MALIGNANT FELINE PRIMARY BONE TUMORS: INTEGRATING CLINICAL, RADIOGRAPHIC AND HISTOPATHOLOGICAL FINDINGS TO IMPROVE DISEASE KNOWLEDGE IN CATS

TUMORES ÓSSEOS PRIMÁRIOS MALIGNOS EM FELINOS: INTEGRANDO ACHADOS CLÍNICOS, RADIOGRÁFICOS E HISTOPATOLÓGICOS PARA MELHORAR O ENTENDIMENTO DA DOENÇA EM GATOS

TUMORES ÓSEOS PRIMARIOS MALIGNOS EN FELINOS: INTEGRANDO HALLAZGOS CLÍNICOS, RADIOGRÁFICOS E HISTOPATOLÓGICOS PARA MEJORAR LA COMPRENSIÓN DE LA ENFERMEDAD EN GATOS

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ABSTRACT: Bone neoplasms are considered rare in feline species. Osteosarcoma (OSA) is responsible for 85% of malignant bone tumors in dogs and 70% in cats, however, demographic information regarding feline OSA is less reliable than in dogs, for being a less common disease. Apparently, cats develop osteosarcoma at a higher age average than dogs. Tumor clinical course is slower compared to canine one, especially in appendicular skeleton. Presented study evaluated 14 cases of primary bone tumors in cats, integrating clinical, imaging and histopathological analysis for better understanding this disease in feline species. Male cats were the most affected ones (71,4%) and age average for neoplasia development was 9 years old. Bone sclerosis predominated in radiographic images, being justified by histopathological findings. Osteosarcoma (n=10) was the most frequent neoplasm, followed by chondrosarcoma (n=3). The most common osteosarcoma subtype was chondroblastic. The only diagnosed benign tumor was an osteochondroma. Metastasis rate was 46,2% affecting lungs, skin and other bones. The knowledge and relationship observed between clinical, radiographic and pathological findings in feline bone tumors must be taken into consideration to better prognostic determination and disease follow-up in cats.

KEYWORDS: imaging diagnosis, osteosarcoma, chondrosarcoma, feline, metastasis.
neoplasias foi de 9 anos. A esclerose óssea predominou nas imagens radiográficas, sendo justificada pelos achados histopatológicos. O osteossarcoma (n=10) foi a neoplasia óssea mais frequente, seguida pelo condrossarcoma (n=3). O subtipo de osteossarcoma mais frequente foi o condroblástico. O único tumor benigno diagnosticado foi um osteocondroma. As metástases corresponderam à 46,2% e ocorreram em pulmão, pele e outros ossos. O entendimento e as relações traçadas entre os achados clínicos, radiográficos e patológicos nas neoplasias ósseas felinas devem ser considerados para melhor determinação de prognóstico e acompanhamento da doença nos gatos.

PALAVRAS-CHAVE: diagnóstico por imagem, osteossarcoma, condrossarcoma, felinos, metástase.

RESUMEN: Las neoplasias óseas en los felinos son raras. El osteosarcoma (OSA) es responsable del 85% de los tumores óseos malignos en perros y aproximadamente del 70% en gatos, pero la información demográfica sobre el osteosarcoma en felinos es menos fiable que en perros, al tratarse de una enfermedad menos común. Los gatos parecen desarrollar osteosarcoma a una edad promedio más alta que los perros. El curso clínico del osteosarcoma en gatos es más lento que en perros, especialmente aquellos que afectan el esqueleto apendicular. El presente estudio evaluó 14 casos de neoplasia ósea primaria en felinos, integrando evaluaciones clínicas, de imagen e histopatológicas para comprender mejor la enfermedad en la especie. Se observó una mayor ocurrencia en los felinos machos (71,4%) y la edad promedio de desarrollo de las neoplasias fue de 9 años. En las imágenes radiográficas predominó la esclerosis ósea, justificada por los hallazgos histopatológicos. El osteosarcoma (n=10) fue la neoplasia ósea más común, seguido del condrosarcoma (n=3). El subtipo más común de osteosarcoma fue el condroblástico. El único tumor benigno diagnosticado fue un osteocondroma. Las metástasis correspondieron al 46,2% y se produjeron en los pulmones, la piel y otros huesos. Se debe considerar la comprensión y las relaciones establecidas entre los hallazgos clínicos, radiográficos y patológicos en las neoplasias óseas felinas para determinar mejor el pronóstico y el seguimiento de la enfermedad en los gatos.

