Primary bone neoplasms in dogs: 90 cases[1]

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ABSTRACT.- Trost M.E., Kommers G.D., Brown C.C., Barros C.S.L., Irigoyen L.F., Fighera R.A., Inkelmann M.A. & Silva T.M. 2012. **Primary bone neoplasms in dogs: 90 cases.** *Pesquisa Veterinária Brasileira 32(12):1329-1335*. Departamento de Patologia, Universidade Federal de Santa Maria, Camobi, Santa Maria, RS 97105-900, Brazil. E-mail: glaukommers@yahoo.com

A retrospective study of necropsy and biopsy cases of 90 primary bone tumors (89 malignant and one benign) in dogs received over a period of 22 years at the Laboratório de Patologia Veterinária, Universidade Federal de Santa Maria, was performed. Osteosarcoma was the most prevalent bone tumor, accounting for 86.7% of all malignant primary bone neoplasms diagnosed. Most cases occurred in dogs of large and giant breeds with ages between 6 and 10-years-old. The neoplasms involved mainly the appendicular skeleton, and were 3.5 times more prevalent in the forelimbs than in the hindlimbs. Osteoblastic osteosarcoma was the predominant histological subtype. Epidemiological and pathological findings of osteosarcomas are reported and discussed.

INDEX TERMS: Osteosarcoma, neoplasms, diseases of the skeletal system, oncology, dogs.

RESUMO.- [**Neoplasmas ósseos primários em cães: 90 casos.**] Através de um estudo retrospectivo dos casos de biópsias e necropsias de cães recebidos no Laboratório de Patologia Veterinária da Universidade Federal de Santa Maria, num período de 22 anos, constatou-se a ocorrência de 90 casos de neoplasmas ósseos primários, sendo 89 malignos e um benigno. Dentre os 89 neoplasmas ósseos malignos, osteossarcoma foi o mais prevalente, correspondendo a 86,7% de todos o neoplasmas ósseos diagnosticados na espécie. A maioria dos casos ocorreu em cães de raças grandes e gigantes e entre seis e 10 anos de idade. Os neoplasmas envolvendo o esqueleto apendicular predominaram e foram 3,5 vezes mais prevalentes nos membros anteriores que nos posteriores. O subtipo histológico predominante foi o osteoblástico. Este estudo aborda os aspectos epidemiológicos e patológicos importantes para o diagnóstico de osteossarcomas.

TERMOS DE INDEXAÇÃO: Osteossarcoma, neoplasmas ósseos, neoplasias, oncologia, cães.

INTRODUCTION

In dogs, unlike what is seen in humans and in some other species of domestic animals, malignant bone neoplasms are much more prevalent than benign neoplasms (Brodey 1979, Misdorp 1980, Dorfman et al. 2002, Thompson & Pool 2002, Thompson 2007). Osteosarcoma (OS) is considered the most common primary bone neoplasm in dogs. However, chondrosarcomas, fibrosarcomas, hemangiosarcomas, among others, also occur but in much lower frequency (Dernell et al. 2001, Egenvall et al. 2007).

Clinical signs associated with primary bone neoplasms depend much more on the location than on the type of the neoplasm itself (Jongeward 1985). The main symptoms are local pain and swelling (Brodey 1979, Jongeward 1985). In advanced cases, lymph edema can occur distal to the tumor (Brodey 1979). The OS commonly exhibit very rapid growth and pathologic fractures may be present in lytic tumors (Brodey 1979).

Osteosarcomas are heterogeneous neoplasms regarding location, radiological presentation, histopathological subtypes, location of metastasis, progression, and response

[1] Received on September 17, 2012.
Accepted for publication on October 29, 2012.
Part of the Doctoral Thesis of the first author.

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to treatment (Selvarajah & Kirpensteijn 2010). Generally, they are aggressive tumors, with local bone destruction, invasion of adjacent soft tissues, and high metastatic potential (Dernell et al. 2001).

Classically, OS affects dogs of large and giant breeds (Owen 1967, Dernell et al. 2001). In most cases the diagnosis is made in dogs around 7 or 8-years-old (Thompson & Pool 2002). There is some evidence that males are more affected than females (Brodey & Riser 1969, Jongeward 1985, Dernell et al. 2001, Selvarajah & Kirpensteijn 2010).

The presumptive diagnosis of primary bone tumors in dogs involves several aspects such as age, breed, anatomical location, and radiological appearance of the lesion. Definitive diagnosis requires histological examination of samples obtained through biopsy, amputation or necropsy (Dernell et al. 2001, Mehl et al. 2001, Thompson & Pool 2002).

