



MANDIBULAR OSTEOSARCOMA: PRESENTATION OF A CHALLENGING CASE INITIALLY MISDIAGNOSED AS MOLAR PERICORONITIS

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ABSTRACT Osteosarcomas are malignant tumors characterized by the formation of osteoid matrix. They are mainly located in the long bones, and rarely (10%) in the head and neck region – only limited data on such lesions being available in the literature. A number of clinical presentations resembling periapical or cement-bony lesions have been documented, with radiologically subtle or manifest tumor growth. No standardized treatment protocol has been established for osteosarcoma of the head and neck unlike that it affects the long bones. It seems that radical surgery could be the treatment chosen because of its rapid advance and high potential for recurrence. The present article describes a case of mandibular osteosarcoma initially misdiagnosed and treated as lower third molar pericoronitis, emphasizing that the prognosis is related to the timely diagnosis of this neoplasm, that is why we emphasize the role of the dentist to quickly investigate the early clinical signs that could make us suspect that a malignancy is developing.

KEYWORDS : Osteosarcoma, mandibular neoplasms, malignant bone tumor, pericoronaritis.

Introduction

Osteosarcoma (OS) is a rare and aggressive bone malignancy characterized by the production of osteoid matrix. It generally develops in the long bones of young individuals between the third and fourth decade of life, and accounts for 15-20% of all primary bone tumors (1). Nearly 10% of all OS develop in the head and neck – this location being unusual in comparison to other locations (2). The mandible is the most commonly affected location, followed by the maxilla, with a similar distribution between sexes (3).

The underlying etiology has not been fully elucidated, though a number of predisposing factors have been described, such as radiotherapy administered as treatment for other malignancies. Paget's disease has also been associated to an increased susceptibility to such tumors, being observed in about 1% of all cases of OS, and with a higher incidence in elderly adults (4). Within its pathogenesis, it has been shown that there is a genetic mutation in p53, RB1 and chromosome 21q (2,3). OS has been associated to fibrous dysplasia, and there have also been less frequent reports linking it to chronic local trauma (4,5). OS of the jaws clinically manifests as a local increase in volume, sometimes accompanied by ulceration, and with possible pain and paresthesia (5). An early sign is tooth mobility or widening of the periodontal ligament space, without associated periodontal disease or other clinical manifestations. (6,7).

Due to its low prevalence and scarce report in the literature, the treatment of maxillary of OS has not been standardized, in contrast to the case of tumors of the long bones (1-4). The gold standard preferred management approach is described as complete surgical resection of the tumor, with adequate safety margins, and radiotherapy or chemotherapy can be applied on a coadjuvant basis in cases where tumor resection is incomplete (8,9). The prognosis of OS of the head and neck tends to be favorable in comparison with OS of the long bones, provided early diagnosis and treatment is established. Nevertheless, the 5-year survival rate is approximately 60% (10). The present article describes a case not reported in the literature of highly malignant mandibular chondroblastic osteosarcoma initially misdiagnosed and treated as molar pericoronitis.

Clinical case

A 19-year-old female with no relevant history of disease was referred to the Department of Oral and Maxillofacial Surgery due to a recently developing (8 weeks) painful swelling in relation to the last right

mandibular molar (tooth 4.8). She had received antibiotic treatment (amoxicillin-clavulanic acid 500/125 mg) and nonsteroidal antiinflammatory medication (ibuprofen 600 mg) for acute pericoronitis in relation to tooth 4.8, with a good initial response.

In his anamnesis, he has no history of neoplasms and in his personal habits he does not smoke, alcohol or drugs. The physical examination showed a normal facial appearance, without asymmetries, and with no palpable submaxillary adenopathies. Intraorally we identified a pediculate tumor mass of rubbery consistency, with clearly defined limits and circumscribed distally to tooth 4.7. The lesion was adhered to the pericoronal portion of tooth 4.8 and measured approximately 1 cm in diameter (Figure 1). The panoramic radiographs showed a semi-impacted tooth 4.8 with mild mesioversion and no evidence of radiopaque or radiotransparent lesions (Figure 2). On the basis of the clinical- radiologic appearance and symptoms, we postulated a differential diagnosis comprising ossifying fibroma, peripheral giant cell granuloma, or infected paradental cyst. Hematological tests within normal parameters without qualitative alteration. Outpatient surgery under local anesthesia partial removal (incisional biopsy) of the lesion was decided, with the extraction of tooth 4.8, previous informed consent.

The microscopic study showed an inflamed pericoronal sac with a proliferative cellular infiltration characterized by cell atypias, hyperchromatic nuclei and numerous mitotic figures. The histopathological diagnosis was highly malignant mandibular chondroblastic osteosarcoma (Figure 3). The oncological committee decided mixed multimodal treatment in the form of neoadjuvant chemotherapy plus surgery, with coadjuvant chemotherapy. After three initial chemotherapy cycles, surgical resection of the right mandibular body and ramus was carried out (Figure 4), with negative bone margins. A further three cycles of coadjuvant chemotherapy were administered after surgery.

