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Osteosarcoma in dogs: clinical-morphological study and prognostic correlation

Osteossarcoma em cães: estudo clínico-morfológico e correlação prognóstica

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Abstract

Osteosarcoma is defined as a bone matrix-producing malignant mesenchymal tumor. It is relatively rare among domestic animals, but corresponds to 85% of all malignant bone tumors in dogs. To study canine osteosarcoma in animals living in Brazil and correlate the clinical-morphological findings with prognosis, forty-six cases of dogs with osteosarcoma were studied retrospectively out of a total of 56 malignant primary bone tumors on file. The animals were assessed in terms of age, sex, breed, topographic tumor distribution, and presence of metastases at diagnosis. The tumors were classified histologically by the method of Pool[1]. Osteosarcomas corresponded to 82% of primary malignant bone dysplasias in the sample studied. Age ranged from 6 months to 14 years (C = 8 y), sex: 32 F/18 M; breed: large dogs (86%), topographic location: appendicular skeleton (64%), axial skeleton (28.5%) and extraskeletal (7.5%); presence of metastases in 17.4%. Histopathology: osteoblastic (32.6%), chondroblastic (9.6%) and telangiectatic (5.8%) patterns; combined: 52%. Osteosarcoma mainly affects adult females. Breed is a predisposing factor, the appendicular skeleton is most often involved, and an osteoblastic histological pattern predominates. The lungs are a common site of metastasis, with pure-bred male dogs being most predisposed regardless of the morphological pattern of osteosarcoma.

Key-words:
Oosteosarcoma.
Dogs

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Introduction

Osteosarcoma is a primary malignant bone neoplasia of mesenchymal origin whose cells produce osteoid or tumoral bone[1]. This neoplasia corresponds to 80% of the primary bone neoplasias affecting dogs and is characterized by aggressive and invasive behavior, with a high metastatic potential[2]. The bones most often affected are those of the appendicular skeleton , in the following order of frequency: humerus, radius, ulna, femur, and tibia[3]. The large or giant dog breeds are those almost exclusively predisposed to the disease and the mean age of affected animals is 8 years.[4]

This is a heterogeneous tumor that, in addition to producing an osteoid matrix, can also present a fibroblastic and cartilaginous matrix, being subdivided into osteoblastic, chondroblastic, fibroblastic, telangiectatic and

giant cell forms depending on the type of matrix.[5]

Regardless of the treatment used for canine osteosarcoma, the estimated survival time is 6 months to 1 year.[2,6] Subclinical micrometastases may be present since the onset of the disease and are not always detected by radiographic examination of the lungs. In general the metastases develop during the first few months after the observation of the primary tumoral lesion and the lungs are the major site of metastases disseminated by the hematogenous route.[7]

In Latin America and in Brazil, there are no epidemiological data or clinical-pathological studies on this disease in dogs. Few papers are available and most of them are reports of isolated cases.[8,9,10] In view of the current situation, the objective of the present investigation was to study canine osteosarcoma in Brazil and to determine possible correlations between clinical-morphological data and prognosis.

Materials and Methods

Animal characterization

Fifty-two cases of canine osteosarcoma were detected in the files of the Department of Veterinary Pathology, Faculty of Veterinary Medicine and Zootechny, University of São Paulo, from 1990 to 2001. Cases with clinical data and histopathological material considered to be insufficient or inadequate for analysis were excluded. The following data were surveyed in the files: age, sex, race, weight, topographic localization of the lesion (axial or appendicular skeleton or extraskeletal site), and presence of metastases detected by radiographic examination at the time of the first examination. The animals were classified as purebred dogs and mixed-breed dogs and as small and large or giant dogs.

Topographic localization

The lesions occurred at the following anatomical locations: a) axial skeleton (craniofacial bones, vertebrae, sacrum and sternum); b) appendicular skeleton (long bones of the fore- and hindlimbs, short bones of the extremities, scapula, ilium and ischium), and c) extraskeletal muscles (soft parts).

Histopathology

Representative specimens of the bone lesions were obtained from the dogs by biopsy, autopsy or surgery. The material was fixed in 10 formalin and decalcified in 5% nitric acid. Tissue sections (5 mm) were obtained, stained with hematoxylin and eosin (H & E), routinely processed for histology, and mounted on slides.

The criterion adopted for the diagnosis of osteosarcoma was based on the detection of osteoid matrix produced by the tumor cells, regardless of its quantity.[11] The tumors were classified according to Pool[1] into the following histological subtypes: osteoblastic, fibroblastic, chondroblastic, telangiectatic, giant cell type, and combined type when more than one histological pattern was present.

