

## Multilobular Tumor of Bone in Bitches: Clinical, Histopathological, Immunohistochemical and Overall Survival Aspects

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### ABSTRACT

**Background:** Multilobular tumor of bone (MTB) is an unusual neoplasm with variable biologic behavior which originates primarily in bone tissues. Radiographs computed tomography (CT), and magnetic resonance imaging (MRI) are useful in diagnoses and surgical planning. Tumor removal with wide surgical margins is the treatment of choice. Immunohistochemistry has been shown as an important tool in veterinary oncology to define therapeutic and prognostic decisions. The goal of this study was to report 2 distinct cases of multilobular tumor of bone, their Cox-2 and Mib-1 immunohistochemical profile and its impact on overall survival.

**Case:** Two bitches were presented at the Oncology Department of the Veterinary Hospital in the Veterinary School of Universidade Federal de Minas Gerais (UFMG). Both had a history of a progressive, painless, circumscribed, and firm facial mass. The 1<sup>st</sup> patient was a 8-year-old intact bitch mixed breed, weighing 50 kg, that presented a fast growing right infraorbital 3-cm mass, causing eye displacement. The 2<sup>nd</sup> patient was a 7-year-old spayed bitch Labrador retriever, weighing 28 kg, that presented a left temporal 8-cm mass. Neurologic examination of both bitches was normal. Skin over the nodules was strained, but with no ulceration. Radiographic exams of the head revealed lytic and proliferative bone reaction, with loss of cortical definition in both cases. These alterations were seen on the left zygomatic arch of the retrobulbar region, involving part of the mandible and of the nasal sinus lateral frontal bone in 1<sup>st</sup> patient, and on the right temporal process of the zygomatic bone in 2<sup>nd</sup> patient. The last one, also showed a granular solid mass with little contact with skull bones. Complete blood count, biochemistry profile, electrocardiogram, and 3-view thoracic radiographs were performed. Results were within normal ranges for the species and no signs of metastasis was seen on the radiographs. Location, size, and density of the mass, adjacent tissue compression, absence of cranial invasion, and lymph node size were rigorously evaluated with CT, allowing an individualized surgical planning to achieve complete mass removal and maintenance of the function of adjacent structures. Both animals were submitted to surgery. Both tumors were fixed on 10% neutral buffered formalin and sent to the Animal Pathology Department of UFMG for histopathological examination and margin assessment. Both tumors were diagnosed as grade I MTB. Tumor immunohistochemistry was performed to identify prognostic factors that could be used to better define therapeutic treatments and to try to clarify the discrepancy in disease progression between both tumors. The 1<sup>st</sup> patient expressed 20% of Mib-1 and was considered score 2 of Cox-2. The 2<sup>nd</sup> one expressed 5% of Mib-1 and was considered score 1 of Cox-2. Considering the diagnoses and histological characteristics of the tumors, it was decided for clinical follow-up of patients without additional therapeutic complementation. Even considering incomplete surgical margins in 2<sup>nd</sup> patient, adjuvant chemotherapy was not performed, due to low mitotic index and low histological grade. The 1<sup>st</sup> patient had an overall survival of 240 days, and death was due to recurrence and disease progression; and the 2<sup>nd</sup> did not show recurrence nor metastasis after 1200 days.

**Discussion:** Proper and individualized surgical planning and histopathological evaluation are extremely important to guide treatment decisions. However, immunohistochemistry can be important in MTB cases, to help define which patients should be submitted to surgery alone and which patients could be benefited from adjuvant chemotherapy.

**Keywords:** MTB, Cox-2 and Mib-1 profile, neoplasm, tumor, oncology, canine, dog, bone tissues.

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## INTRODUCTION

Multilobular tumor of bone (MTB) is an unusual neoplasm which originates primarily in bone tissues. It is frequently located on the skull. This slow growing, locally invasive tumor has the potential to compress and invade the brain [12]. MTB can metastasize to the lungs late in the course of the disease, and pulmonary metastatic nodules are normally small and clinically silent [6].