The patient returned 6 months later with signs of lesion relapse. Radical surgery in the form of a hemimandibulectomy was proposed but rejected by the patient, who only accepted coadjuvant radiotherapy plus chemotherapy. The patient finally died 1.5 years after this last treatment, secondary to local invasive growth of the disease.

Discussion

Osteosarcoma is a very rare primary malignancy affecting 1:1,000,000

individuals annually (11,12). It accounts for approximately 20% of all sarcomas and is typically found in the growth zones of the long bones in individuals between 15-30 years of age, and approximately 6-13% of all OS are located in the maxillofacial region (1,3). The biological behavior of tumors located in the maxillas differ from that of the malignancies of the long bones, with an older patient age at onset (third and fourth decade), a lesser metastatic potential (9,11), longer survival, and a high rate of local recurrences that are difficult to control (1).

The tumor is clinically characterized by swelling, pain, dental mobility and displacement, and paresthesia. A radiopaque, radiotransparent or mixed appearance can be observed in the conventional radiological study, in some cases exhibiting a sun ray pattern. Widening of the periodontal ligament space and/or root resorption can be seen in the case of tumors related to teeth (8). It is important to mention that in some cases OS has been initially confused with other disorders such as cement-bone or periapical lesions (13,14). A careful differential diagnosis is therefore required, avoiding inappropriate treatments as in this case, which delay the definitive diagnosis and worsen the clinical situation.

The tumor can be histologically classified as osteoblastic, chondroblastic or fibroblastic. The chondroblastic form is the most common presentation, representing 41% of all cases, followed by the osteoblastic and fibroblastic tumors (33% and 26%, respectively) (15). Chondroblastic lesions are characterized by a predominance of cartilage tissue with marked cellular atypia and growth in the form of cell islets, while osteoblastic tumors produce abundant osteoid tissue. Fibroblastic lesions are the least common presentation of OS and are characterized by abundant filamentous cells similar to those seen in fibrosarcoma. Our case was consistent with the chondroblastic variant.

With regard to the complications of OS, local recurrence has been reported in 33% of all patients subjected to surgical treatment. Distant metastatic spread in maxillary OS is infrequent, occurring in about 18% of all cases – this representing a distinguishing feature with respect to OS of the long bones (7).

The low incidence of this type of tumor has precluded the definition of a standard treatment protocol. Nevertheless, the literature describes multimodal management in which radical surgery, accompanied by chemotherapy, appear to be the central elements of patient care (5).

Although in the beginning the patient was presented with a radical surgery (hemimandibulectomy) with delayed reconstruction, it was rejected from the beginning by eventual aesthetic and functional deformations, which could have positively modified the prognosis of the disease. Because the mandibular bone tissue had a normal appearance in the tomography without invasion and involvement of the basilar edge, an alternative multimodal treatment consisting of neoadjuvant chemotherapy, segmental surgery and adjuvant chemotherapy was indicated as an alternative. Due to its high recurrence rate and local aggressiveness of this neoplasm, it is recommended that we perform a radical surgery from the beginning. The prognosis is variable but is mainly conditioned to early diagnosis and opportune treatment, disease-free resection margins, the presence or absence of micrometastases, and the efficacy with which these are controlled (4).

It is important to mention that the prognosis is related to the timely diagnosis of this neoplasm, that is why we emphasize the role of the dentist to quickly investigate these lesions in early stages that may suspect that a malignancy is developing.

Conclusions

It is important to establish differential diagnoses and apply complementary tests to avoid a delay in the definitive diagnosis and worsen the patient's clinical condition. An early and timely diagnosis could have favorably changed the patient's prognosis, so we emphasize the role of the dentist in screening these lesions in early stages that may have incipient clinical signs, in order to perform treatments in the early stages, thus not compromising the patient's life.

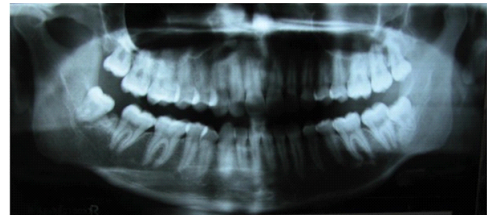
The low incidence of oral OS has hindered the standardization of the treatment protocol, however, due to its aggressiveness and high rate of recurrence and low metastatic potential, radical surgical treatment with or without chemotherapy seems to be indicated.

Figure 1.



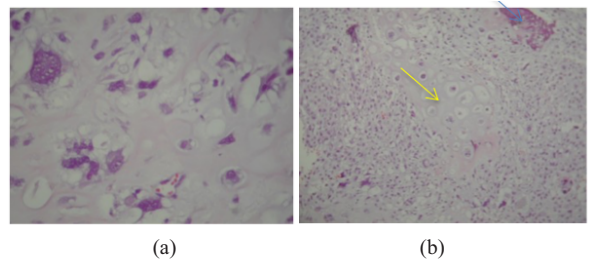
Note the increase in volume in quadrant 4, with dental imprints from the upper arch. A pediculate tumor mass of rubbery consistency was observed, with clearly defined limits and circumscribed distally to tooth 4.7. The lesion was adhered to the pericoronal portion of tooth 4.8 and measured approximately 1 cm in diameter. The buccal and lingual cortical layers were preserved, with no occupation of the vestibular zones.

