

Chondroblastic osteosarcoma in a feline: a case report

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Abstract

Osteosarcomas are noteworthy as one of the main malignant bone tumors in dogs and cats, comprising an important cause of limb amputation in these species. Literature reports for felines are, however, scarce. Therefore, the aim of the present study was to characterize the clinical and histopathological findings of a chondroblastic osteosarcoma case in a female cat. The chondroblastic osteosarcoma diagnosis was based on radiographic, cytological, histopathological and immunohistochemical findings. Clinical, radiographic, and cytological findings suggested a presumptive osteosarcoma diagnosis, while histopathological and immunohistochemical findings confirmed a chondroblastic osteosarcoma diagnosis.

Keywords: Biopsy; Diagnosis; Immunohistochemistry; Histopathology; Mesenchymal tumors.

Introduction

Malignant bone tumors are important neoplasms in dogs and cats and their diagnosis is often challenging, both from a clinical and pathological point of view. As bone tissue is topographically associated with different types of mesenchymal tissues, lesions that cause localized swelling

may macroscopically suggest different pathological origins such as inflammatory, hyperplastic, or neoplastic processes, which may, in turn, originate in any locomotor system constituent tissue [1,2].

Osteosarcoma is noteworthy as one of the main malignant bone tumors in dogs and cats [3,4], comprising an important cause of limb amputation in

these species. Its occurrence, however, is better documented in canines [1-4] compared to felines. Although there is no precise frequency as to its occurrence in other species, this tumor has been reported both in domestic [1-3,5-7] and wild [8-10] species.

These neoplasms originate in bone tissue and are characterized by osteoid production by malignant osteoblasts, whose matrix quantity and quality can vary considerably between and within tumors [11]. This matrix production variation can be used in tumor subclassification. Therefore, the aim of this study was to characterize the clinical and histopathological findings in a chondroblastic osteosarcoma case in a feline.

Case report

The clinical and anatomo-pathological findings of a chondro-blastic osteosarcoma case in a six-year-old cat, mixed breed, from the metropolitan area of Natal, Rio Grande do Norte, Brazil, were reviewed. The animal exhibited a nodulation about 12.0 cm in length in the right hind limb, accompanied by lameness. At the time of care, radiography and Fine Needle Aspiration (FNA) exams were performed on the affected limb.

A radiographic examination identified periosteal proliferation in the distal portion of the femur, with a

heterogeneous and radiopaque appearance (Figure 1), while the FNA indicated the presence of a malignant mesenchymal cell tumor. Clinical, radiographic, and cytological findings suggested a presumptive osteosarcoma diagnosis. The animal was, thus, submitted to an amputation and the excised limb was sent for a histopathological analysis. Macroscopically, the nodulation measured about 12.0 cm, was covered by skin and the cut surface was irregular and grayish brown.

Post-surgical treatment consisted of antibiotic therapy based on amoxicillin and potassium clavulanate (10mg/kg + 2.5mg/kg) every 12 hours for 15 days. In the anti-inflammatory and analgesic therapy, meloxicam (0.1 mg/kg) was used every 24 hours for 5 days, dipyrone (12.5 mg/kg) every 12 hours for 5 days and tramadol (4 mg/kg) every 12 hours for 7 days.

Nodule fragments were collected and fixed in 10% buffered formalin for histopathological examinations following Tolosa et al. [12]. In addition, 5µm thick paraffin block sections were obtained using a LEICA RM 2125 RT® microtome, adhered to glass slides, and left in an oven at 60 °C overnight for subsequent staining with hematoxylin and eosin (HE). The histological slides were then analyzed under a LEICA DM 500 HD light microscope coupled to a

LEICA ICC50W camera, and images were obtained using the LAS EZ Ink

program.