Due to its invasive growth, direct infiltration to adjacent structures is a common finding in patients with MTB [5,8], neurologic signs, nasal sinus obstruction, impaired mastication, exophthalmia, and face and head disfiguration can occur depending on the location of the protruding mass [8,10].

Radiographs, computed tomography (CT), and magnetic resonance imaging (MRI) are useful in diagnoses and surgical planning [5].

The goal of this study was to report 2 distinct cases of multilobular tumor of bone, their Cox-2 and Mib-1 immunohistochemistry profile and its impact on overall survival.

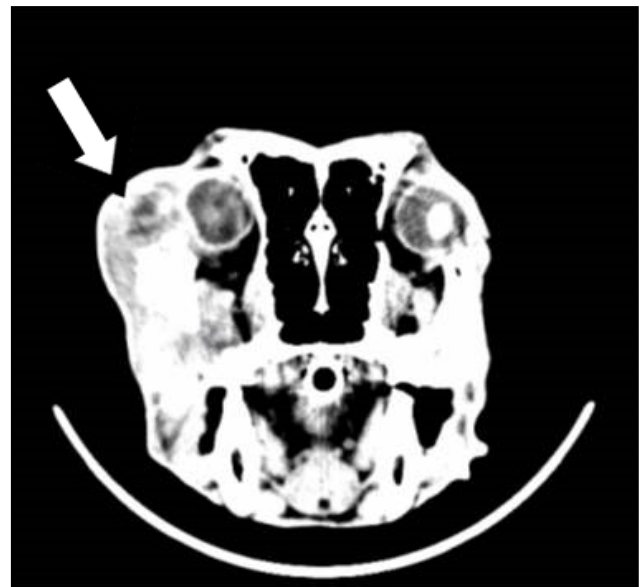
## CASES

**Case 1.** A 8-year-old intact bitch mixed breed, weighing 50 kg, that presented a fast growing right infraorbital 3-cm mass, causing eye displacement was presented at the Oncology Department of the Veterinary Hospital in the Veterinary School of Federal University of Minas Gerais (UFMG) with a history of a progressive, painless, circumscribed, and firm facial mass.

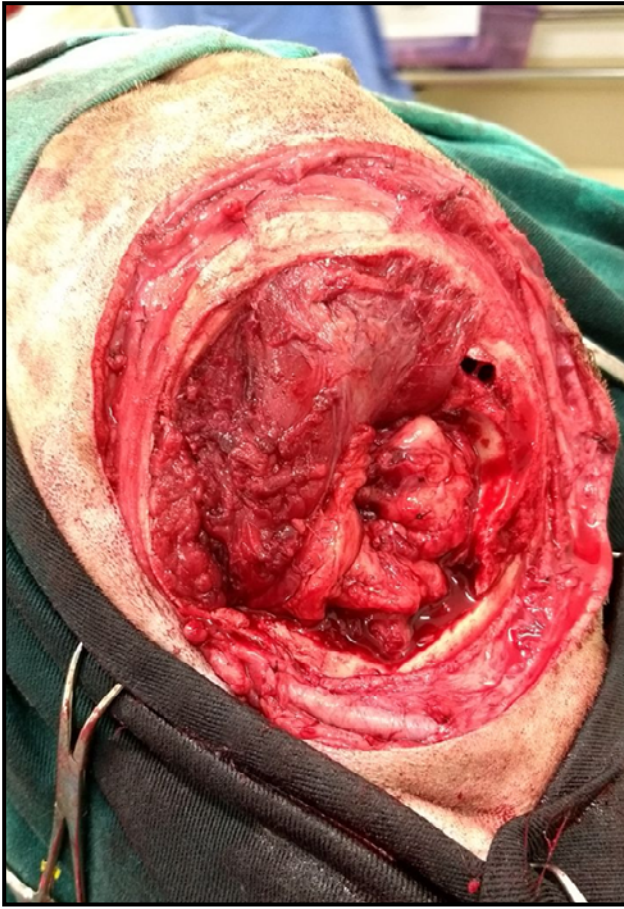
Neurologic examination was normal. Skin over the nodules was strained, but with no ulceration. Radiographic exams of the head revealed lytic and proliferative bone reaction, with loss of cortical definition. These alterations were seen on the left zygomatic arch of the retrobulbar region, involving part of the mandible and of the nasal sinus lateral frontal bone. Complete blood count, biochemistry profile, electrocardiogram, and 3-view thoracic radiographs were performed. Results were within normal ranges for the species and no signs of metastasis was seen on the radiographs. CT was performed to assess each mass and its relationship with surrounding tissues. Alkaline phosphatase serum levels were within range. Location, size, and density of the mass, adjacent tissue compression, absence of cranial invasion, and lymph node size were rigorously

