




Case-report

Keywords:

bisphosphonate-associated osteonecrosis of the jaw, neoplasm metastasis, diagnosis, drug-related side effects and adverse reactions

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Metastatic cancer in a patient with suspected Medication-Related Osteonecrosis of the Jaw

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Abstract

Metastasis to the oral cavity represents 1% of all tumors in this location, and the molar area of the mandible is the most common region of metastasis. Tumors that metastasize to the oral cavity have clinical characteristics that can mimic reactive or inflammatory lesions, making their diagnosis a clinical challenge.

We present a case of a 30-year-old female patient, with breast adenocarcinoma with lymph node and bone metastasis, who underwent chemotherapy, mastectomy and had been under therapy with zoledronic acid. The patient had pain in the left hemiface region, and mandibular bone exposure at the extraction site of tooth 37. The radiography showed massive bone sequestration in the posterior left mandibular body, distally to tooth 36. The main diagnostic hypothesis was Medication-Related Osteonecrosis of the Jaws (MRONJ). The histopathological examination revealed a metastasis of the previously diagnosed breast cancer. The patient was treated with palliative care and died six months after the biopsy.

Being an uncommon diagnosis, necrotic lesions in metastatic cancer of the oral cavity can be misinterpreted as MRONJ in patients with history of antiresorptive medication. A biopsy and histopathological examination prior to treatment is essential once it changes the therapeutic strategy of these patients.

Highlights

1- Oral cavity metastasis is uncommon and in this location is a sign of widespread disease. 2 - It's clinically and radiographically difficult to distinguish metastasis from Medication Related Osteonecrosis of the Jaw. 3 - There is a significant number of metastatic cancer lesions in areas with suspected MRONJ. 4 - All the MRONJ suspected cases should be confirmed by biopsy and histopathological examination before treatment.

1. Introduction

Oral cavity metastasis is uncommon, accounting for approximately 1% of all tumors in this location [1, 2]. Some authors suggest that the actual incidence of metastatic spread to the jaws may be higher. Micrometastatic foci in the jaws were found in 16% of autopsied carcinoma cases despite the absence of radiologic findings [3].

The presence of metastasis in this location is a sign of widespread disease; nevertheless, in up to a quarter of the cases, oral metastasis was found to be the first indication of an occult malignancy at a distant site⁴. The primary sites differ between sexes. For men the most common sites are prostate, lung, kidney and liver, and for women breast, genital organs, kidney, and colorectal [4, 5].

The location of the metastasis in the jawbones is twice the frequency of the oral mucosa, and the mandible more common than the maxilla. The molar region of the mandible is the most affected site [1, 6].

Clinically, there are no specific manifestations. Patients can have paresthesia, ulcerated, inflamed, bleeding, painful or necrotic oral lesions that can be confused with other lesions, increasing the difficulty of the final diagnosis [2].

Antiresorptive and/or antiangiogenic drugs are frequently used to treat patients with bone metastasis. These drugs improve the overall survival and the quality of life by preventing skeletal-related events but can have as potential side effect the development of medication-related osteonecrosis of the jaws (MRONJ) [6]. Several risk factors contribute to development of MRONJ: medication-related risk factors, local factors and demographic and systemic factors and other medications [7]. The most common identifiable factor for developing MRONJ are dentoalveolar surgeries, ranging from 62 to 82% as the pre-disposing factor [7]. For cancer patients exposed to bisphosphonates, the risk of developing MRONJ after tooth extraction ranges from 1.6 to 14.8% [7]. Some authors have pointed out that bone metastasis can secrete an array of cytokines that are known to down regulate normal tissue homeostasis and up regulate their own blood supply and proliferation, leading the development of MRONJ [8].

In this report, the authors present a case of a patient suspected of having MRONJ that ended up diagnosed with breast cancer metastasis of the jaw.

2. Case presentation

Female patient, 30 years old, with a medical history of breast adenocarcinoma diagnosed in 2014 and was treated with chemotherapy and modified radical mastectomy. In May 2019 she had disease progression with bone (skull, spine, right clavicle, hip bone, left scapula and ribs) and ganglion metastasis. Therefore, she started zoledronic acid, fulvestrant and palbociclib, and had spine surgery and radiotherapy. Right before starting zoledronic acid, she had a tooth extraction (tooth 37) in a private office. The extraction socket never healed completely and six months later she had bone exposure and was treated with regularization of the alveolar ridge.

