

Fine needle aspiration biopsy of mandible: an effective alternative to conventional biopsy for the differential diagnosis between metastasis and osteonecrosis in oncologic patients treated with bisphosphates - Case report

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Abstract:

Bisphosphonates are the drugs of choice for the prevention and treatment of bone metastases of breast cancer, especially in more advanced cases. Osteonecrosis of the jaw (BRONJ) is the most common, debilitating complication of the use of this drug, caused mainly by bone manipulation. Because of this, the indication for biopsy for differential diagnosis is critical in cases of radiographic findings without mandibular exposure, and less invasive diagnostic methods have been discussed in the literature. The objective of this study was to describe a case of differential diagnosis of mandibular metastasis of breast cancer and BRONJ by fine needle aspiration (FNA). A 67-year-old woman was referred to the Dentistry and Stomatology Service of Ribeirao Preto General Hospital, Brazil, in January 2015, for investigation of pain followed by paresthesia in the lower lip. The patient had a history of mixed breast carcinoma in 1999, recurrent in 2010, treated with chemotherapy and Zometa from 2010 to 2013. Although no significant alterations were detected at clinical examination, the CT scan revealed osteolytic lesions involving the anterior and posterior right jaw. Because of the risk of bone necrosis after biopsy, FNA was chosen as the diagnostic method. Cytology confirmed metastasis of breast cancer and the patient had no complications in the puncture area. FNA was shown to be a viable, safe option for differential diagnosis between BRONJ and mandibular bone metastasis.

Keywords: Biopsy, Fine-Needle; Breast Neoplasms; Neoplasm Metastasis; Bisphosphonate-Associated Osteonecrosis of the Jaw.

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INTRODUCTION

Breast cancer is the second most frequent cancer among women around the world. Its relatively high survival rates (61% in the first five years) have been associated with the occurrence of chronic conditions, including metastasis¹. Approximately 11% of metastatic tumor to the jaw originates from breast cancer².

Metastasis in the gnathic bones is associated with many signs and symptoms, especially pain, teeth loss tumor volume enlargement, and mass formation. Involvement of the lower alveolar nerve may cause a condition “numb chin syndrome”, which is a neurological condition characterized by paresthesia of lower lip and chin. However, these symptoms are not exclusive to metastatic lesions and may be also associated with inflammatory diseases and necrosis of the gnathic bones. Some cases may even be asymptomatic and the lesion may be occasionally identified in radiographic images.

The lesions may be identified as well-circumscribed, radiolucent lesions, but most of the time, radiographs reveal poorly defined, “silverfish damage-like” lesions. Some carcinomas, especially prostate and breast carcinoma, may stimulate the formation of new bone in the metastatic site, resulting in radiopaque, radiolucent or mixed lesions³.

Bisphosphonates are a class of drugs used in the treatment of metastatic bone lesions from different types of cancer, and more recently, they have been used in the treatment of osteoporosis¹. Studies suggest that in addition to the effect on the osteoclasts, these drugs also present some activity in tumor cells. Bisphosphonate-related osteonecrosis of the jaw (BRONJ) has been reported as a debilitating, difficult-to-treat side effect among bisphosphonate users⁴. BRONJ is identified by the appearance of exposed bone in the maxillofacial region, persistent for more than eight weeks, in patients who have been treated with bisphosphonate, with no history of radiation therapy to the jaws⁵.

Local signs and symptoms of BRONJ include inflammation or infection, fistulas, paresthesia and pain⁶. Bone manipulation is the main triggering factor of BRONJ, and it is expected that approximately 39% of cases of osteonecrosis related to bisphosphonates have a history of exodontia in the affected regions^{7,8}. Regardless of the classic definition of bone exposure, Khan et al. have proposed the term “stage 0” disease, which refers to the presence of radiographic findings – alteration of bone density, bone sequestrum, periosteal

bone formation and mixed lesions, commonly mistaken as bone metastasis^{9,10} – without bone exposition^{9,10}.