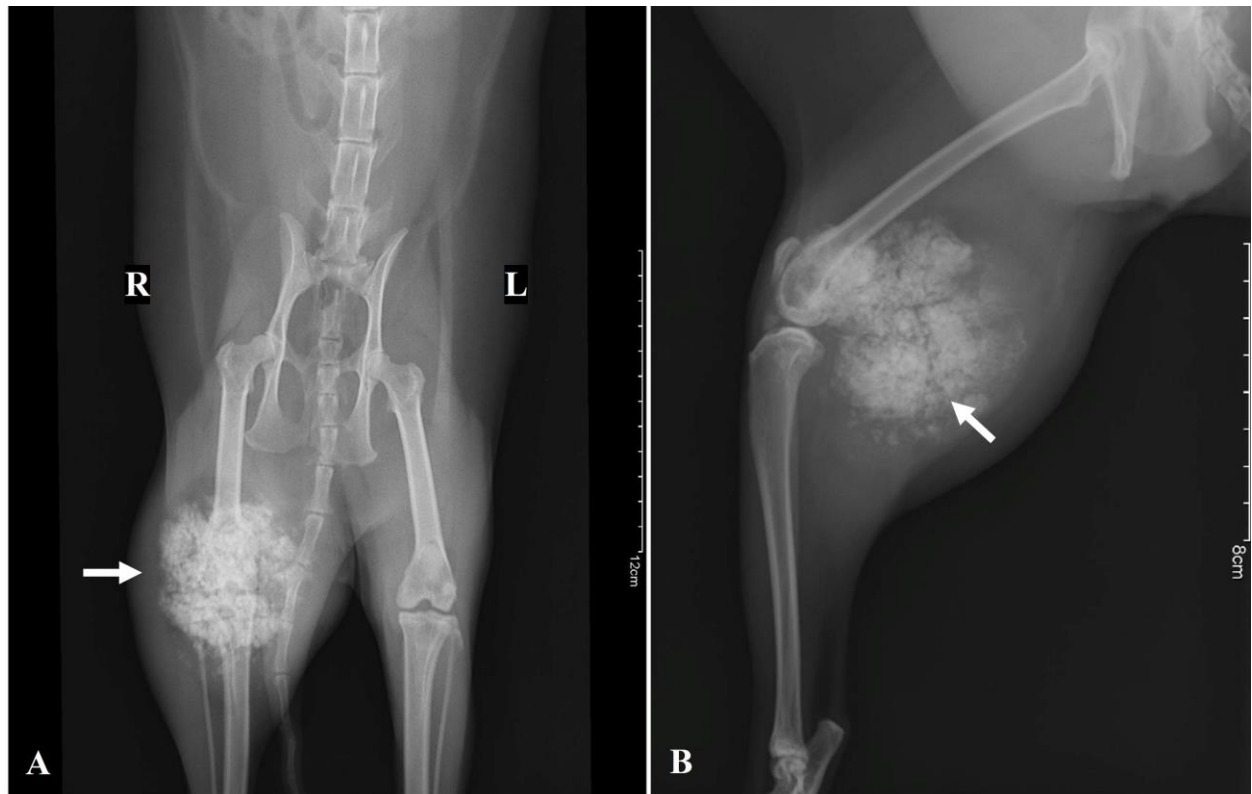


Figure 1. Radiographic examination of a feline with chondroblastic osteosarcoma. A and B: Periosteal proliferation in the distal portion of the right femur, with a heterogeneous and radiopaque appearance (arrows). Right antimer (R), and left antimer (L).

Histopathologically, a lobular mesenchymal neoplastic proliferation presenting expansive growth was noted. The mass was composed of atypical chondrocytes and chondroblasts immersed in a marked amount of chondroid matrix. Some fields exhibited randomly arranged cell bundles containing small osteoid matrix aggregates. Endochondral ossification areas were also

observed, rounded or fusiform, presenting an acidophilic cytoplasm, eventually clear and vacuolated. The nuclei were round, sometimes hyperchromatic, with some-times inconspicuous and sometimes prominent nucleoli. Mild to moderate anisokaryosis and an average of one mitosis per high-power field were also observed (Figure 2).

