Multiple myeloma: a clinical case report

Mieloma múltiplo: relato de caso clínico

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ABSTRACT

Objective: To report and discuss the clinical and histopathological findings of a case of multiple myeloma in the jaw region. Case Report: A 58 year old female patient came to UNIPAR Dentistry School complaining of "increased volume on the left side of the face". On physical examination it was observed intact mucosa with buccal cortical expansion in the region of the teeth 34/35/36 and asymptomatic. Radiographic examination revealed a radiolucent area approximately 25 mm in diameter. An incisional biopsy was performed and the histopathological diagnosis was suggestive of plasmacytoma/multiple myeloma, and after finding other lesions it was confirmed as multiple myeloma. The patient was then referred to a hematologist who, together with the oncologist, established the treatment. Conclusion: Although treatment is a medical responsibility, the dental surgeon has an important role in the early diagnosis of this disease, since some of its first clinical and radiographic findings are related to the maxillomandibular complex.

Keywords: malignant neoplasms; plasmacytoma.

RESUMO

Objetivo: Relatar e discutir sobre os achados clínicos e histopatológicos de um caso de mieloma múltiplo na região dos maxilares. Detalhamento do caso: Paciente do gênero feminino com 58 anos de idade, procurou o Curso de Odontologia da UNIPAR com queixa de "aumento de volume do lado esquerdo da face". Ao realizar-se o exame físico observou-se mucosa íntegra com expansão da cortical vestibular na região dos dentes 34/35/36 e assintomática. No exame radiográfico observou-se área radiolúcida com cerca de 25 mm de diâmetro. Foi realizada a biópsia incisional e o diagnóstico histopatológico sugestivo de plasmocitoma/mieloma múltiplo e após achado de outras lesões confirmou-se como sendo mieloma múltiplo. A paciente foi então encaminhada a um médico hematologista que em conjunto com o oncologista estabeleceram o tratamento. Conclusão: Apesar de o tratamento ser de responsabilidade médica, o cirurgião-dentista tem papel importante no diagnóstico precoce dessa doença, uma vez que alguns dos seus primeiros achados clínicos e radiográficos estão relacionados ao complexo maxilo-mandibular.

Palavras-chave: neoplasias malignas; plasmocitoma.
INTRODUCTION

Multiple myeloma (MM) is a malignant disease characterized by spinal cord infiltration with plasmocytes derived from an anomalous clone, supported by prominent angiogenesis (SALEMA; DE CARVALHO, 2019; SOUSA et al., 2020), which is anchored in growth-stimulating factors of the endothelium and fibroblasts, associated with the action of adhesion molecules, interleukins (IL), factors boosting the growth of granulocytes and monocytes and tumor necrosis factor-alpha (BITTENCOURT et al., 2004).

Factors predisposing to the development of MM include exposure to ionizing radiation and hair dyes, certain occupations (farm workers), benzene, and petroleum products, although causality is not strongly proven. With regard to family history of the disease, the presence of cases in first-degree relatives increases the risk of developing the disease by about two times (DOS SANTOS et al., 2022).

It is a malignant tumor that develops in the bone marrow and causes disseminated bone destruction (SALEMA; DE CARVALHO, 2019). Although any bone may be affected, the maxillary bones' involvement is reported in 30% of the cases (NEVILLE; DAMM; WHITE, 2004). The disease represents about 1% of all malignancies and is considered the second most common onco-hematological disease globally, second only to lymphomas and reaching 10-15% of cases (NEVILLE; DAMM; WHITE, 2004; SALEMA; DE CARVALHO, 2019).

The estimated incidence of new cases of Multiple Myeloma in the United States is approximately 32,270 cases, corresponding to 1.8% of malignancies, with continued growth in both females and males (SIEGEL et al., 2020). Its prevalence is higher from the fifth decade of life, rarely occurring before 40 years of age, and men are slightly more affected than women being the black race twice as affected as white (BITTENCOURT et al., 2004).

According to information available by Oncologia Brasil on its own website in the year 2019, the most prevalent average age of MM carriers was 63 years, being mostly male (VO et al., 2019). Of the individuals who have MM, about 66% have no symptoms, or present nonspecific symptoms, which causes the diagnosis to be based on clinical signs, making it often incorrect. Because of this, it is important that the professionals involved in the investigation are aware of the clinical and laboratory characteristics of the disease. And it is because of the lack of multi-professional knowledge that cases are usually diagnosed at an advanced stage (SALEMA; DE CARVALHO, 2019).

Of those who are symptomatic, 58% have constant bone pain. Bone pain is the most characteristic present symptom, being the pelvis, skull, sternum, ribs, clavicles, and jaws, the places that can be affected (COELHO et al., 2020). The bone can be resorbed, leading to excessive calcium in the blood, central or peripheral nervous system deficiencies, and loss of sensation and mobility (MILANI; FERNANDES, 2018). Most cases progress with severe anemia and renal
failure (SALEMA; DE CARVALHO, 2019). Fever may be present due to neutropenia, which increases susceptibility to infections (MILANI; FERNANDES, 2018; COELHO et al., 2020).