PALABRAS CLAVE: diagnóstico por imagen, osteosarcoma, condrosarcoma, felino, metástasis.
1. Introduction

Cancer is the primary cause of death nowadays, whether in man or dogs and cats, and has become an increasing concern for companion animals’ owners, who look for oncological treatments to minimize pet suffering and provide overall survival increment (Simpson et al., 2017).

Bone tumors comprise 1.8% of all feline tumors (Manuali et al., 2020), while osteosarcoma is responsible for 70% to 80% of all primary malignant bone tumors diagnosis in cats. In this species, osteosarcoma occurs mostly in old animals, between 9 and 10 years old, without any breed predilection and female cats are more frequently affected than male ones. Feline osteosarcoma presents lower tumoral growth when compared to its canine counterpart (Al Attar et al., 2016; Chun, 2005; Harasen; Little, 2015; Helm; Morris, 2012). Primary bone tumors incidence is 7.9/100.000 in dogs and 3.1-4.9/100.000 in cats (Vanel et al., 2013). Still, feline osteosarcoma demonstrates lower metastasical rate, figuring in 5-10% of reported cases, and less aggressive behavior when compared to canine osteosarcoma, although the reason for such differences between both species is still unknown (Dimopoulou et al., 2008; Gebhard et al., 2016; Meyer; Walter, 2015). Patient overall survival time will be influenced by factors such as location, tumor diameter and volume, tumoral grade and distant metastasis, with cats presenting better prognosis than dogs (Daleck et al., 2016; Gebhard et al., 2016; Helm; Morris, 2012).

Due to this behavioural difference toward an improved prognosis, feline appendicular osteosarcoma, when initially diagnosed, is often treated by amputation, which in cats is curative, with concomitant chemotherapy seldomly required (Gebhard et al., 2016; Harasen; Little, 2015; Helm; Morris, 2012;).

This studied aimed to evaluate primary feline bone tumors, integrating clinical, imaging diagnosis and histopathological information, drawing
relevant connexions to better understand feline disease development and improve prognostic accuracy.

2. Methodology

**Ethical approval:** The study was approved by Universidade Federal Fluminense Ethics Committee in Animal Use under protocol n. 7046100123/2023 and informed consent was obtained from all participants included in the study.

**Animal selection and inclusion criteria:** Clinical data, radiographic and histopathological exams were collected from 14 cats, male and female, neutered or not, from any breed, including cats from no specific breed (NSB), independently of age, who presented radiographic image suggesting primary bone neoplasia with concomitant histopathological confirmation, between 2020 and 2024.

**Clinical data:** Data collected included age, sex, breed, affected bone, disease-free interval and overall survival time. Disease-free interval was defined as the time from surgical excision until any detectable metastasis. Overall survival was defined as the time from neoplastic diagnosis until decease (natural death or euthanasia).

**Radiographic images:** Images were retrieved from veterinary clinics and hospitals from which included cats were attended. Target lesions were from appendicular skeleton, since it is the most affected location; however, axial lesions attending inclusion criteria were also included. At least two complimentary radiographic images from the affected site were obtained, including proximal and distal joint. Radiographic images were evaluated by the same radiologist (LCRC).

**Histopathological evaluation:** Hematoxylin-eosin-stained histological sections were reviewed and blindly analyzed under optical microscope by two pathologists (JSL and CBA). Histopathological diagnosis was established
according to World Health Organization (WHO) proceedings histopathological classification (Slayter et al.,1994).

**Statistical analysis:** Descriptive statistical tools were used to evaluate studied variables.

### 3. Results and Discussion

Clinical data and histopathological diagnosis of 14 included cats is shown on Table 1.

Table 1. Clinical data (sex, age and affected bone) and histopathological diagnosis from 14 cats included in the study.