Accurate diagnosis of OS is important because it often involves radical therapeutic decisions (e.g. amputation of limbs). Over the years, some advances in the treatment of these tumors has occurred. However, amputation remains the standard treatment for appendicular OS cases, and even then, the prognosis is generally poor (Spodnick et al. 1992; Thompson & Pool 2002, Selvarajah & Kirpensteijn 2010). The aim of this paper is to report and discuss prevalence, epidemiological, and pathological characteristics of primary bone neoplasms, especially OS diagnosed in dogs at the Laboratório de Patologia Veterinária, Universidade Federal de Santa Maria (LPV-UFSM).

MATERIALS AND METHODS

The necropsy and biopsy files of the LPV-UFSM were retrospectively reviewed looking for cases of primary bone neoplasms in dogs. The period of time encompassed by this review was from 1990 through 2011 (22 years). Data retrieved from the files included age, breed, gender, anatomical location of the neoplasms, histological features and occurrence of metastasis in the necropsy cases.

Dogs with the breed specified in the protocols were classified by size according to the classification used by kennel clubs: a) dogs with less than 10 kg were classified as small, b) between 10 and 25 kg as medium, c) between 25 and 45 kg as large, and d) between 45 and 90 kg, as giant (Grandjean 2001). The classification of the neoplasms was based on the categories for the primary bone neoplasms used by the World Health Organization and adapted by Thompson & Pool (2002). The Osteosarcoma (OS) cases in which the histologic subclassification was not included in the protocols were classified by the observation of new histological sections stained with hematoxylin and eosin (HE), when paraffin blocks were available on the LPV-UFSM archives.

RESULTS

This series of primary bone neoplasms in dogs comprises 90 cases, 89 being malignant and one benign (chondroma of a rib). Forty-five cases were biopsy samples (which included amputated limbs and tumor masses) and accounted for 0.56% of 7,936 histopathological examinations in dogs during the studied period. In the same period of time, 5,114 dogs were necropsied and primary bone neoplasms were diagnosed in 45 cases (0.87%).

Within the malignant neoplasms, Osteosarcoma (OS) was the most prevalent histological subtype, with 78 cases diagnosed, which accounted for 86.7% of all malignant bone neoplasms observed in this study. Other malignant bone neoplasms diagnosed, in descending order of prevalence, were chondrosarcoma (five cases), hemangiosarcoma (two cases, one in a vertebra and the other one in the tibia), multilobular bone tumor (skull), giant cell bone tumor (head), fibrosarcoma (humerus) and maxillary fibrosarcoma (Fig.1), the last four with one case each. In the five diagnosed cases of chondrosarcoma, two were in the femur, one in the radius, one in the scapula, and one in a rib (Fig.2).

Due to the high prevalence of OS among primary bone neoplasms in this case series, only the epidemiological and pathological characteristics of OS are presented herein. The main results regarding the OS are summarized in Table 1.

The number of affected females and males was similar with a ratio of 1.08 males per affected female. In one case, the sex of the dog was unknown. The distribution of the

Fig.1. Maxillary fibrosarcoma, mixed breed dog. Enlargement of the left side of the maxillary bone with neoplastic invasion of the palate and adjacent soft tissues.

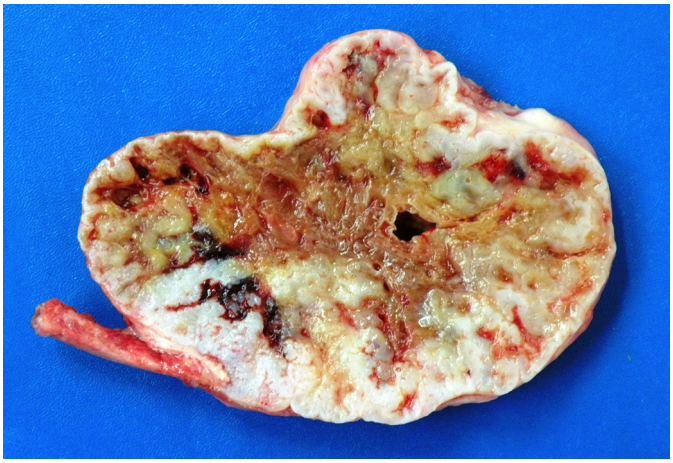

Fig.2. Chondrosarcoma, rib, dog, Boxer. The tumor mass involves and replaces an extensive portion of the rib. The mass is composed of multiple whitish cartilaginous nodules in the periphery and contains a large, soft, and pale yellow centrally located area.