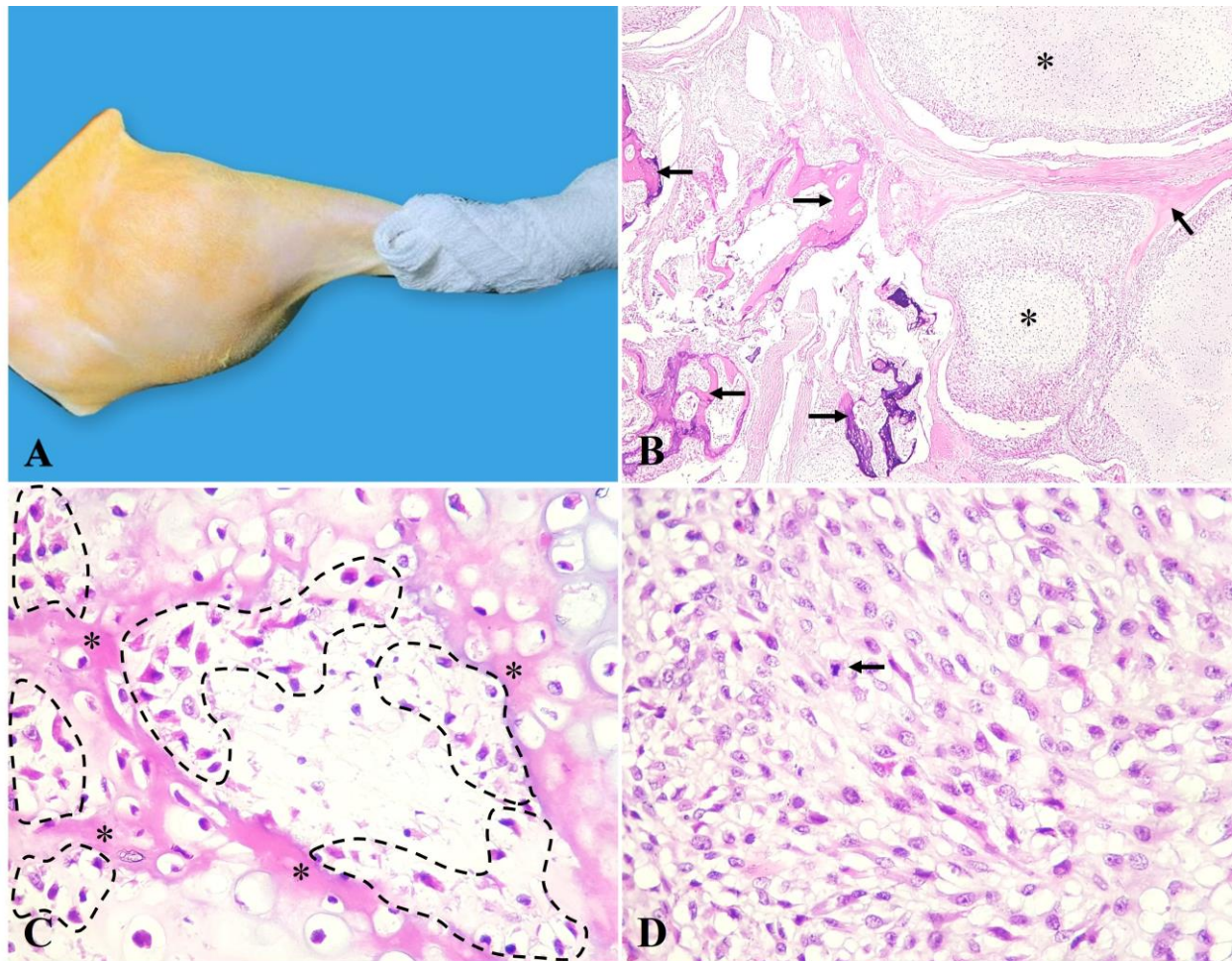


Figure 2. Feline chondroblastic osteosarcoma. A: Anatomical location of the mass at the height of the femur. Note the increased volume presenting well-defined contours and covered by skin. B: Mass constituted by a pleomorphic mesenchymal proliferation containing both bone matrix (arrows) and chondroid matrix (asterisks). Hematoxylin-Eosin (HE), 40x magnification. C: Evidence of osteoblast rhyme close (dashed line) to the osteoid (asterisks). HE, 400x magnification. D: Bundles of neoplastic cells compatible with malignant osteoblasts. Note the atypical mitosis in between. HE, 400x magnification.

A paraffin block was used to perform an immunohistochemical profile for diagnostic confirmation levels, for the following markers: Osteocalcin, Desmin, 1A4, GFAP, IBA1, and the Ki67 proliferation marker. Tissue sections embedded in paraffin were placed on previously silanized

slides. Antigen retrieval by the moist heat method was performed in a steamer for 20 -30 min. Incubation with primary antibodies was performed overnight at 4 °C. The Advance system was used for development. Staining was performed with 3,3-diaminobenzidine and counterstaining with hematoxylin.

External and/or internal controls were used to validate the reaction.

The neoplastic cells immune-expressed osteocalcin and the Ki67 proliferation marker was positive in about 20% of the neoplastic cells, favoring a chondroblastic osteosarcoma

diagnosis (Figure 3). After recovery from limb removal surgery, chemotherapy treatment was suggested to the tutor, but it was not performed. After 3 months of surgery, the animal was admitted to another veterinary hospital with symptoms of respiratory disease.