Determination of the presence of metastases

The possible presence of metastases was determined at the time of the first visit by clinical and radiographic examination of the chest.

Statistical analysis

To determine the association between two variables, comparison of the proportions was made using the chi-square test or the exact Fisher test, as indicated. In all cases, the level of significance was set at 5% ($P < 0.05$).

Results

On the basis of the medical records of the 52 dogs with osteosarcomas, it was possible to determine the age of 40 of them, which ranged from 6 months to 14 years, with a mean of 8 years. The sex of 50 animals was recorded, with 31 being females (62%)

and 19 being males (38%). The distribution of the neoplasia according to race is given in figure 1 for 40 animals. Twenty-seven were purebred (67.5%) and 13 (32.5%) were mixed-breed. Thirty-two animals were evaluated in terms of size, with the large animals being the most affected ones (71.9%). Weight was recorded for only 12 animals and ranged from 9 to 50 kg, with a mean of 29 kg.

In 41 animals it was possible to determine the topography of the lesions (Figure 2). In 31 (75.6%) of them, the lesions were located in the appendicular skeleton in the following decreasing order of frequency: radius and ulna (26.8%), femur (24.8%), tibia (20.3%), scapula (14.3%), humerus (9%), and phalanges (4.8%). The forelimbs presented lesions in 56% of cases and the hindlimbs in 44%. Lesions of the axial skeleton occurred in 7 animals (17.1%), affecting spinal bones (three cases), skull (two cases), mandible (one case), and sacrum (one case). Extraskeletal localization of osteosarcoma was observed in three cases (7.3%).

With respect to the morphological findings, both osteosarcomas of a pure pattern (27 cases) (52%) and osteosarcomas of a combined pattern (25 cases) (48%) were identified. The pure pattern showed the following histological subtypes in decreasing order of frequency: osteoblastic (19 cases) (70.4 %) (Figure 3), chondroblastic (6 cases) (22.2 %) (Figure 4), and telangiectatic (2 cases) (7.4 %) (Figure 5). On the basis of the amount of osteoid present, osteoblastic

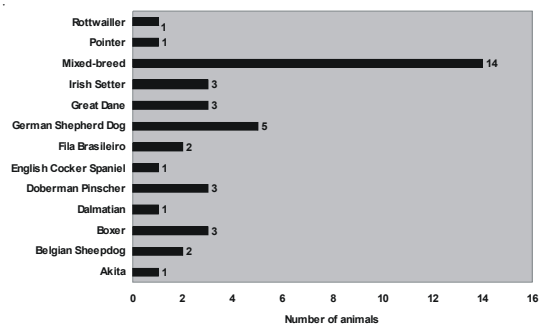

Figure 1
Distribution of 40 animals by race

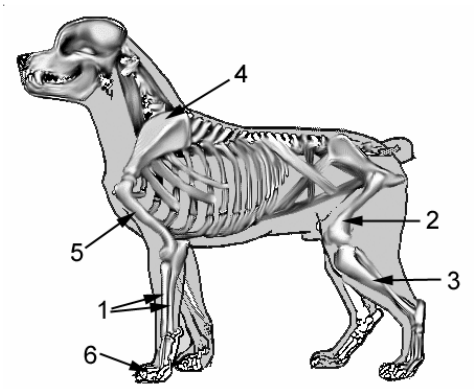

Figure 2
Distribution of osteosarcoma lesion in decreasing order of frequency: 1 – radius and ulna (26.8%); 2 – femur (24.8%); 3 – tibia (20.3%); 4 – scapula (14.3%); 5 – humerus (9%); 6 – phalanges (4.8%)

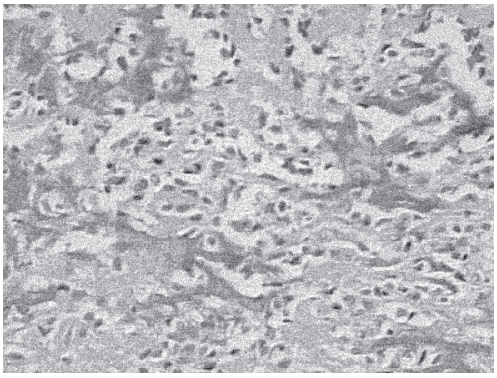

Figure 3
H&E. Original 10x. Osteoblastic osteosarcoma. Observe the atypical osteoblasts characterized by hyperchromatism and increased nuclear volumes. Abundant production of partially mineralized osteoid matrix can be seen throughout, between the neoplastic cells