Medical history and clinical evolution of the patient are the main diagnostic criteria⁹, since biopsy is exclusively used for specific cases, because of the risk of BRONJ progression with manipulation of the tissues exposed to the medication. However, in some cases, the differential diagnosis is essential, especially in patients at risk of metastasis and symptomatic patients with radiographic lesions without exposure of necrotic bone⁶. In these cases, incisional biopsy is the most used method, despite the risk of BRONJ progression.

Fine needle aspiration biopsy (FNA) is a practical, safe, little invasive diagnostic method. Although it has a high precision rate in oral lesions (80% to 94.5%), FNA has been rarely used in the diagnosis of intraosseous jaw lesions due to technical difficulties in approaching lesions in the cortical bone¹¹.

This study aimed to report the use of the FNA, guided by radiographic findings, in the differential diagnosis of osteolytic bone lesion in breast cancer patient, chronic user of bisphosphonate.

CASE REPORT

AERG, 67 years old, female, was referred to the Dentistry and Stomatology Service of Ribeirão Preto General Hospital, Brazil, in January 2015, in order to investigate pain followed by lower lip paresthesia. The patient had a history of mixed carcinoma of the right breast in 1999, which recurred in the left breast in July 2010, and as vertebral bone metastasis in November of the same year.

The patient received chemotherapy and Zometa™ (zoledronic acid) from 2010 until 2013. In clinical examination, there were no notable alterations, but the panoramic radiography revealed areas of changes in jaw bone density. For a better definition of the radiographic findings, a CT scan was conducted, which showed osteolytic lesions in the right anterior and posterior regions of the mandible, with loss of cortical bone in the anterior region and in the angle of the mandible. (Figures 1 to 7)

Based on patient’s history, clinical data and radiographic findings, the diagnostic hypotheses were bone metastasis and necrosis due to the use of bisphosphonate. Since confirmation of the diagnosis was essential to determine the clinical approach, and considering the fact that an incisional biopsy could lead to the worsening or development of bone necrosis,



Figure 1. Clinical aspect: intact oral mucosa.



Figure 3. CT Scan - Sagittal section: right mandibular ramus region: osteolytic lesions.

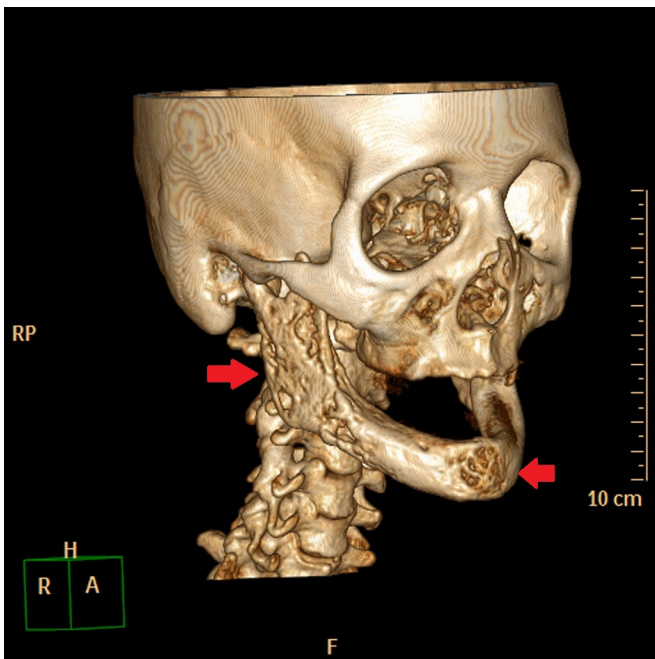


Figure 2. CT imaging with 3D reconstruction: osteolytic lesions in the mental region and in the right posterior mandibular region (red arrows show areas of structural loss of the cortical bone).