Patients with MM are at high risk for thromboembolic complications, mainly related to patient factors (age, comorbidities, immobility), intrinsic factors of the disease (pro-thrombotic effects of monoclonal components secreted into the blood and the hypercoagulable environment generated by the tumor) and factors related to the treatment (immunomodulatory drugs, corticosteroids, chemotherapy). The main adverse events include deep vein thrombosis, central venous catheter thrombosis, pulmonary thromboembolism, and superficial vein thrombosis (FOTIOU et al., 2016).

The recognition of myeloma first occurred in 1844, and since then the presence of the abnormal protein has been linked to bone destruction. Only recently, however, have the mechanisms involved in the process been determined. The first clue was the presence of myeloma cells and a high number of osteoclasts at the sites of bone destruction. The study of mechanisms evolved from the observation that myeloma cells produce osteoclast-activating factors (FAOs) to the characterization of local cytokines such as IL-1β, IL-6, and TNF-α and β, chemokines such as MIP-α, and cell-cell adhesion processes involving αvβ3-integrin, all of which are important in increasing osteoclast production and activity. Following this, a substance called RANK ligand (RANK L) has been identified as a key mediator for osteoclast activation. Studies are being conducted to evaluate the clinical efficacy of specific RANK L inhibitors (RANK.Fc and osteoprotegrin [OPG]), which have shown promise in laboratory examinations and preliminary clinical trials. In addition to osteoclast activation, osteoblast inhibition also occurs, which is another important feature of bone disease. The balance between osteoclast and osteoblast function is responsible for normal bone repair and remodeling, which is disrupted in cases of myeloma (ACQUAH et al., 2019).

Microscopically, a monocyte infiltration of cells with a plasma cell profile is observed. Differentiation is variable, but the positioning of the nucleus eccentrically is usually suggestive of the diagnosis. Besides, it is observed mitotic figures and atypical nuclei (NEVILLE; DAMM; WHITE, 2004).

MM is considered an incurable disease, but it is treatable. It is common that its carriers present modifications in the production of other blood cells, being observed alterations in the hemogram, such as anemia, thrombocytopenia and leukopenia (DOS SANTOS et al., 2022; VO et al., 2019; MILANI; FERNANDES, 2018).

The treatments available for this neoplasm involve chemotherapy, radiotherapy, interferon-alpha (as maintenance treatment), bone marrow transplantation and peripheral stem cell transplantation (PSCT), peripheral stem cell collection, plasmapheresis, symptom control regimens such as drug administration to control hypercalcemia, bone destruction, pain, and infections (SOUZA et al., 2004).
Salema and De Carvalho (2019) describe that a standard way to assess tumor burden is to analyze bone marrow cells, as it is also an indicator of prognosis and treatment response. Circulating plasma cells (CPC) also have prognostic value in MM, as they show the timing of tumor progression. The morphology of circulating plasma cells, LDH and C-reactive protein are risk factors for survival. Thus, the objective of this study is to present a case of a 58-year-old female patient who sought the Dentistry Course of UNIPAR complaining of "increase on the left side of the face".

MATERIALS AND METHODS

This rare case report was submitted to the Ethics Committee of Paranaense University (UNIPAR) and approved under the number of CAAE: 40167020.0.0000.0109.

CASE REPORT

Patient M.M.F, female, 58 years old, married, leucoderma, from the city of Foz do Iguaçu, state of Paraná, sought the Dentistry Clinic of the Paraná University (UNIPAR), campus of Cascavel city, state of Paraná, complaining of an increase in volume on the left side of the face that hindered the adaptation of her prosthesis (removable partial dentures). When performing the physical examination, the patient presented intact mucosa with an expansion of the vestibular cortical in the teeth region 34/35/36, asymptomatic (figure 1).
Figure 1. Physical exam

Source: the authors (2023).

Radiographic examination was performed, in which the radiolucent area on the body of the left mandible was evidenced; the diameter was about 25 mm, without clear edges (figure 2).
**Figure 2.** A panoramic x-ray of the mandible.

Source: the authors (2023).

An incisional biopsy was then performed with the patient's consent and authorization due to the risk of possible paresthesia of the inferior and mentonian alveolar nerve, which was close to the lesion (figure 3). The material was sent for histopathological examination, which observed the presence of foci of plasmacytoid cells with moderate atypia and areas of resorptive trabecular bone tissue, which allowed the diagnosis of multiple myeloma to be established (Figures 4a and 4b). After the diagnosis, the patient was referred to the oncologist and hematologist.
Figure 3. View of the lesion at the time of the incisional biopsy.

