

Osteonecrosis of the jaw in a patient treated with bisphosphonates for metastatic breast cancer: about an observation

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Abstract: Bisphosphonates are widely used in medical practice. Osteonecrosis of the jaw (ONJ) was first reported in the dental literature in 2003. Eighteen years later, this pathology is still topical and increasingly publicized, particularly because of its disabling clinical consequences and the complexity of treatment. The objective of this work is to focus on this pathology which is disabling, very difficult to treat and to show that preventive treatment based on patient information in relation to the risks of this therapy, the restoration of the oral cavity before the introduction of bisphosphonate treatment and the eviction of avulsions except in extreme cases of mobility remains the only way to avoid this complication

Keywords: osteonecrosis, Bisphosphonates, metastatic breast cancer

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I. Introduction:

Bisphosphonates (BP) are widely used for the treatment of osteoporosis and bone complications of cancers. The benefits associated with their use are widely recognized. However, some risks are associated with their use, including Osteonecrosis of the jaw (ONJ), a complication often publicized, but which is only rarely encountered in medical practice (Marx 2003) [1]. Maxillary osteonecrosis is a serious and disabling complication and a major public health problem that can affect the quality of life of patients. The ONJ corresponds to an exteriorization of necrotic bone in the oral cavity that does not heal after 8 weeks of evolution of a dental extraction or oral surgery, in a patient who has been treated with bisphosphonates, but who has not undergone cervical-facial radiotherapy [2].

The accompanying signs are pain (inconstant), numbness, heaviness of the jaw, dental mobility, delayed healing, and an appearance of alveolitis. The most frequently affected site is the posterior mandibular region. The unfavourable evolution is manifested by the appearance of cutaneous or mucous fistula, mucous erythema, suppuration, cellulitis, sinus oral communication and spontaneous fracture.

Radiological signs are absent at the beginning of the ONJ on conventional radiography (retroalveolar, orthopantomogram). After several months of evolution, a poorly defined osteolytic image is visible with sometimes appearance of a bone sequester. Computed tomography and scintigraphy allow earlier visualization of bone lesions [3,4,5]. The incidence of osteonecrosis in patients treated with intravenous bisphosphonates for malignant conditions is estimated to be between 1% and 10%. The incidence of osteonecrosis in patients treated with oral bisphosphonates for mild conditions remains low, between 0.001% and 0.10%. However, caution should be exercised in estimating the incidence, on the one hand because of the evolution of treatments and, on the other hand, because of the disparity in the current data: disparity attributed to the quality of the studies and whether or not they are taken into account, risk factors [6, 7,]. The pathophysiological process is not fully understood, but some risk factors are identified, including dental extraction, prosthetic trauma and comorbidities such as diabetes and osteoporosis. The risk increases significantly with treatment duration and cumulative dose. Management requires a multidisciplinary approach and most of the time conservative treatment is preferred. Faced with this rather rare but disabling and difficult to treat condition, it is important to identify patients at risk and apply preventive measures [8].

II. Observation:

A 53-year-old post-menopausal patient who had been treated with Zolédronate for less than a year for metastatic breast cancer presented for consultation following mandibular bone exposure. The inaugural clinical sign was dull mandibular pain. The clinical examination revealed a generalized mandibular bone exposure (fig. 01) associated with an infection and mandibular edentation with a healing delay at several post extractional sites that had been evolving for several months, and maxillary bone exposure and infection in position 15 (fig. 02).

The orthopantomography (fig. 03) showed a diffuse bone osteolysis in position 15 and 16 ,a thickening of lamina dura in position 34 ,35 and 44 as well as a bone-sequester-free osteocondensation at the left horizontal branch. A bone scan objectified maxillary and mandibular bone hyperfixation (fig. 04). Treatment with poly antibiotic and analgesic level 2 was initiated and Zolédronate was stopped after multidisciplinary consultation. A milling of spicules irritating to the mucous membrane was carried out. Pain and infection were controlled but bone exposure appears to have increased in size

III. Discussion:

In recent decades, there has been the emergence of an iatrogenic pathology, Osteonecrosis, attributable to bisphosphonates and certain targeted therapies. Zolédronate is an intravenous third-generation bisphosphonate. It is a powerful antiresorptive inhibiting differentiation, function and osteoclast survival. Bone resorption is thus decreased. The incidence of Osteonecrosis in patients treated with intravenously administered bisphosphonates for malignant conditions is estimated to be between 1% and 10% [2]. The incidence of NMP induced by Zolédronate is 2.1%[3]. The average time to onset of ONJ is 28 months after initiation of Zolédronate [4]. Our patient developed an ONM in less than 12 months. The average cumulative dose of Zolédronate involved is 26 doses [5]. In our case, the patient received 08 doses and thus significantly less than that reported in the literature. The average time to diagnosis is 9 to 14 months with Zolédronate after an invasive act [6]. Our patient underwent dental extraction 03 months after a dental avulsion. The average age of onset of osteonecrosis is 62 years[7]. Our patient was 52 years old. The ONM appears to affect both sexes with no statistically significant difference according to the AAOMS [8]. It is likely that the combination of several treatments with bisphosphonates promotes the development of ONJ . An association with chemotherapy is described in 67% of cases, corticosteroids in 61% of cases and radiotherapy in 11% of cases [9]. . In this case, one could question the role of osteoporosis in the occurrence of this ONM. Indeed, several studies have shown that patients with such a pathology have developed ONJ more frequently [10]. Osteoporosis would therefore be a risk factor for the occurrence of osteonecrosis.

IV. Conclusion:

ONJ is a rare complication in osteoporosis but more common in the presence of oncological involvement. In the vast majority of cases, it occurs after a dental extraction. Prevention plays a major role. It is important to identify patients at risk and apply risk reduction strategies. Informing patients about the risks of ONJ should not be a barrier to the prescription of bisphosphonates or adherence to this treatment. The prevention and treatment of ONJ requires multidisciplinary management between the general practitioner, oncologist, dentist and maxillofacial surgeon. Research still needs answers on pathophysiology, treatment and effectiveness of preventive measures.

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Fig 01: intra-oral photo showing mandibular bone infection and exposure



Fig 02: intra-oral photo showing bone exposure and infection in position 15.



Fig. 03: panoramic radiograph showing diffuse osteolysis in position 15, thickening of lamina dura position 34, 35 and 44 as well as bone sequester-free osteo-condensation at the left horizontal branch



Fig 04 : scintigraphie osseuse montrant une hyperfixation osseuse maxillaire et mandibulaire

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