evaluated with CT, allowing an individualized surgical planning to achieve complete mass removal and maintenance of the function of adjacent structures. CT showed an invasive mass on the right zygomatic bone, most evident on the maxillary portion, associated with ipsilateral eye displacement (Figure 1). The mass had hypo attenuated and hypo permeative areas after contrast injection. Bone trabeculation changes with lytic areas and irregular bone proliferation were seen on the invasive bone lesion. Due to the compressive and invasive characteristic, an elliptical incision was performed around the right eye, with a 2-cm margin around the tumor to perform an osteotomy of zygomatic, maxillary, and temporal bones (Figure 2). Enucleation was necessary because of periorbital muscular invasion, for an *en bloc* resection (Figure 3).

The tumor was fixed on 10% neutral buffered formalin and sent to the Animal Pathology Department of UFMG for histopathological examination and margin assessment. The tumor was diagnosed as grade I MTB, according to the criteria proposed by Dernell *et al.* [3]. The tumor was characterized as a partially encapsulated poorly delimited bone tumor, arranged in lobes separated by septa of well-differentiated collagenous connective tissue with abundant blood vessels. The center of the lobes consisted of predominantly non-mineralized immature chondroid and osteoid matrix forming trabeculae. There is polygonal cellular proliferation between the trabeculae, with indistinct cell borders, round to oval nuclei, sparse chromatin,



**Figure 1.** Computed tomography showed lesion in the lower orbit (arrow) due to tumor infiltration up to the zygomatic bone (Case 1).



**Figure 2.** An elliptical incision around the right eye, with a 2-cm margin around the tumor to perform an osteotomy of zygomatic, maxillary, and temporal bones (Case 1).

prominent nucleoli, and intense anisokaryosis. There is also numerous multinucleated cell (osteoclasts). No mitotic figures were seen. Cavities filled with erythrocytes and some osteoclasts, lined with osteoblasts and osteoid matrix were visualized. Surgical margins were considered histologically clean. Considering the diagnoses and histological characteristics of the tumor, it was decided for clinical follow-up of patients without additional therapeutic complementation. The dog had an overall survival of 240 days, and death was due to recurrence and disease progression. Patient showed metastatic foci in many organs, such as lungs, liver, and kidneys.

**Case 2.** A 7-year-old spayed bitch Labrador retriever, weighing 28 kg, that presented a left temporal 8-cm mass was referred to the Oncology Department of the Veterinary Hospital in the Veterinary School of Federal University of Minas Gerais (UFMG). The patient had a history of a progressive, painless, circumscribed, and firm facial mass.



**Figure 3.** Enucleation, for an *en bloc* resection (Case 1).

Neurologic examination was normal. Skin over the nodules was strained, but with no ulceration. Radiographic exams of the head revealed lytic and proliferative bone reaction, with loss of cortical definition, as the first case. These alterations were seen on the right temporal process of the zygomatic and showed a granular solid mass with little contact with skull bones. Complete blood count, biochemistry profile, electrocardiogram, and 3-view thoracic radiographs were performed. Results were within normal ranges for the species and no signs of metastasis was seen on the radiographs. Alkaline phosphatase serum levels were within range. Location, size, and density of the mass, adjacent tissue compression, absence of cranial invasion, and lymph node size were rigorously evaluated with CT, allowing an individualized surgical planning to achieve complete mass removal and maintenance of the function of adjacent structures. CT showed a hyperdense expansive amorphous irregular tumor with bone like heterogeneity. The mass was multilobulated (“popcorn like”), non-permeant to the contrast medium, and located on the left retrobulbar region. Conservative surgery was performed with a partial orbitectomy through an osteotomy of the articular region of the zygomatic process of the temporal bone and temporal portion of the left zygomatic bone.

