake in right mandible (red narrow), vertebral bodies and costal arcs.

Under local anesthesia, a puncture aspiration was performed that ruled out the presence of cystic liquid. An incisional biopsy of the mandibular lesion was therefore performed as well, the specimens of which were sent to the oral pathology laboratory (figure 3A and B). A histopathologic examination revealed malignant neoplasm (figure 3C) characterized by cells with eosinophilic cytoplasm, pleomorphism, large and hyperchromatic nuclei, numerous atypical mitotic figures, and vascular invasion (figure 3D). The histopathological diagnostic was malignant neoplasm. An immunohistochemical reaction was performed to determine the histogenesis of the lesion, and a positive reaction for AE1/AE3, CK7, and estrogen receptor was observed, as was a negative reaction for CK20, synaptophysin, progesterone receptor, and human epidermal growth factor receptor 2. The final diagnosis was the metastasis of breast cancer. Endodontic treatment was completed (figure 4A), and the patient was referred to an oncologist for further management.

Chemotherapy was performed in 33 sessions, and the patient submitted to follow-up. A panoramic x-ray was requested after 1 year of oncological treatment, the results of which revealed osteogenesis in the apical region (figure 4B). The patient died 2 years after the diagnosis of metastasis in the jaw and ribs.



**Figure 3.** A) Periapical region after surgery of incisional biopsy. B) Macroscopical examination showed two collected fragments that measured about 2cm of diameter. C) Histological sections in hematoxylin-eosin staining (HE) demonstrated proliferation of neoplastic cells in a solid pattern (HE, magnification 25x). D) Neoplastic cells presented pleomorphism, large and hyperchromatic nuclei, atypical mitosis and vascular invasion (HE, magnification 400x).



**Figure 4.** Comparative panoramic x-ray. A) image requested after the conclusion of the endodontic treatment of the first premolar of right side in mandible. B) One year after conclusion of the endodontic treatment, demonstrating bone repair of periapical region.

## DISCUSSION

A unilocular radiolucency in the periapical region presented a range of possible diagnoses, including inflammation, which could not be ruled out given the presence of pain and pulp necrosis. In response, the first differential diagnosis considered chronic apical periodontitis [8] in the form of a periapical cyst or granuloma.

If healing does not occur following the endodontic treatment of a tooth associated with a periapical radiolucency, it is necessary to perform surgery and subject the specimen to histological examination. In the case reported here, paresthesia and pain returned a few days after pulpectomy. The localization of the radiolucency around the roots of teeth, especially if vitality is negative or doubtful, can complicate diagnosis and delay appropriate treatment [9].

Odontogenic lesions are the most common intraosseous lesions – a study of 7,117 oral biopsies reported that 16.54% were odontogenic lesions [10] – and require differential diagnoses. In a retrospective analysis, nonendodontic periapical lesions misdiagnosed as endodontic apical lesions represented 2.95% of the histopathological diagnoses; keratocystic odontogenic lesions were

the most frequent nonendodontic periapical lesions, followed by fibro-osseous lesions, dentigerous cysts, and ameloblastoma [11]. At the same time, different odontogenic lesions show variation in clinical presentation and aggressiveness. In the lesion reported here, well-defined margins common in benign odontogenic lesions were not observed radiographically; however, the diffuse margins could have derived from secondary infection.

Epithelial and mesenchymal intraosseous lesions can be radiologically unilocular and apically located. Whether benign or malignant, intraosseous lesions are rare, although the mandible is their most common location. Although squamous cell carcinoma is the fifth-most common nonendodontic periapical lesion [11], intraosseous mesenchymal tumors mimicking periapical lesions have also been reported. Schwannoma in the mandibular alveolar bone [12] and malignant peripheral nerve sheath tumors in the maxilla [13], both mimicking an inflammatory periapical lesion, have also been reported.

Although extranodal non-Hodgkin lymphomas are rarer in the oral region than other diseases of odontogenic origin, two cases were initially misdiagnosed as reactive periapical lesions [14-15]. Furthermore, a primary intraosseous Kaposi's sarcoma presenting as an asymptomatic periapical radiolucency has also been reported [16]. In the case reported here, an intraosseous malignant lesion, particularly a metastasis of breast cancer, was an important differential diagnosis confirmed after additional imaging examinations and an incisional biopsy. However, it is important to emphasize that for the inclusion of metastasis of breast cancer as a differential diagnosis is necessary a well-conducted anamnesis. Therefore, the differential diagnoses of metastasis is important if the team of professionals obtained the information of the general physical state of the patient, specifically the presence of breast cancer.

In an analysis of 157 cases of metastases in the oral mucosa, Hirshberg et al. [2] observed a man-to-woman ratio of 1.6 to 1.0 among patients aged 9–88 years, with a mean age of 54 years. Those findings corroborate the results of a review of 390 cases [17] and 453 cases [3] of metastasis to the jaw bones. The most common primary sites of metastatic tumors were the lungs for men and the breasts for women [2-3,17]. Metastasis in distant organs is not random and is regulated by site-specific processes [18]; breast cancers usually metastasize in the jaw bones, whereas lung carcinomas commonly metastasize in

soft oral tissues [17]. Although the pathogenesis of the metastatic process in the jawbones remains unclear, a pathway that may be critically responsible for defining the microenvironment favorable to bone metastasis in breast cancer has been identified [18].

Most patients who present with metastatic tumors in the oral cavity have also developed metastases at other sites [1]. In the case reported here, bone scintigraphy demonstrated osseous metastasis in vertebral bodies and costal arcs in addition to the mandible. In general, for cases with metastases at other sites, a palliative regimen is the only management option [1]. Although treatment with chemotherapy was chosen for the patient in the case presented here, local treatment of jaw bone metastases nearly always involves radiotherapy, while metastases in soft oral tissues may be more readily approached surgically [1]. Prognosis for patients is poor, and the median survival time is 6 months [1,3]. The patient in the case reported here died 2 years after the diagnosis of metastasis in jaw and ribs.

Advanced stages of cancers usually result in metastases. Unfortunately, the interval between the appearance of metastasis and death is often brief [19]. The diagnosis presents a challenge to professionals given the lack of pathognomonic signs and symptoms, including lesions to the oral cavity. Therefore, complete information about a patient's medical history and physical examination, including all complementary exams, are important for appropriate diagnosis and treatment. Furthermore, the adequate follow-up of long-term cases, as suggested by the case reported here, underscore the importance of the differential diagnosis of oral lesions to the maintenance and management of patients' health.

## CONCLUSION

In conclusion, dentists and general physicians should investigate the presence of oral metastasis in cases involving atypical symptoms, especially among patients with known malignant disease, for which cone beam computed tomography and bone scintigraphy can offer important information. In addition, a well-conducted anamnesis detailing the patient's general condition before treatment is of great importance, taking as much information as possible, even if it takes a significant amount of time from the professional.

## Collaborators

The authors JLBMC, GRS and MFPC were involved in the design and conception of the project. The data collection was carried out by all authors, and analysis and interpretation of results carried out by JLBMC, GRS and MFPC. JLBMC and GRS drafted the manuscript and carried out the critical revision. All authors have read and approved the final version of the manuscript.

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