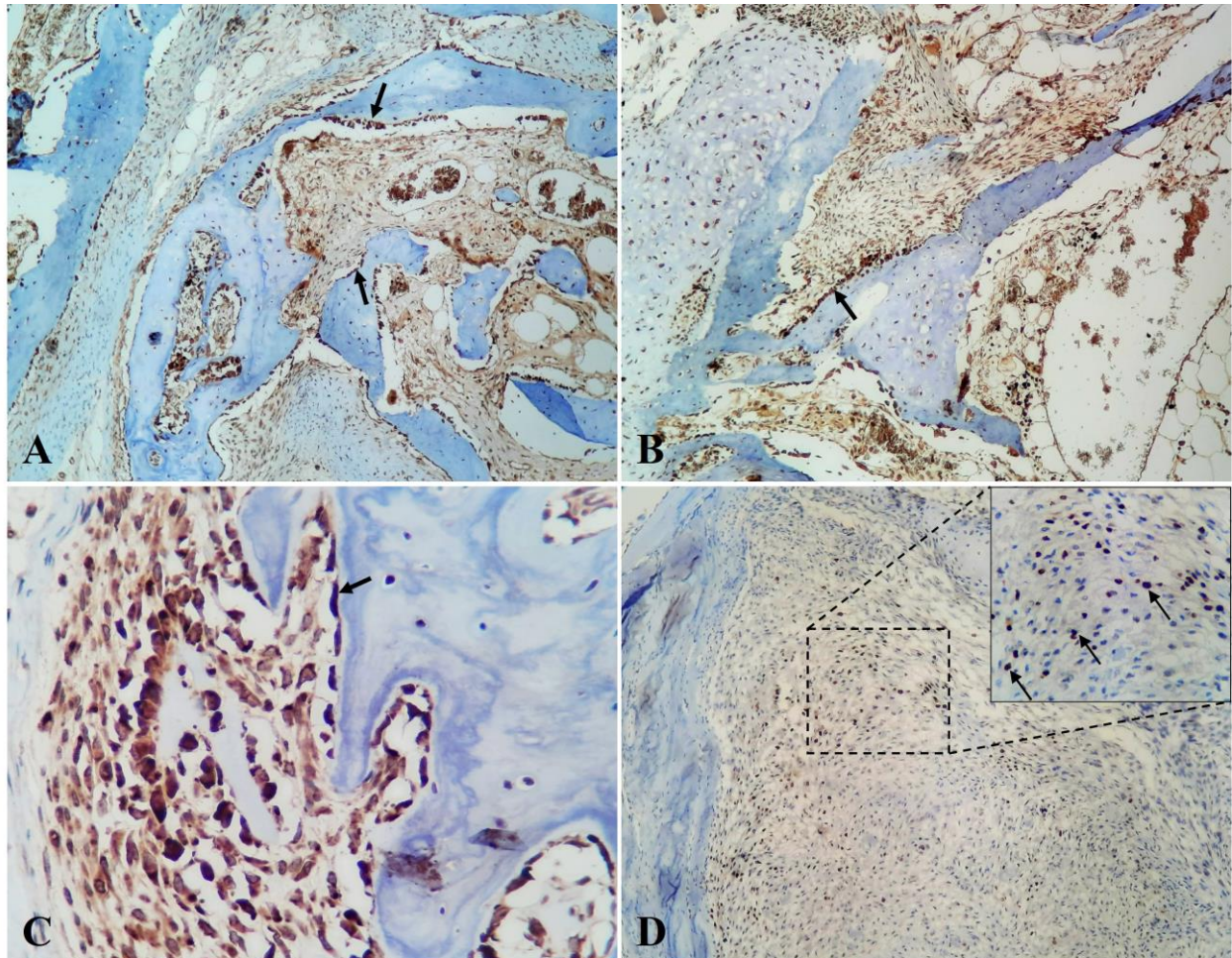


Figure 3. Immunohistochemical profile of chondroblastic osteosarcoma in a feline. A-C: Positive immunostaining for osteocalcin (arrows). D: for the Ki67 proliferation marker (arrows - enlargement of the area enclosed by the rectangle in panel D). Counterstaining with hematoxylin. (A, B and D - 40x magnification; C - 400x magnification).

Clinical examination revealed the presence of yellowish nasal discharge, noisy breathing, sneezing, inappetence,

fever and apathy. After 7 days of hospitalization, the animal presented complications, and its death was

confirmed, however, the diagnosis was not defined. No metastasis was verified by chest radiography and abdominal ultrasound.

Discussion and Conclusion

The chondroblastic osteosarcoma diagnosis in the present study was established based on clinical, radiographic, and histopathological findings. Osteosarcomas are malignant tumors of a mesenchymal origin, frequently observed in the appendicular skeleton in companion animals. Despite being better explored in canines, its occurrence has been described in both domestic and wild species [5-10].

Regarding epidemiology, studies report that the casuistry of this condition can reach up to 38.97% in dogs and up to 9.09% in cats [13], denoting a much lower frequency in felines when compared to canines, affecting mainly dogs large and giants [1-3,5,13-15]. This discrepancy between species may reflect the number of available literature reports [16] and emphasizes the need for more routine reports, as in the present study.

Apparently, there are no specific predisposing osteosarcoma occurrence factors, although some studies point to radiation as a probable cause in another case reported in a feline [17]. Herein, factors that could be implicated in the genesis of the tumor were not detected.

Clinically, the findings may vary according to the case evolution, that is, the degree of tumor expansion and invasion of adjacent tissues. In the present case, the patient presented claudication due to the affected neoplastic site, but the absence of metastases associated with complete limb excision favored life improvement and condition resolution.

However, osteosarcoma cases accompanied by cachexia and wasting have also been previously reported [18], potentially resulting in poor prognoses. Fractures, although less common, can also affect cats with osteosarcoma or up to 10 years after removal [19]. In the present case, the patient responded well to tumor removal, dying months after the diagnosis from other unrelated causes.