<table>
<thead>
<tr>
<th>Animal</th>
<th>Sex</th>
<th>Age</th>
<th>Affected bone</th>
<th>Histopathological diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>12 years</td>
<td>Radius</td>
<td>Fibroblastic OSA</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>9 years</td>
<td>Humerus</td>
<td>Fibroblastic OSA</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>NI</td>
<td>Radius</td>
<td>Fibroblastic OSA</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>4 years</td>
<td>Rib</td>
<td>Osteochondroma</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>10 years</td>
<td>Metatarsus</td>
<td>Chondroblastic OSA</td>
</tr>
<tr>
<td>6</td>
<td>Male</td>
<td>11 years</td>
<td>Scapula</td>
<td>Chondroblastic OSA</td>
</tr>
<tr>
<td>7</td>
<td>Female</td>
<td>7 years</td>
<td>Radius</td>
<td>Chondroblastic OSA</td>
</tr>
<tr>
<td>8</td>
<td>Female</td>
<td>6 years</td>
<td>Femur</td>
<td>Osteoblastic OSA</td>
</tr>
<tr>
<td>9</td>
<td>Male</td>
<td>10 years</td>
<td>Metacarpus</td>
<td>Chondrosarcoma</td>
</tr>
<tr>
<td>10</td>
<td>Male</td>
<td>10 years</td>
<td>LPL</td>
<td>Chondrosarcoma</td>
</tr>
<tr>
<td>11</td>
<td>Male</td>
<td>7 years</td>
<td>Femur</td>
<td>Chondrosarcoma</td>
</tr>
<tr>
<td>12</td>
<td>Male</td>
<td>14 years</td>
<td>LTL</td>
<td>Osteoblastic OSA</td>
</tr>
<tr>
<td>13</td>
<td>Female</td>
<td>6 years</td>
<td>Tarsus</td>
<td>Osteoblastic OSA</td>
</tr>
<tr>
<td>14</td>
<td>Male</td>
<td>11 years</td>
<td>Metacarpus</td>
<td>Chondroblastic OSA</td>
</tr>
</tbody>
</table>

LPL: left pelvic limb; LTL: left thoracic limb  
Source: Lyvia C. R. Carvalho, 2024

All cats were of no specific breed (NSB). Male cats predominated over female ones (71,4%; 10/14 x 28,6%; 4/10). Age average were 9 years old, varying from 4 to 14 years. In one patient’s medical record, age was not identified (NI), however, it was an adult cat.

Appendicular skeleton comprised the majority of affected sites, with eight lesions on thoracic limb (57,1%; 8/14) and five in pelvic ones (35,7%;
Only one lesion was located in axial skeleton (1/14; 7.2%), on right rib.

Radius was the most affected bone (25%; 3/12), followed by femur and metacarpus (16.7%; 2/12 each). The remaining bones were singularly affected each. In two cases, affected bone was not identified and only left pelvic limb and left thoracic limb was addressed.

From evaluated neoplasias, 13 (92.8%; 13/14) were malignant and only one (7.2%; 1/14) benign. From primary malignant bone tumor, ten (76.9%; 10/14) were diagnosed as osteosarcoma (OSA) and three (23.1%; 3/14) chondrosarcomas (CSA). All diagnoses were obtained from excised lesions submitted to histopathological diagnosis.

In studied cats, osteosarcoma radiographic image was predominantly sclerotic. One case presented both lysis and bone sclerosis, but permeative bone lysis was slightly prevalent. Chondrosarcoma radiographic alterations were composed of sclerotic bone lesions, without evident cortical bone lysis. The sole benign lesion, an osteochondroma, was voluminous, with heterogenous opacity, destroying part of the sixth left rib (Figure 1, A to F).
Figure 1: Radiographic and tomographic images. (A, B) Case 14: Voluminous tumoral bone lesion, with proliferative and lytic areas in feline left metacarpus. Dorsopalmar and lateral incidences. Diagnosis: Osteosarcoma. (C) Case 9: Voluminous tumoral bone lesion, predominantly sclerotic in feline right metacarpus. Dorsopalmar incidence. Diagnosis: Chondrosarcoma. (D) Case 11: Proliferative periosteal reaction with no evidence of bone lysis and apparently preserved femoral cortical bone. Lateral incidence. Diagnosis: Chondrosarcoma. (E) Case 4: Transversal section of expansive heterogenic lesion on left sixth rib (arrows). An intrathoracic tumoral portion is observed. Diagnosis: Osteochondroma. (F) Case 4: Sagital reconstruction of expansive heterogenic lesion on left sixth rib (arrows). An intrathoracic tumoral portion is observed deviating thoracic trachea (arrow head). Diagnosis: Osteochondroma.