Table 1. Epidemiological and pathological characterization of osteosarcomasin 78 dogs

Sex	Age (years)	Breed	Size*	Anatomical location	Histological type
M - 51%	Mean - 7.4	Mixed - 24%	Md - 5%	Ap- 79.5%	Osteoblastic- 44.9%
F - 48%		Pure - 76%	L - 40%	Ax - 19.2%	Telangiectatic- 10.2%
NA - 1%			G - 55%	Ap/Ax - 1.3%	Fibroblastic - 7.7%
					Chondroblastic - 7.7%
					Giant Cell - 6.4%
					NC - 23.0%

M = male, F = female, NA = not available. *From pure breed. Md = medium, L = large, G = giant, Ap = appendicular, Ax = axial, NC = not classified.

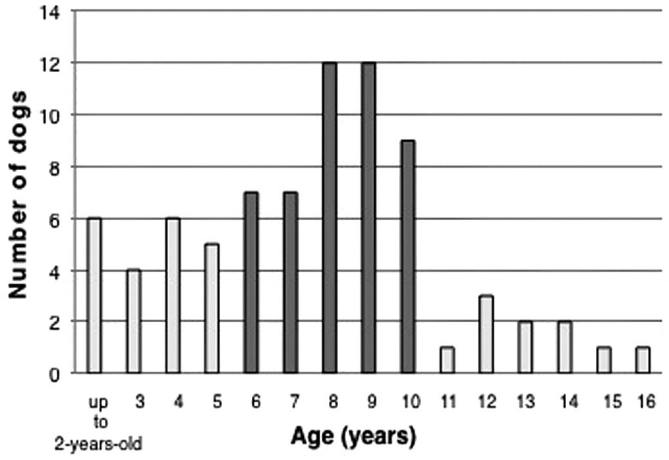

Fig.3. Pattern of age distribution of the 78 dogs with osteosarcoma.

Fig.4. Osteoblastic osteosarcoma, humerus, 5-year-old female dog, Rottweiler. The radiographic image show extensive lysis characterized by multiple bony spicules in the proximal portion of the humerus (arrow). The neoplasm produces an extensive area of fracture (mainly involving the humeral head) and expands into the surrounding soft tissues, creating a radiopaque image.

dogs according to age is shown in Figure 3. In one case the age of the dog was unknown. Most cases (60%) occurred in dogs between 6 and 10-years-old (mean of 7.48-years-old). Six cases (7.7%) occurred in dogs between 1.4 and 2-years-old. Twenty dogs were mixed breed. In this study, in cases in which the dog breed was available, about 90% were large or giant dogs and 43% were Rottweilers. No cases occurred in small breeds.

Table 2. Anatomical location of osteosarcomas in 78 dogs

Location	Number of cases	% category	% total
APPENDICULAR	62	100	79.48
Forelimb	48	77.41	61.53
Humerus	20	32.25	25.64
Radius/ulna	13	20.96	16.66
Scapula/humerus	5	8.06	6.41
Scapula	4	6.45	5.12
Carpal/metacarpal bones	3	4.83	3.84
Not specified	3	4.83	3.84
Hindlimb	14	22.58	17.94
Femur	8	12.90	10.25
Tibia	3	4.83	3.84
Femur/tibia	1	1.61	1.28
Calcaneus	1	1.61	1.28
Digital bones	1	1.61	1.28
AXIAL	15	100	19.23
Head	7	46.66	8.97
Vertebral bones	4	26,66	5.12
Ribs	3	20.00	3.84
Pelvic bones	1	6.66	1.28
APPENDICULAR/AXIAL	1	100	1.28
Femur/pelvic bone	1	100	1.28
TOTAL	78	-	100

Regarding to the anatomical location, OS of the appendicular skeleton was about five times more prevalent than OS of the axial skeleton. In one case, the neoplasm involved both axial (pelvic bones) and appendicular skeleton (femur). Fifteen neoplasms were located in the axial skeleton, most of them occurred in the head (seven cases; approximately 47%), and the others in the vertebrae (four cases), ribs (three cases) and in the pelvic bones (one case). Anatomical location findings of the 78 OS cases are presented in Table 2.