Figure 2.



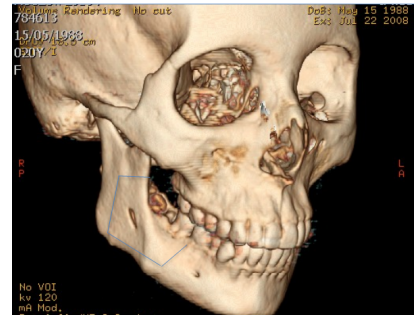
Panoramic radiograph showing a semi-impacted tooth 4.8 with mild mesioversion (Pell and Gregory class 2B). Note the mild widening of the periodontal space corresponding to the mesial root of tooth 4.8.

Figure 3.



(a) Histological view showing a proliferative cellular infiltration with abundant cell atypias, hyperchromatic nuclei and numerous mitotic figures. (b) Some areas exhibit a cartilaginous appearance (yellow arrow), while others show osteoid tissue formation (blue arrow).

Figure 4.



(a) Three-dimensional reconstruction of the computed tomography scan. Initial marginal osteotomy design at first surgery. Resection of the right mandibular body and ramus to the right first lower molar was carried out, with a 2 cm safety margin. Note the mild buccal cortical involvement.



(b) Axial computed tomographic view showing continuity, without interruption at lingual cortical level. No soft tissue invasion of the parapharyngeal space is observed.

Reference:

- 1-. Pardhe ND, Jamdade A, Bajpai M, et al. Giant Osteosarcoma of the Mandible. *J Coll Physicians Surg Pak.* 2017 Sep;27(9):S117-S119.
- 2-. Asioli S, Righi A, Rucci P, et al. p16 protein expression and correlation with clinical and pathological features in osteosarcoma of the jaws: Experience of 37 cases. *Head Neck.* 2017 Sep; 39(9): 1825-31.2
- 3-. Chaudhary M, Chaudhary SD. Osteosarcoma of jaws. *J Oral Maxillofac Pathol.* 2012;16:233–238.
- 4-. Nthumba PM. Osteosarcoma of the jaws: a review of literature and a case report on synchronous multicentric osteosarcomas. *World J Surg Oncol.* 2012;10:240
- 5-. Chittaranjan B, Tejasvi MA, Babu BB, Geetha P. Intramedullary osteosarcoma of the mandible: a clinicoradiologic perspective. *J Clin Imaging Sci.* 2014;31:4–6.
- 6-. Soares RC, Soares AF, Souza LB, et al. Osteosarcoma of mandible initially resembling lesion of dental periapex: case report. *Rev Bras Otorrinolaringol.* 2005;71:242–245.
- 7-. Yamamoto-silva FP, Silva BS de F, Batista AC, et al. Chondroblastic osteosarcoma mimicking periapical abscess. *Journal of Applied Oral Science.* 2017;25(4):455-461.
- 8-. Arora P, Rehman F, Girish KL, Kalra M. Osteosarcoma of mandible: Detailed radiographic assessment of a case. *Contemp Clin Dent.* 2013 Jul;4(3):382-5.
- 9-. Paparella ML, Olvi LG, Brandizzi D, et al. Osteosarcoma of the jaw: an analysis of a series of 74 cases. *Histopathology.* 2013;63:551–557.
- 10-. Ferrari D, Codecà C, Battisti N, et al. Multimodality treatment of osteosarcoma of the jaw: a single institution experience. *Med Oncol.* 2014 Sep;31(9):171.
- 11-. van den Berg H, Merks JH. Incidence and grading of cranio-facial osteosarcomas. *Int J Oral Maxillofac Surg.* 2014 Jan;43(1):7-12.
- 12-. Praveena NM, Maragathavalli G. Osteosarcoma of maxilla. *J Indian Acad Oral Med Radiol.* 2012;24:236–238.
- 13-. Fang Z, Jin S, Zhang C, et al. Misdiagnosis of osteosarcoma as cementoblastoma from an atypical mandibular swelling: A case report. *Oncol Lett.* 2016 Jun;11(6):3761-3765.
- 14-. Almeida E, Mascarenhas BA, Cerqueira A, et al. Chondroblastic osteosarcoma. *J Oral Maxillofac Pathol.* 2014 Sep-Dec;18(3):464-8.
- 15-. Agrawal RR, Bhavthankar JD, Mandale MS, Patil PP. Osteosarcoma of Jaw with Varying Histomorphologic Patterns: Case Report. *Journal of Orthopaedic Case Reports.* 2017;7(1):61-64.