Research Article

Oral squamous cell carcinoma mimicking osteonecrosis of the jaw: a case report

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Osteonecrosis of the jaw (ONJ) is a well-known adverse drug reaction to bisphosphonate (BP) treatment.

ONJ diagnosis is usually based on the patient's medical/medication histories and on the clinical/radiological features of necrotic bone (frequently exposed). Furthermore, in case of mandibular involvement, patients may present pain and/or hypesthesia of the inferior alveolar nerve. There are no pathognomonic clinical and radiological signs of ONJ, and in doubtful cases, the histologic examination is recommended.

We report a case of a woman attending to our sector of Oral Medicine (AOUP "P. Giaccone" Palermo, Italy) with a mandibular bone exposure after implants loss and a medical history of BPs. Biopsy specimens demonstrated proliferation of oral squamous cell carcinoma (OSCC). Even if the role of biopsy in diagnosis ONJ is still a controversial issue, it is mandatory in case of OSCC suspicious.

Background: Osteonecrosis of the jaw (ONJ) is an adverse effect of therapy with bisphosphonates (BP) and other anti-resorptive agents. [1] The majority of cases of ONJ observed in osteoporotic patients, treated for many years with anti-resorptive drugs, with an average of 4.6 years. [2] Clinically, it can occur as an ischemic jawbone exposed through fenestration of the oral mucosa or facial skin; other manifestations include pain, secondary infection, tooth loss, fistula formation and pathological fractures. [3] The risk of ONJ in osteoporotic patients treated with BP remains low, compared with that of oncologic patients. However, the incidence of ONJ in patients in treatment with oral BPs, after dental surgical procedures, especially dental implant placements, remains uncertain. [4]

Oral squamous cell carcinoma (OSCC) accounts for \approx 90% of oral malignant neoplasms with a 34.70% 5-year mortality rate. [5] Current treatment of OSCC includes a combination of surgery, radiotherapy, and chemo-therapy that significantly impact patient' quality of life. [6][7] On consequence, early diagnosis is mandatory.

<u>Materials and Methods</u>: We report a case of a woman who has attended our sector of Oral Medicine (AOUP "P. Giaccone" Palermo, Italy) with a local inflammation around the socket of an implant failure and slight pus excretion on the left mandible.

<u>Results</u>: A 62-year-old Caucasian woman presented at our sector of Oral Medicine in October 2020 with complaints of pain and swelling in his left mandible. Her medical history revealed OSCC on the left mandible on 2006, chronic drug-induced pancreatitis and osteoporosis treated with alendronate from 2016 to 2018.

The patient reports mandibular rehabilitative treatment by 3 dental implants; 2 of them failed to integrate after 2 months. She had intermittent swelling and pain in the implant site and lack of soft tissue healing since the time of the fixture's explanations. Oral clinical examination showed characteristic signs of ONJ, but also an unusually high quantity of surrounding granular tissue. Due to the clinical aspects of the lesions and to medication history, a suspicion of medication-related osteonecrosis of the jaw was raised.

However, as the patient had a positive history for OSCC and due to the clinical appearance of the lesion, diagnostic protocol for OSCC, by magnetic resonance imaging (MRI) and incisional biopsy for histological examination, was also performed. Based on the histological and radiological findings, the definitive diagnosis of OSCC was done and appropriate oncological management has therefore been started.

<u>Conclusions</u>: Bisphosphonates are used in skeletal disorders, including osteoporosis, Paget's disease, bone metastases and hypercalcemia. Even though direct mechanism for ONJ is not fully elicited, they inhibit osteoclastic activity. The osteoclast inhibition interrupts bone resorption and weakens bone turnover remodelling and mechanical properties of the skeletal. Several local risk factors, such as periodontal disease, dental extraction, implant placement, oral infection, can increase the adverse effect of the bisphosphonates such as alendronic acid. Signs and symptoms potentially evocative of ONJ, such as bone sequestrums, suppuration, mucosa or cutaneous fistula might appear in patients

with a long background of the BP administration. $^{[1][10]}$ The diagnosis of ONJ is made after clinical and radiologic investigation. $^{[1]}$

Patient with ONJ are commonly treated with a combination of surgical and medical treatment. [4]

Local recurrences of OSCC occur in about 10-30% of the cases with advanced tumors, even with histopathological tumor-free surgical margins after resection. The gold standard diagnostic process for OSCC are imaging and histological confirmation.

The American Society for Bone and Mineral Research recommends that the diagnosis of ONJ should specifically exclude other intraoral conditions, including bone tumors and metastases. [13] Although the presence of a lesion at the site of an implant failure in a patient who has taken bisphosphonates, inevitably leads to a diagnosis of suspected osteonecrosis, biopsy and histological confirmation could be mandatory in suspicious cases.

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