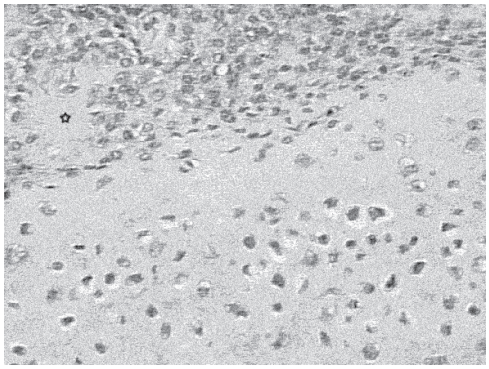

Figure 4
H&E. Original 40x. Osteosarcoma of chondroblastic pattern. Predominance of areas with cartilaginous differentiations. Observe the chondrocytes with atypical, voluminous and hyperchromatic nuclei and with focal osteoid matrix (star)

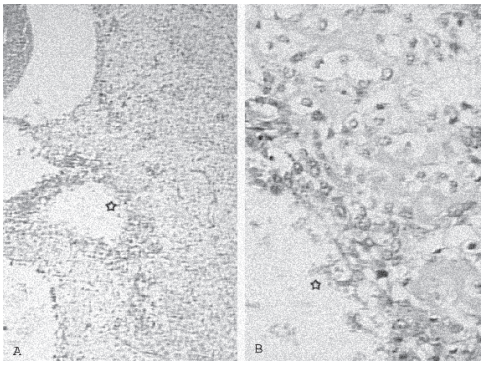

Figure 5
H&E. A: original 10x e B: 40x. Telangiectatic osteosarcoma. Cystic cavities filled with blood (star) surrounded by atypical neoplastic cells with osteoid matrix (A). Observe the detail (B)

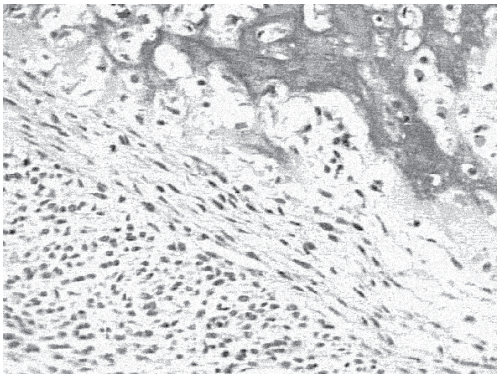

Figure 6
H&E. Original 40x. Combined pattern osteosarcoma: osteoblastic (above) and fibroblastic in a longitudinal section (center), and in a transverse section (below)

osteosarcoma was further classified into productive (47.6%) and poorly productive (52.4%). The combined pattern tumors presented two (66.7%) or three types of cell elements (33.3%), the most frequent being the combination of osteoblastic and chondroblastic patterns. Tumors showing sparse giant cells of the osteoclast type or areas of a myxoid pattern were also identified. No pure osteosarcoma variant of giant cells and fibroblastic cells was detected.

Forty-one animals were evaluated for the presence of metastases, which were detected in 17.1% of the animals, being located in the lungs in all cases. Generalized metastases involving other organs such as the spleen and liver in addition to the lungs were observed in a single case.

No significant correlation was detected between race and the following variables: distribution of the lesion in the skeleton ($p = 0.23$), histological classification ($p = 0.40$), and presence of metastases ($p = 0.53$).

There was no significant correlation between the presence of metastases and the following variables: size ($p = 0.53$), age ($p = 0.39$) and histological pattern ($p = 0.35$). However, males ($p=0.05$) and purebred animals ($p = 0.08$) tended to develop metastases.

Discussion and Conclusions

In the present study we observed that osteosarcoma is more common in adult dogs, as also reported by Heyman et al.[6], Zezza Neto et al.[10] and Delisle and Devauchelle[12]. Studies by Pool[1] and Brodey and ABT[13] demonstrated a discrete predominance of osteosarcoma among male dogs, except for the St. Bernard race, in which females were more affected.[1, 13] In the present study, however, we detected a predominance of osteosarcoma among females (62%) regardless of race. A similar result was also observed by Feeney, Johnston and Grindem[14] and Smith and Sutton. [15]

According to Spodnick et al.[4], Berg[7] and Delisle and Devauchelle[12], race is a significant risk factor for osteosarcoma, with animals of large or giant races being the most affected.[4,7,12] These findings were also confirmed in the present study. Large animals weigh 20 to 40 kg.[11] According to TJALMA , dogs weighing more than 36.5 kg have a 61- to 180-fold higher chance of developing skeletal tumors than dogs weighing less than 9 kg[16]. In the present study, weight data were obtained for only 12 animals, preventing a comparative analysis. Osteosarcoma predominated in purebred animals, with the following races being affected in decreasing order of frequency: German Shepherd, Boxer, Doberman Pinscher, Great Dane, and Irish Setter. Hammer et al.[17] also reported a higher incidence of osteosarcoma in German

Shepherds.[17] According to Dalleck,[8] the race most affected in Brazil is the Fila Brasileiro.