Source: Lyvia C. R. Carvalho, 2024
Regarding histopathological evaluation, feline osteosarcomas was subclassified as osteoblastic (30%; 3/10), chondroblastic (40%; 4/10) and fibroblastic (30%; 3/10), according to extracellular matrix content produced besides osteoid. Both chondrosarcomas presented neoplastic chondrocytes but one sample was well-differentiated and the other one moderately differentiated. Osteochondroma displayed all its typical features: peripheral chondroid tissue with central endochondral ossification, with ongoing-formation bone lacunae, lined with normal cuboid osteoblasts. Many multinucleated, osteoclast-like cells were observed in addition to high-density capillary vasculature (Figure 2, A to F).
Figure 2: Photomicrography of feline primary bone tumors: (A) Osteoblastic osteosarcoma: high-density tumor, with small bone lacuna (arrow head) scattered among neoplastic cells. Multinucleated, osteoclast-like cells are visible (circle). Bar: 71 µm.

(B) Chondroblastic osteosarcoma: two types of extracellular matrix are observed: basophilic chondroid matrix with occasional central endochondral ossification (asterisk) and eosinophilic osteoid matrix (arrow head) in the same neoplastic sample. Bar: 51 µm.

(C) Fibroblastic osteosarcoma: intramedullary neoplastic cells are observed (triangle). Cortical bone is noted (asterisk). Bar: 153 µm. (D) Fibroblastic osteosarcoma: scarce osteoid deposition is observed (arrows) within a whirl pattern of dense fibroblastic matrix. Multinucleated, osteoclast-like cells are visible (arrow head). Bar: 46 µm. (E): Chondrosarcoma: neoplastic chondrocytes haphazardly disposed among basophilic chondroid matrix. Bar: 71 µm. (E): Osteochondroma: peripheral chondroid matrix (asterisk) with endochondral ossification: bone lacuna in formation, with osteoblasts lining (arrow head). Multinucleated, osteoclast-like cells are visible (circle). Bar: 100 µm. Hematoxylin-eosin staining.

Source: Lyvia C. R. Carvalho, 2024
From 10 osteosarcoma-bearing patients, four were euthanized due to poor clinical evolution. One of them presented firm nodular lesions in the skin, bones and one solitary pulmonary nodule. The second one presented long bone increased volume and diffuse nodules in the skin, but no metastasis confirmation was reported. Another patient was euthanized due to bone metastasis identified on radiographs (Figure 3, A to C). The fourth cat was euthanized due to respiratory distress caused by hemorrhagic pleural effusion, without post-drainage radiographic information.

Figure 3: Radiographic images. (A) Case 7: Voluminous proliferative sclerotic primary tumoral bone lesion in distal left radius. Lateral incidences. Diagnosis: Osteosarcoma. (B) Proliferative predominantly sclerotic secondary tumoral bone lesion in right fourth thoracic digital phalange (arrow). Dorsopalmar incidences. (C) Expansile predominantly sclerotic secondary tumoral bone lesion in left scapula. Scapular spine is signed (arrow).

Two chondrosarcoma-bearing patients died within 1 and 2 years after initial diagnosis, with pulmonary metastasis development report. Information regarding clinical evolution and follow-up of the third patient with chondrosarcoma was not available.
The cat with osteochondroma was submitted to surgical tumor removal but died within the first hours after the procedure, apparently for reasons not related to the primary disease.

Informed metastasis frequency in malignant bone lesions was 46.2% (6/13), being 40% (4/10) in osteosarcomas and 66.7% (2/3) in chondrosarcomas.