The tumor was fixed on 10% neutral buffered formalin and sent to the Animal Pathology Department of UFMG for histopathological examination and margin assessment. The tumor was diagnosed as grade I MTB, according to the criteria proposed by Dernell *et al.* [3]. The tumor was characterized as a non-encapsulated bone tumor forming coalescent nodules. Center of the nodules consisted of mineralized osteoid matrix and the border showed well-differentiated osteocytes.

No mitotic figures were seen. Surgical margins were considered incomplete. Considering the diagnoses and histological characteristics of the tumor, even incomplete surgical margins, adjuvant chemotherapy was not performed. It was decided for clinical follow-up. The bitch had a good clinical evolution and did not show recurrence nor metastasis after 1200 days. Patient death was unrelated to the tumor.

Tumor immunohistochemistry was performed to identify prognostic factors that could be used to better define therapeutic treatments and to try to clarify the discrepancy in disease progression between both tumors. *Case 1* expressed 20% of Mib-1 and was considered score 2 of Cox-2. *Case 2* expressed 5% of Mib-1 and was considered score 1 of Cox-2 [6].

## DISCUSSION

Both cases presented as locally invasive, solid, and fixed mass in skull bones causing face deformity and adjacent tissue compression, in accordance with literature [12]. *Case 1* had a lesion in the lower orbit due to tumor infiltration up to the zygomatic bone, which shows possible infiltrative tumor growth [8].

Image exams were important for clinical staging and individualized surgical planning. Pathognomonic characteristics such as well-defined borders and coarse granular appearance (“popcorn balls”) were seen on radiographs and CT scan (*Case 2*) [5]. Image exams were important to show differences between both cases regarding tumor appearance and extent; *Case 1* was an infiltrative mass, permeable to contrast medium and *Case 2* had less contact with adjacent bones and was not permeable to contrast medium. Therefore, it was possible to establish the best surgical plan for each patient, with a more aggressive surgery in *Case 1* and a conservative surgery in *Case 2*, while seeking long term disease control [4].

The histological grade criteria [3] are important in MTB and, when in association with clinical history, are useful for treatment decisions, such as not to offer additional therapeutic complementation [11]. However, this can be questioned due to short overall survival seen in *Case 1* patient, even with clean surgical margins and

low histologic grade. Individualized clinical follow-up and immunohistochemistry are important to evaluate the neoplasm and its prognostic factors.

Surgical excision is the best option for tumor control, however local recurrence and metastasis may occur. Therefore, routine follow-up exams were performed, to clinically assess patients and for a better understanding of the biologic behavior of this uncommon neoplasm. *Case 1* patient had clean surgical margins but developed local recurrence and distant metastasis, with a shorter overall survival.

Mib-1 cut-off value for MTB has not been established. A comparison with canine appendicular osteosarcoma, an aggressive and highly metastatic tumor, can be done. Mib-1 values was found of 5.6% to 65.1% when studying appendicular osteosarcoma in dogs. The same author found that animals with Mib-1 values of 20% or higher had a significantly shorter overall survival time when compared with animals with Mib-1 values lower than 20% [1].

When both cases are compared, a relatively high proliferation index is found in *Case 1* tumor (20%), which could explain the poor outcome and short overall survival. The authors believe this patient could have benefitted from adjuvant chemotherapy after surgery, with a longer overall survival and disease-free interval.

Cox-2 expression was not relevant as a prognostic or predictive factor since it showed low values in both cases [6]. However, more studies are necessary to evaluate its relevance as a prognostic factor for MTB.

Proper and individualized surgical planning and histopathological evaluation are extremely important to guide treatment decisions. However, immunohistochemistry can be important in MTB cases, to help define which patients should be submitted to surgery alone and which patients could benefit from adjuvant chemotherapy.

## MANUFACTURER

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