With respect to anatomical distribution, there was a considerable prevalence of osteosarcoma in the appendicular skeleton (75.6%), with the radius, ulna, femur and tibia being the most affected bones, in decreasing order of frequency. These findings agree with data reported by Thompson and Fugent[2], Brodey and Riser[18], and Cooley and Waters[19] who observed that the appendicular skeleton is three to four times more affected than the axial skeleton.

Knecht and Priester[20] demonstrated that the forelimbs are twice more frequently affected than the hindlimbs, and Liu et al.[3], also reported a similar distribution and frequency. In the present study the percentage of lesions affecting the axial skeleton was 17.1%, with spinal and cranial bones being more affected, in agreement with data reported by Cooley and Waters[19], Heyman et al.[6] and Knecht and Priester.[20] Osteosarcomas are frequently located in the metaphysis of long bones,[13] but in the present study it was not possible to obtain precise data about this feature. It is possible that the high incidence of osteosarcomas in the appendicular skeleton, especially in the forelimbs of large dogs, and in long bone metaphyses is related to the high growth rate of bone tissue in the metaphyseal region and the weight overload supported by the forelimbs.

Histologically, a slight predominance of the pure pattern over the combined pattern was observed, with the following histological subtypes being also observed in decreasing order of frequency: osteoblastic, chondroblastic and telangiectatic. In the tumors with a combined pattern, the most common combination was osteoblastic and chondroblastic subtypes, as also reported by Kirpenstain et al.[11] These findings disagree with those reported by Hammer et al.[17] who observed the following frequencies: 64% osteoblastic tumors, 16% combined tumors, 2% chondroblastic tumors, 9 % fibroblastic tumors, and 9% telangiectatic tumors.[14] In the present study we did not detect a significant correlation between histological type of the tumor and other variables studied, although Misdorp and Hart[21] reported that dogs with fibroblastic osteosarcomas have a better prognosis than dogs with other variants of the tumor.

Osteosarcoma is a highly metastatic neoplasia, mainly towards the lungs, with 90% of the animals developing metastases within one year after limb amputation[18]. Previous studies have detected the presence of pulmonary metastases in 5 to 11% of cases at diagnosis.[5,17]. In the present study, the percentage of pulmonary metastases was slightly higher (17%). There was no correlation between the presence of metastases and the various clinical and morphological aspects of the tumor, with purebred male dogs only showing a tendency to develop distant lesions.

Main conclusions: osteosarcoma mainly affects adult females. Breed is a predisposing factor, the appendicular skeleton is most often involved, and an osteoblastic histological pattern predominates. The lungs are a common site of metastasis, with pure-bred male dogs being most predisposed regardless of the morphological pattern of osteosarcoma.

Although important, the clinical and morphological aspects of canine osteosarcoma have been little studied in Brazil. Despite the limitations of a retrospective study, the present results contribute important data for a better understanding and management of canine osteosarcoma.

Resumo

O osteossarcoma é definido como um tumor maligno mesenquimatoso produtor de matriz óssea. É relativamente raro entre os animais domésticos, contudo em cães, corresponde a aproximadamente 85% das neoplasias ósseas malignas. A finalidade

Palavras-chave:
Osteossarcoma.
Cães

deste trabalho foi estudar o osteossarcoma canino, em nosso meio, correlacionando os achados clínico-morfológicos com o prognóstico. Retrospectivamente foram levantados 52 cases de cães com osteossarcoma. Foram avaliados quanto a idade, sexo, raça, peso, porte físico, distribuição topográfica e presença de metástases ao diagnóstico. Os tumores foram classificados histologicamente segundo POOL[14]. A idade variou de 6 meses a 14 anos (média = 8 anos); sexo: 31 F/ 19 M; cães de raça pura (67.5%) e sem raça definida (SRD) (32.5%); cães de grande porte foram os mais afetados (71,9%). Esqueleto apendicular (75,6%), axial (17.1%) e extraesquelético (7.3%); Metástase ao diagnóstico em 17.1%. Histopatologia: padrão puro (52%); osteoblastic (38.6%); condroblastic (9.4%) e telangiectásico (4%) e padrão combinado 48%. Conclusão: Afeta, em geral, fêmeas adultas e o esqueleto apendicular é o mais comprometido. A raça é fator predisponente e histologicamente predomina o padrão puro osteoblastic. Os pulmões são sede comum de metástases, sendo os cães machos e de raça pura os mais predispostos, independente do padrão morfológico do osteossarcoma.

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