Pulmonary parenchyma was the most affected site by metastasis, identified on radiographs, occurring in four patients, followed by bones (three patients) and skin (two patients), whether single or multiple lesions. Metastases from chondrosarcoma were restricted to lungs while osteosarcoma metastasis compromised other locations.

Overall survival time (OST) from patients with available follow-up information varied from 5 to 40 months, with 17.8 months average (Table 2). One male cat, diagnosed with chondroblastic osteosarcoma is under surveillance, 30 months after diagnosis and without any clinical sign of metastasis.

<table>
<thead>
<tr>
<th>Animal</th>
<th>Sex</th>
<th>Age</th>
<th>Primary Site</th>
<th>Diagnosis</th>
<th>Metastasis Site</th>
<th>OST</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Male</td>
<td>11 years</td>
<td>Scapula</td>
<td>Chondroblastic OSA</td>
<td>Lung</td>
<td>15 months</td>
</tr>
<tr>
<td>7</td>
<td>Female</td>
<td>7 years</td>
<td>Radius</td>
<td>Chondroblastic OSA</td>
<td>Bones</td>
<td>40 months</td>
</tr>
<tr>
<td>10</td>
<td>Male</td>
<td>10 years</td>
<td>LPL</td>
<td>Chondrosarcoma</td>
<td>Lung</td>
<td>12 months</td>
</tr>
<tr>
<td>11</td>
<td>Male</td>
<td>7 years</td>
<td>Femur</td>
<td>Chondrosarcoma</td>
<td>Lung</td>
<td>19 months</td>
</tr>
<tr>
<td>12</td>
<td>Male</td>
<td>14 years</td>
<td>LTL</td>
<td>Osteoblastic OSA</td>
<td>Lung, bone, skin</td>
<td>16 months</td>
</tr>
<tr>
<td>14</td>
<td>Male</td>
<td>11 years</td>
<td>Metacarpus</td>
<td>Chondroblastic OSA</td>
<td>Bone, skin</td>
<td>5 months</td>
</tr>
</tbody>
</table>

Table 2. Clinical data (sex, age and affected bone), histopathological diagnosis, metastasis site and overall survival time of six feline patients with primary malignant bone tumors who developed metastasis.

None of the patients was submitted to chemotherapy or any other kind of treatment for metastatic disease, excepting primary lesion surgical excision such as amputation.
Osteosarcoma was the most frequent neoplasm found in this study, as observed by Al Attar et al., (2016), Chun (2005), Harasen and Little (2015), Helm and Morris (2012) and Nakano et al., (2022).

Feline osteochondroma is a spontaneous osteocartilagenous exostosis associated to feline leukemia or autosomal diseases (Gomez et al., 2023). No information regarding feline leukemia virus (FeLV) infection was available for presented patient, unabling such correlation.

Male cats were the most affected ones, similarly to Heldmann; Anderson; Wagner-Mann (2000) who reported male cats to be the majority of bone neoplasm-bearing felines, but discordant with Manuali et al., (2020) who observed equal commitment between male and female cats in their study. This finding can be related to regional feline population profile. A populational study recorded prevalence of male cats (54%) in Cachoeiras de Macacu municipality, Rio de Janeiro state (Cruz; Cardoso; Moutinho, 2019). Preference for male cats was also stated in Barbacena city population, from Minas Gerais state (Silva et al., 2010). This was be explained by absence of inconvenience concerning estrus, pregnancy, litter care and destination. This considered, male cat predominance in studied sample is possibly related to cultural factors rather than a sexual predisposition to primary bone tumor development in feline species.