In July 2020 she went to the stomatology emergency department with pain on the left side of the face, that increased during the night, and started three days earlier. She had bone exposure of 2 cm in the alveolar socket of the extraction of tooth 37. There was no discharge and no other symptoms. In the panoramic dental radiograph, we could see bone sequestration in the mandible distally to tooth 36 (Fig. 1). The patient was medicated with paracetamol, amoxicillin and clavulanic acid for two weeks, local application of chlorhexidine and referred to the outpatient clinic for evaluation by computed tomography (CT) of the jaws. In the CT we could see diffuse medullary sclerosis, cortical erosion and periosteal reaction located in the position of teeth 37/38, reaching the entire alveolus up to the depth of the inferior alveolar nerve (Fig. 2). The case was discussed with the oncology department and the zoledronic acid was suspended in order to plan a bone sequestrectomy of a highly suspected MRONJ lesion. Before the surgical treatment, a biopsy of the bone lesion was done and the histopathological

examination revealed a bone metastasis of breast cancer (Fig. 3). Therefore, the surgical treatment was cancelled, the patient was treated with palliative chemotherapy, and kept the follow-up in the stomatology department. The patient died six months after the biopsy.



Figure 1. Panoramic dental radiograph: bone sequestrum in 4th sextant (white arrow).

3. Discussion

In the presence of a patient treated with zoledronic acid for bone metastasis, the first diagnosis for bone exposure with more than eight weeks of progression was MRONJ.

Nevertheless, in a patient with breast cancer and bone metastasis, must be considered the chance of a jaw metastasis, a primary cancer of the jaw or other nature lesion. Metastasis in the jaw can often appear both clinically and radiographically, similarly to those seen in MRONJ. Clinically, exposed bone while radiographically, findings of osteolytic lesions, cortical erosion, bone sclerosis and sequestration, persisting alveolar sockets can be present in both lesions. The final diagnosis can only be given with the histological exam of a sample of the lesion.

The presence of metastasis in lesions suspected of MRONJ has been described by several authors [6]. Carlson *et al.* (2013) highlighted that osteolytic bone diseases, including metastatic breast cancer, disrupt the normal skeletal equilibrium such that bone formation and bone resorption are no longer coupled. That disruption can be related to the release of factors that affect the survival of osteoblastic precursor cells derived from the marrow stroma by inducing both apoptosis and cell necrosis. Other factors are the expression of matrix metalloproteinases, that are implicated in cancer progression and destruction of the extracellular matrix [8].

Metastatic cancer in the oral cavity although rare must be taken in consideration when approaching a patient with MRONJ suspicion. In a literature review, Sacco (2021) found the histologic presence of malignant cells in 4.6% of the samples of patients with MRONJ suspicion, who had not been previously diagnosed. In patients with previous diagnosis of metastatic disease, this number increases to 9.3% of the samples [6].

The presence of bone metastasis is usually a sign of widespread primary cancer and is a sign of poor progno-

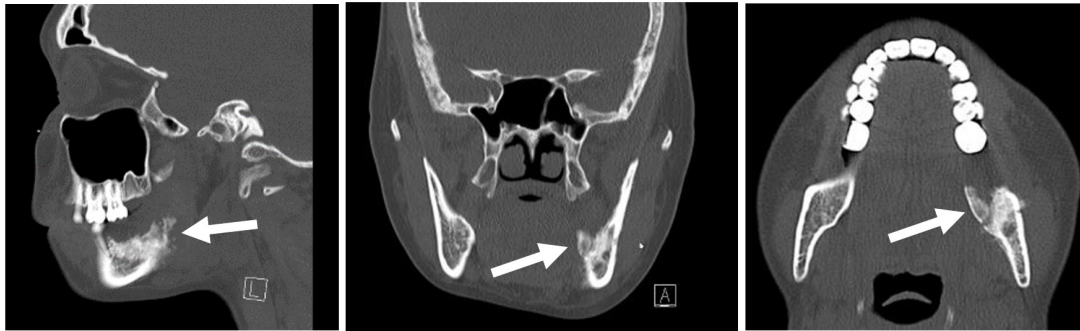


Figure 2. CT: medullary sclerosis, cortical erosion and periosteal reaction (white arrow).