Macroscopic as well as radiographic appearance, when available, varied among the cases. Cases with predominantly lytic (Fig.4 and Fig.5), proliferative (Fig.6) or a mixture of destructive and proliferative elements were seen. In some cases, the occurrence of these particular patterns could be better evaluated in macerated specimens (Fig.7). At gross inspection most of the lytic tumors appeared as expansive, poorly demarcated masses with variably sized hemorrhagic and necrotic areas (Fig. 5), while productive tumors were more solid, compact, and whitish in appearance (Fig.6).

In this case series, the neoplasms in the forelimbs were about 3.5 times more prevalent (48 cases) than those in the hind limbs. The humerus was the major (41.6% of the forelimb OS) individually affected bone and accounted for

Fig.5. Osteoblastic osteosarcoma, humerus, 5-year-old female dog, Rottweiler. Tumor mass, longitudinal cut surface. The mass is poorly demarcated and constituted peripherally by whitish and solid areas with a soft, necrotic and hemorrhagic central area. The humeral head is fractured. The correspondent radiological image is presented in Fig.4.

Fig.7. Telangiectatic osteosarcoma, femur, 8-year-old male dog, Rottweiler. Macerated specimen. The extension of the bone lysis is better evaluated. There is a major oblique fracture in the diaphysis. Multiple bone spicules are also seen in the metaphysis. A normal bone from another dog with similar body size was used as control.

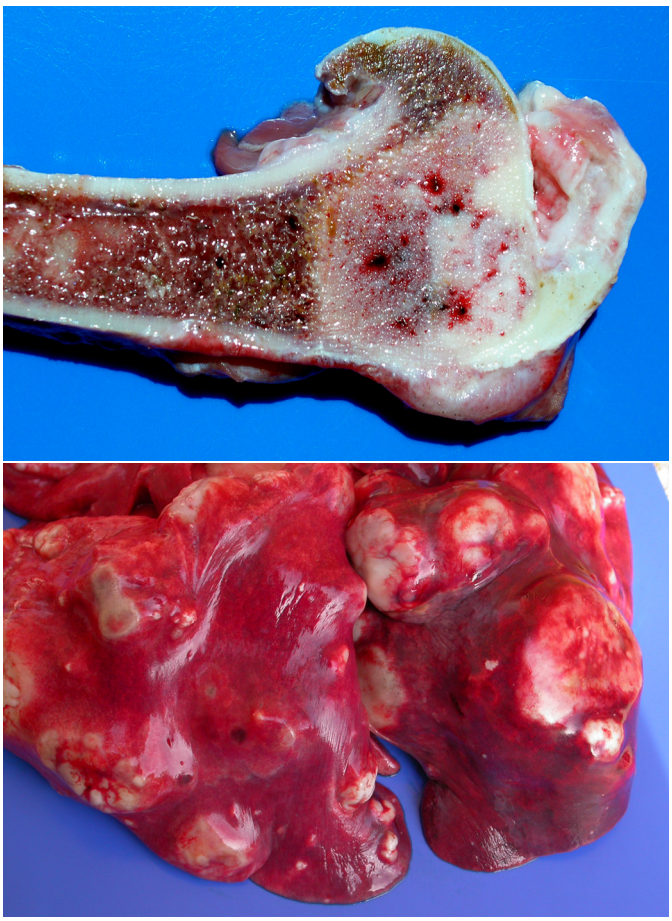

Fig.6. Osteoblastic osteosarcoma (productive type), humerus, dog, German Shepherd. Bone longitudinally sectioned. The proximal metaphysis and epiphysis contain a whitish, compact and well-demarcated mass.

Fig.8. Pulmonary metastasis from an osteoblastic osteosarcoma (productive type), dog, German Shepherd. Scattered throughout the pulmonary parenchyma are multiple whitish and salient neoplastic nodules.

about one-fourth (25.6%) of all OS evaluated in this study. The other mainly affected appendicular bones (or combinations of bones) were: radius and ulna (16.6%), femur (10.2%), scapula and humerus (6.4%), scapula (5.1%), and tibia (3.8%).

Metastases could be evaluated in dogs submitted for necropsy (43 cases) and were detected in 26 (60.5%) of them; 16 cases were single metastases and ten involved more than one organ. The most frequent sites of metastases, in descending order of prevalence, were: lung (24) (Fig.8), regional lymph nodes (7), heart (3), bone (2), liver (2), and kidney (2). Adrenal gland, mesentery, diaphragm, and brain had one occurrence each. One case (osteoblastic OS in a rib) was associated with a paraneoplastic syndrome know as pulmonary osteopathy, characterized by partially circumferential periosteal new bone formation, mainly observed in the diaphysis of long bones.