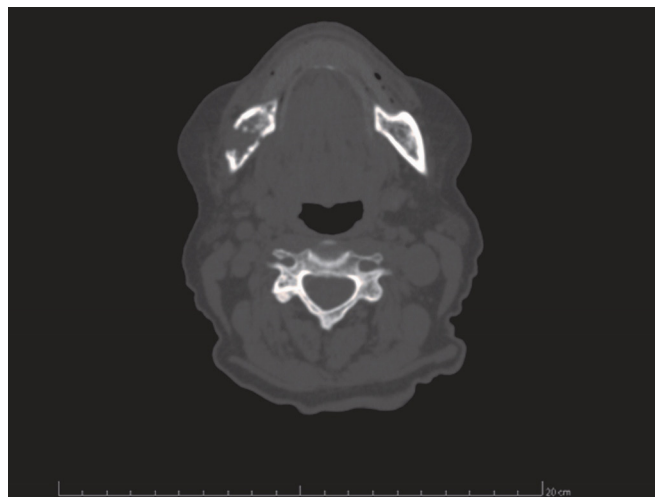


Figure 4. CT Scan - Transversal section: right posterior region of the mandible with cortical bone loss.

FNA was used as a less invasive diagnostic method. The anterior mandibular region was chosen as the biopsy site based on its easy accessibility and small thickness showed on the CT scan. The cytology confirmed the presence of neoplastic cells and the patient did not have any complications in the puncture site.

DISCUSSION

Metastatic tumors are more frequent in gnathic bones than in oral mucosa. The red bone marrow is the most common site of metastatic depositis, due to high

vascularization and metabolic activity of the tissue that enable the availability and development of tumor cells. With the ageing process, relatively little active marrow remains in the mandible, which explains the prevalence of metastatic lesions in this area in elderly patients².

Clinical presentation of oral metastasis differs according to the affected region. In the mandible, they are frequently associated with edema, pain and paresthesia, usually with a short duration¹², which are often mistaken for dental infections. On the other hand, in some cases, the disease may be totally asymptomatic. Clinical manifestations of osteonecrosis vary from small areas of exposed necrotic bone to necrosis of the whole area affected, or from simple edema in soft tissues to more

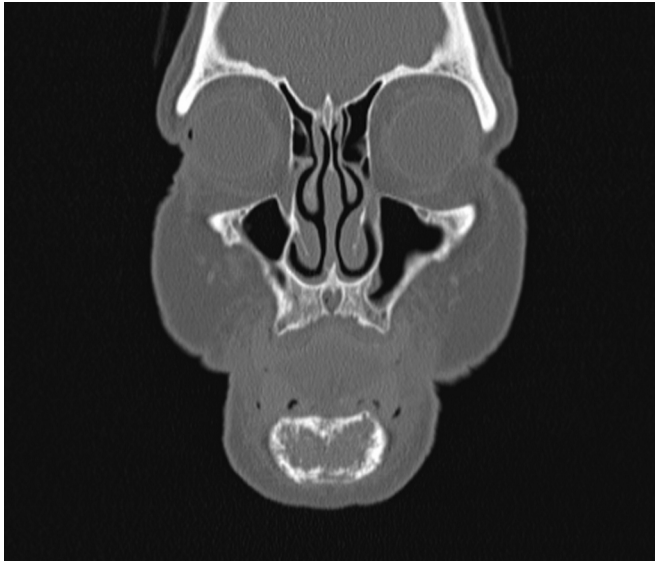


Figure 5. CT scan - Coronal section: osteolytic lesion in the anterior region of the mandible, and significant thinning of the cortical bone.