In cases of bone lesions, radiographic findings are essential, especially to assess the degree of lesion involvement and extent. In osteosarcoma cases, radiological examinations may indicate, for example, osteolysis, osteodensification or mixed forms presenting different evolution degrees [13]. This is similar to the case reported herein, with the exception of the absence of bone lysis, which was not present, which may have contributed to the favorable prognosis.

In the present case, cytological examinations indicated a mesenchymal

tumor, although it is important to note that osteosarcoma cytological slides usually consist of moderately cellular content comprising malignant mesenchymal cells, either isolated or clustered in the midst of an amorphous eosinophilic material (suggestive of bone matrix).

These cells may exhibit well-defined contours, a rounded to fusiform profile, basophilic cytoplasm with occasional peripheral intracytoplasmic vacuoles and scattered eosinophilic granules, and the nuclei are, in general, rounded and containing single to multiple nucleoli [20]. Combining cytology with radiographic findings can be useful in the clinical routine as a presumptive diagnosis.

Macroscopically, osteosarcoma masses exhibit very variable sizes and aspects, and, in general, are described as lobulated, fixed, semi-hard, reddish and/or whitish masses that may display mineralized areas when cut [16], similar to that observed in this case report. The femoral region is constantly described as the main site of occurrence of these tumors [21]. Extraskelatal osteosarcomas are considered rare but have been described in a domestic cat [22] and in a bat [23].

From a microscopic point of view, osteosarcomas are subdivided according to their morphology as osteoblastic, fibroblastic, chondroblastic,

telangiectatic and mixed [24]. The chondroblastic subtype is characterized by a mesenchymal cell proliferation that forms both bone and cartilaginous tissue, that is, with the production of both chondroid and osteoid matrices [16,18], similar to the findings reported herein.

Some studies indicate that morphological subtype may exhibit prognostic value in the face of an osteosarcoma diagnosis [14,25,26], although these efforts are of limited prognostic significance [11]. Important histopathological criteria comprise matrix type, vascular invasion, degree of pleomorphism, mitotic rate, among other factors [27]. The mitotic index seems to be an important factor related to survival rates, which may explain the patient's survival in the present study, where a low mitosis count was observed.

The metastasis rate in felines with osteosarcoma is lower when compared to canines [27,28], although an incisional biopsy can be an important exam prior to limb extraction in aggressive cases, in order to determine mitosis rate and predict the possibility of tumor recurrence. In this sense, this approach can contribute to the removal of tumors with a wide margin and reduce the recurrence rates, fractures, and possible clinical complications. The median survival rate can range from 24-44

months in animals with extensive local resection or amputation [28,29].

Naturally, osteocalcin corresponds to the main non-collagenous protein found in the bone matrix [30] and its labeling is a potential confirmation of bone formation [15]. The significant expression of Ki67 is an important cell proliferation indicator and may be associated with rapid tumor progression and unfavorable outcomes in cancer patients [31], although this relationship could not be established in the present case, given the premature death of the patient. The negative expression of other markers contributed to the exclusion of tumors of skeletal, nervous, and joint muscle origin, and highlights the importance of performing immunomarker panels in cases of mesenchymal neoplasia.

Concerning differential diagnoses, other osteosarcoma subtypes should be ruled out microscopically [32]. Osteosarcomas may vary in histological appearance, and a definitive diagnosis is based on the production of osteoid and/or bone by malignant mesenchymal cells. Some reports regarding osteosarcomas similar to osteoblastomas are available [33], although this is a more uncommon clinicopathological entity.

Chondroblastic osteosarcomas comprise an important bone neoplasm and the diagnosis should be based on

radiographic, histopathological and immunohistochemical findings.

Although not significantly predictive of prognosis, microscopic examinations coupled to morphological classifications can aid in the diagnosis of musculoskeletal system tumors, with the aim of supporting professionals in the field in the diagnosis of this disease, in order to promote important knowledge regarding the feline medical clinic routine and surgery.

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