Source: the authors (2023).
Figure 4a. Atypical plasmacytoid cells (400x) (a)

Source: the authors (2023).
Figure 4b. Atypical plasmacytoid cells in greater proximity (1000x) (b)

Source: the authors (2023).

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DISCUSSION

Several strategies can be applied to patients with multiple myeloma to minimize the disease's complications (MELO et al., 2005). Significant advances include the prevention and treatment of hypercalcemia and bone injuries, pain control, and, in some cases, a decrease in the incidence of pathological fractures (BITTENCOURT et al., 2004; ACQUAH et al., 2019). In the evolution of multiple myeloma, neoplastic lesions are initially restricted to bone and bone marrow, with late extramedullary involvement; this behavior reflects the natural history of B-cell neoplasia, with preliminary involvement of lymph nodes and bone marrow and subsequent dissemination to other organs and skin (SOUSA et al., 2019). In this clinical case, we observed that the primary lesion was located in the mandible, which is in accordance with the literature that
demonstrates that the jaws are affected in 30% of cases, with the mandible being the preferred site in this region (NEVILLE; DAMM; WHITE, 2004).

Although the literature is unanimous with regard to pain as the most characteristic symptom of such pathology (NEVILLE; DAMM; WHITE, 2004; SOUZA et al., 2004; LASKARIS, 2004), the patient in question did not present painful symptoms. A striking feature is the presence of resorption points in the skullcap; this was one of the findings in the case described, which allowed the disease to be defined as multiple myeloma and not plasmacytoma, which refers to the manifestation of the exclusive disease in a bone.

Multiple myeloma is a complication that is difficult to treat because it involves several bones and metabolic changes, has a dismal prognosis, and may be uni or multifocal (DOMINGOS, et al., 2020). It is a neoplasm that triggers many other diseases, such as kidney failure, infections in the urinary tract, respiratory, bloodstream, among others (SALEMA; DE CARVALHO, 2019).

A recent review showed that a high percentage of MM patients have severe anemia, probably due to advanced MM disease and renal impairment. The results also showed a significant increase in creatinine (ACQUAH et al., 2019).

The case reported is a localized lesion in the jaws, and we opted for biopsy and histopathology to define the diagnosis. But it is also important to evaluate the prognosis in these cases, and one factor to consider is serum lactate dehydrogenase (LDH), as a result of the reversible conversion of muscle lactic acid into pyruvic acid, this change being accomplished by the catalysis of LDH, and is found in various tissues of the human body and only a lesion characterized by cells can raise the levels of this marker, Unfortunately, it was not possible to determine the value of LDH in this patient, but other reports show that although LDH is predictive of prognosis, in some situations its values may permeate within the reference for normality, indicating that this enzyme has limited diagnostic value (DOS SANTOS et al., 2022).

In case of any symptoms, medical imaging and laboratory tests must be performed. Surgery can be used to shrink or remove tumors, repair bone changes, and reduce pain. A range of pain medications and procedures are available to relieve discomfort (SALEMA; DE CARVALHO, 2019). Therefore, it is a disease that can be treated and controlled for a long time, and the patients can have a quality of life, with little interrupted activities, if their treatment and follow-up are carried out correctly.

It is also important to emphasize that in clinical practice, in elderly patients presenting with anemia, bone pain, spinal cord compression syndrome and/or renal failure, the possibility of multiple myeloma should be investigated, allowing diagnosis and early initiation of treatment. Therefore, it is known that an effort to better disclose MM in our environment is urgent, since early diagnosis has an impact in terms of survival and in reducing the progression of symptoms (COELHO et al., 2020; ACQUAH et al., 2019).
Considering that the impaired function of the various types of immune cells ends up favoring the dissemination of the tumor and, consequently, its growth, in recent years researchers have dedicated themselves to the study of immunotherapy using dendritic cells, natural killer cells, and genetically engineered T-cells represent a new therapeutic era. The application of these treatments is growing rapidly, based on their capacity to eradicate MM (VO et al., 2019).

CONCLUSION

Multiple myeloma is a malignant neoplasm whose involvement is beyond the oral cavity. This disease requires multi-professional diagnosis; however, because it has a high prevalence in the jaws, dentists need to know about this disease because they need to establish the diagnosis, which is crucial for greater speed and effectiveness in the treatment of this pathology.

Ethic
This study was carried out in accordance with the principles of the Ethics Committee Statement under CAAE number: 40167020.0.0000.0109.

Author Contributions
All authors contributed to the design of the study, analysis, and interpretation of the results and conclusions. All authors critically revised the manuscript, gave final approval, and agreed to be accountable for all aspects of the work.

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Conflict of Interest
The authors declare no conflict of interest.
REFERÊNCIAS