Age average of affected patients was high, as observed by Al Attar et al., (2016), Chun (2005), Harasen and Little (2015), Helm and Morris (2012). Shida et al., (2010) reported mean age of 9,9 ± 3,8 years for general feline neoplasia development, not bone tumors exclusively, in Japan. Likewise, an Italian study reported age from 8 to 11,9 years old for cats presented with neoplasms (Vascellari et al., 2009). It is interesting to highlight that, although being the only benign bone tumor, osteochondroma affected a rather young cat, with 4 years old. Again, this was expected due to this disease development and progression, usually impairing young individuals (Szilasi et al., 2022; Thompson & Dittmer, 2017).
Thoracic limbs were the most frequent affected anatomical location for bone tumor development, pointing out to proximal humeral epiphysis, differing from previous reports where pelvic limbs are more affected by osteosarcoma in cats (Chun, 2005; Heldmann; Anderson; Wagner-Mann, 2000). This finding may be attributed to studied samples inner characteristics rather than any kind of predisposition.

Malignant bone tumors radiographic appearance was prevalently sclerotic. Osteosarcoma radiographic appearance varies from sclerotic to mixed and lytic type in dogs and cats (Dittmer; Pemberton, 2021). Sclerotic radiographic aspect was particularly observed in chondroblastic osteosarcoma and chondrosarcoma, differing from what was expected since cartilaginous tissue is radiotransparent (Dittmer; Pemberton, 2021). Such radiopacity can be attributed to endochondral ossification of cartilaginous matrix in both cases, as observed in histopathological analysis. On the other hand, osteoblastic osteosarcoma was predominatly lytic, reflecting high tumoral cellularity and, although numerous, small fragments of mineralized bone lacunae.

Discriminating osteosarcoma from chondrosarcoma on radiographs is more related to tumor location than bone alteration morphology, with osteosarcoma occurring in long bones and chondrosarcoma more commonly observed in flat bones (Dittmer; Pemberton, 2021). However, in this survey, all three chondrosarcoma cases were located in long bones. Analyzing specially metarcapic lesions, although being one osteosarcoma and one chondrosarcoma, both radiographic patterns were very similar, not allowing any reasonable radiographic differentiation between both tumor types.

Most frequently diagnosed osteosarcoma subtype was chondroblastic one, disagreeing with previous study reporting osteoblastic subtype as the most common one (Dimopoulou et al., 2008). Still nowadays, there is no agreement concerning prognostic value of osteosarcoma subtypes in man (Basile et al., 2020) and dogs (Simpson et al., 2017) and no information is
reported in cats. But it is consensual osteosarcoma mesenchymal cells hability to produce different extracellular matrix types besides osteoid in what can be considered “the same” microenvironment (Corre et al., 2020).

Osteosarcoma metastasis frequency was higher than Dimopoulou et al. (2008), Gebhard et al., (2016) and Meyer; Walter, (2015) reports but a little lower than Nakano et al., (2022) (46.3%). Unfortunately, in many patients’ records disease evolution and overall survival time (OST) was not available in order to better characterize these findings.

As in canine osteosarcoma, lung was the main metastatic affected site in studied malignant feline bone tumors (Nakano et al., 2022). However, other bones and skin are less frequently reported as osteosarcoma or chondrosarcoma metastatic sites in dogs (Thompson; Dittmer, 2017). Nevertheless, cutaneous metastasis is considered to decrease OSA prognosis in dogs (Marin et al., 2022; Parachini-Winter et al., 2019). Further studies are required to clarify this clinical finding in cats.

Axial chondrosarcoma usually has slow clinical progression with low metastasis rate in dogs and cats (Thompson; Dittmer, 2017). The same may not be true to appendicular forms of this tumor, since OST in studied cases was 1 to 1.5 years. However, it is important to take into consideration that no included patient received adjuvant chemotherapy. In malignant canine bone tumors, adjuvant chemotherapy usually decelerates disease progression leading to an improve in disease-free interval (Marconato et al., 2021). This therapeutical management does not seem to provide the same beneficial result in cats (Heldmann; Anderson; Wagner-Mann, 2000; Nakano et al., 2022).

4. Conclusion

Osteosarcoma was the most frequent primary bone tumor in studied cats, followed by appendicular chondrosarcoma. Radiographic imaging
provided tumor location, affected bone integrity and tumoral mass radiopacity information but was not able to differentiate both tumor types. Histopathological analysis clarified radiological findings and revealed similar osteosarcoma subtypes observed in dogs and man. Metastases were reported in lungs, skin and bone resulting in reduced survival time.

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