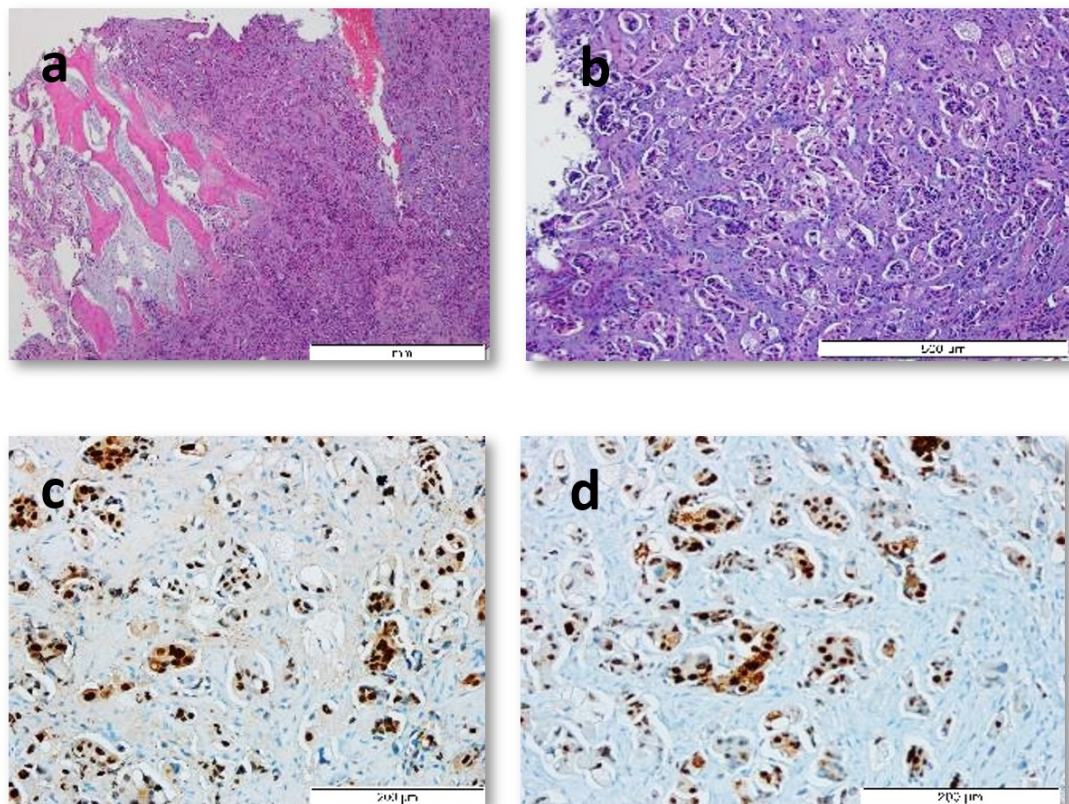


Figure 3. Histology of the biopsy of the lesion. a. (10x) H&E (Hematoxylin and eosin stain) Bone tissue partially occupied by malignant epithelial neoplasia; b. (20x) H&E Neoplasm with characteristics of carcinoma consisting of tubules, cells with ample cytoplasm and eosinophils; c. (20x) ER (estrogen receptor) positive neoplastic cells; d. (20x) GATA - 3 positive cells.

sis. The mean survival of these patients varies between series from 6-7 months, to 9.8 months[2].

4. Conclusions

In the management of MRONJ a correct diagnosis is essential. There can be an overlap between the symptoms and radiologic appearance, between MRONJ and jaw metastasis, that can lead to an inadequate treatment if the diagnose is inaccurate. This case highlights the importance of the biopsy and histopathological examination as part of the flowchart of the management of suspected MRONJ cases.

Funding: This study did not receive any specific grants or aid from funding agencies in the public, commercial, or non-profit sectors.

Competing Interests: None of the authors of the manuscript has any conflict of interest related to this study.

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