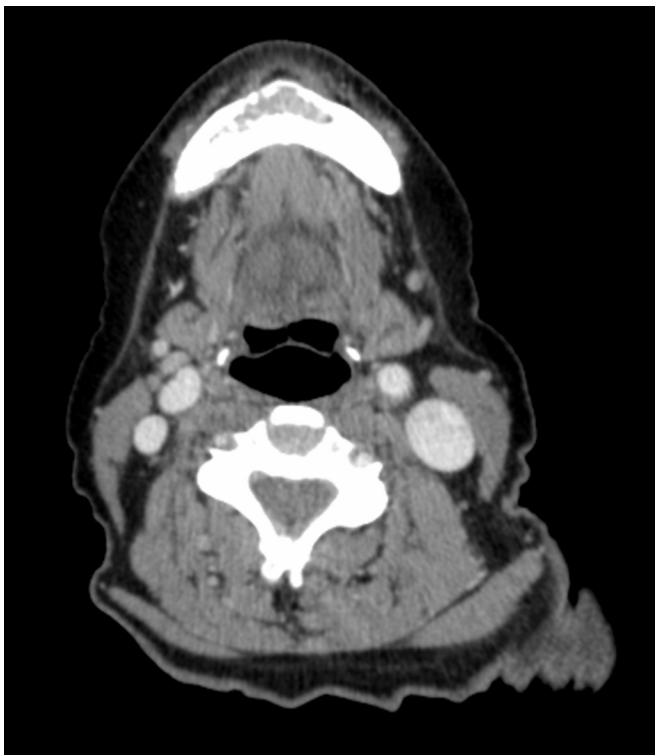


Figure 6. CT scan - Transversal section: osteolytic lesion in the anterior region of the mandible, and significant thinning of the cortical bone.

complex cases that progress to fistula and diffuse pain. BRONJ lesions may be asymptomatic until a trigger event occurs, such as an infection, trauma or an invasive dental procedure (e.g. a biopsy of intraosseous lesion)¹³.

The diagnostic confirmation of tumor metastasis and the exclusion of infectious complications of necrosis are essential not only to control disease progress, but also

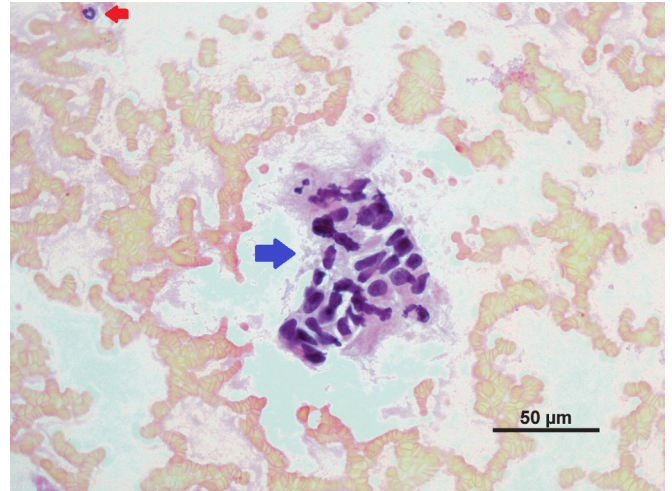


Figure 7. Fine needle aspiration cytological study, HE staining, and magnification of 40 times, showing hemorrhagic background, tumor cell islands (blue arrow), and isolated neutrophils (red arrow).

to develop strategies (e.g. radiotherapy) to prevent or control symptoms and complications, such as pathologic fractures, even in cases of advanced stages of primary disease. On the other hand, antineoplastic treatment of the infectious or necrotic area could be determinant to the development of local or systemic complications.

Despite the fact that many patients with oral metastatic lesions also have metastasis in other regions, the differential diagnosis is of great importance. For example, Jain et al.¹³ reported a disease-free survival of 15 years in 24% of 134 patients with only one metastatic tumor, treated with surgical resection, systemic therapy and radiotherapy^{14,15}.

FNA offers a conservative alternative to some invasive procedures, such as the incisional biopsy, which is the main diagnostic method in bone lesions¹⁶. Limitations of the method may be related to difficult accessibility of the lesion, clinical condition of the patient, or special conditions, such as the risk of osteonecrosis, as in the present case.

CONCLUSION

In the present case, FNA proved to be an efficient diagnostic method that enabled the identification of tumor cells and prevented the development of necrosis or infectious complications in the area. The main determinant factors for the successful approach were the control of predetermined parameters and the identification of rupture areas or thinned cortical bone by CT scan, which facilitated the access.

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