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Letter to the Editor:
Dental Prostheses and Risk of Medication-related Osteonecrosis of the Jaw

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Dear Editor

Medication-related Osteonecrosis of the Jaw (MRONJ) is a rare complication associated with the use of three classes of drugs: Bisphosphonates (BP), denosumab, and angiogenesis inhibitors [1]. BP and denosumab are anti-resorptive drugs, which despite having different mechanisms of action, are used to control bone loss in the skeleton in diverse clinical situations such as osteoporosis, bone metastases, Paget›s disease, and multiple myeloma [1-3]. Anti-angiogenic agents, such as bevacizumab, sunitinib, and aflibercept, represent a broad and ever-growing group of drugs indicated to treat various types of cancers [4].

In 2003, Marx reported the first cases of necrosis in the jaws related to intravenous BP (pamidronate and zoledronic acid) [5]. Since then, MRONJ has become an increasingly concerning worldwide health problem caused by both the widespread use of BP and denosumab and the increasing number of new drugs constantly being produced by pharmaceutical companies, especially anticancer drugs, most with the potential to induce osteonecrosis in the jawbones.

According to the most recent definition provided by The American Association of Oral and Maxillofacial Surgeons (AAOMS) [6], the diagnosis of MRONJ must be based on the following criteria: presence of exposed bone (or bone that can be probed through an intraoral or extraoral fistula) that persists for more than 8 weeks, current or previous treatment with BP, denosumab or anti-angiogenic drugs, and absence of a history of radiation therapy to the jaw or evident bone metastasis.

The pathogenesis of MRONJ is multifactorial, with synergistic participation of a local precipitating factor (trauma or infection) in a gnathic bone predisposed to necrosis because of reduced osteoclast turnover and anti-angiogenic effects caused by such drugs [1, 2]. Plausible explanations for the occurrence of MRONJ exclusively in the gnathic bones could include a massive accumulation of the medicines in these bones because of higher cellular turnover, with more active osteoclasts (site of action of the drugs), the proximity of the jawbones to the external environment and the constant presence of mechanical trauma, infection from dental biofilm, [2, 3] and even functional loading of dental implants [7].

Although MRONJ can occur spontaneously, it is assumed that the local precipitating factor plays a pivotal role in the initiation of osteonecrosis [3]. A recent study

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by Yazdi and Schiodt showed that the main precipitating factor of MRONJ was dental extraction, while the second most prevalent factor involved causes related to prostheses [8]. Indeed, other studies have convincingly established that the use of fixed, removable prostheses and dentures could be considered precipitating factors capable of initiating the MRONJ process [8-12].

Although further research is warranted, one can hypothesize that the synergistic action of mechanical trauma caused by a dental prosthesis (especially if it is ill-fitting) and the microbial infection from dental biofilm could trigger MRONJ in the maxilla and mandible, which are predisposed to necrosis due to their low vascularization, and the decrease in cellular turnover induced by drugs. An example of this clinical situation can be seen in Figure 1.

An exposed necrotic bone which appeared spontaneously in the pontic area of a fixed partial denture located in the left maxilla can be seen.

It should be emphasized that MRONJ is an infectious condition that can cause considerable morbidity and, depending on local and general aspects, could be very difficult to manage and can even have a fatal outcome [13]. As it is a complex disease, the approach to and management of MRONJ requires the involvement of primary care physicians, oncologists, oral and maxillofacial surgeons, and dentists [14].

However, some studies have shown an insufficient level of knowledge of MRONJ among dentists [15, 16]. Bearing in mind that the fitting of fixed and removable prosthetic pieces could be a precipitating factor for MRONJ, the dentist, particularly the prosthodontist, plays a decisive role in identifying at-risk patients and preventing this condition. With the evolution of medical treatments and the discovery of new anticancer drugs, there has been an increase in life expectancy and increased the number of patients needing dental rehabilitation. Thus, the prosthodontist must carry out a comprehensive anamnesis and physical examination and should ideally be acquainted with the commercial brand names of medications. Besides, all medications being used must be carefully recorded and checked.

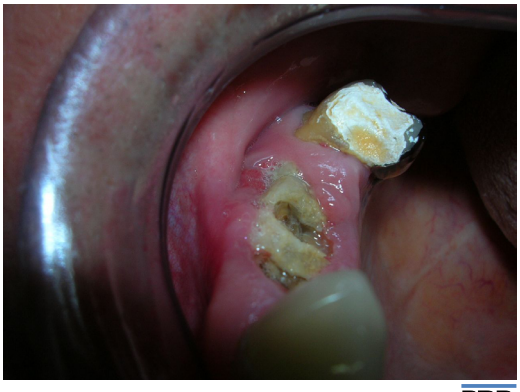

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Figure 1. Intraoral photography of medication-related osteonecrosis of the jaw in a 72-year-old male undergoing zoledronic acid therapy

The incidence of MRONJ in osteoporotic patients undergoing oral BP therapy is low and ranges from 0.01% to 0.04% [17], but it can reach 9.64% [18] in cancer patients treated with intravenous bisphosphonates. An accurate risk assessment is complicated and depends on factors associated with type, route of administration, and length of time the drugs have been used, as well as local and systemic factors [2, 3]. Consultation and referral to an experienced oral surgeon are recommended [1].

During the examination of the oral cavity, the prosthodontist should identify bony spikes, spicules, and exostoses, which are potential risk factors for MRONJ associated with prostheses. Preprosthetic surgery could be imperative in these cases. The precise and careful impression is also crucial to avoid trauma during the process and demands the construction of well-fitting prostheses, which minimize trauma during mastication. Instructions on the maintenance of a good oral hygiene routine are also highly recommended [19].

It is vital to clarify that patients treated with BP, denosumab, and anticancer drugs can safely undergo prosthetic rehabilitation. However, both dentist and patient should know that risk, which, although low, does exist and is greater in patients receiving intravenous BP, denosumab, and anticancer drugs. It is recommended that the patient sign an informed consent form and be regularly monitored by the prosthodontist to check adaptation to the fitted prostheses, and thereby reduce the risk of MRONJ.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this paper.

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Authors' contributions

Conceptualization: Luciano Alberto de Castro; Methodology: Luciano Alberto de Castro and Luciano Leite de Castro; Writing original draft, review, and editing: Luciano Alberto de Castro, Satiro Watanabe and Luciano Leite de Castro; Investigation: All Authors; Supervision: Luciano Alberto de Castro.

Conflict of interest

The authors declared no conflict of interest.

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