The classification of OS, according to the histological subtype, was done in 60 cases: 35 (44.9%) were osteoblastic (Fig.9), eight (10.2%) telangiectatic, six (7.7%) fibroblastic, six (7.7%) chondroblastic, and five (6.4%) were giant cell OS.

DISCUSSION

This retrospective study revealed that 86.7% of the malignant primary bone tumors diagnosed were osteosarcoma (OS). The prevalence of OS is considered the highest among all malignant bone neoplasms in dogs, with values that exceed 80% and can reach up to 98% of them (Dernell et al. 2001, Thompson & Pool 2002, Morello et al. 2010).

Reports have attributed a higher prevalence of OS in male dogs, and although a slightly higher prevalence of OS in males occurred in this case series, this finding is not consistent among several studies (Brodey 1979, Misdorp &

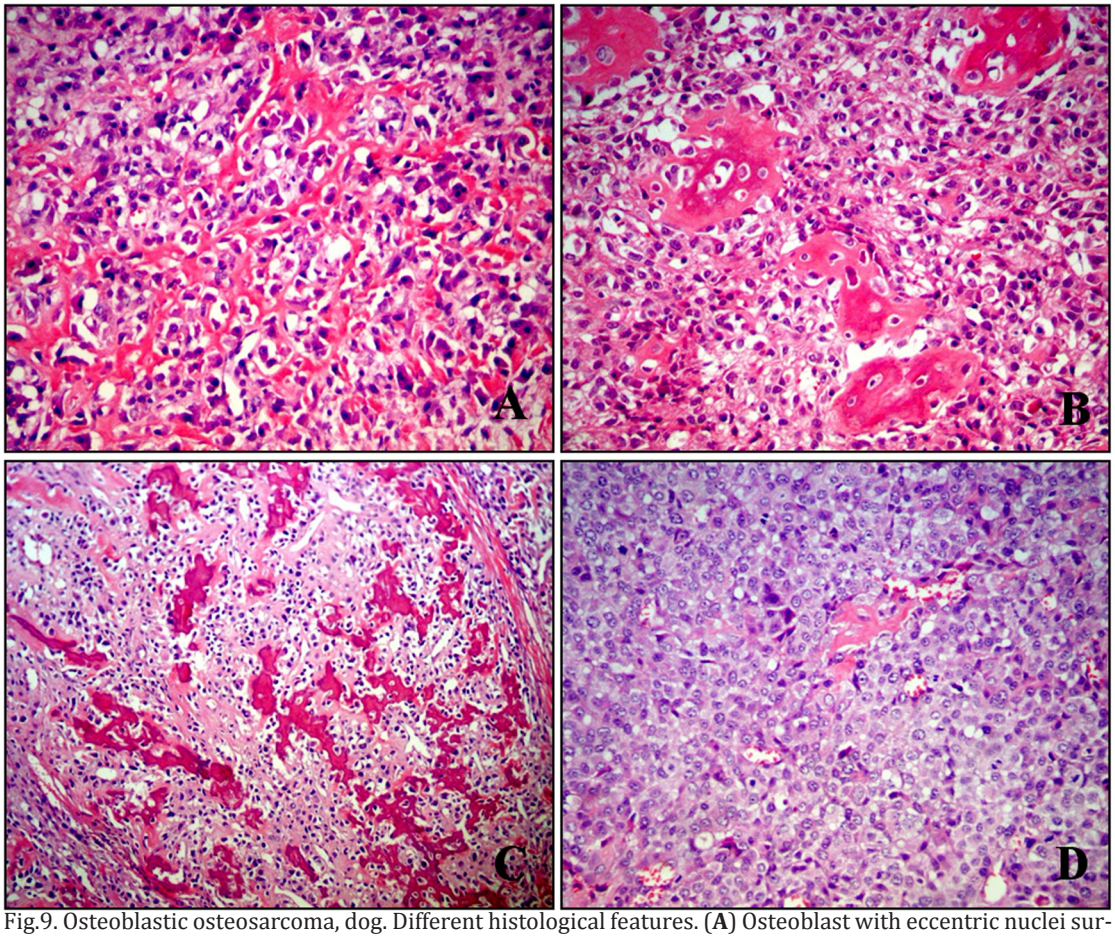

Fig.9. Osteoblastic osteosarcoma, dog. Different histological features. (**A**) Osteoblast with eccentric nuclei surrounding thin bony trabeculae. HE, obj.40x. (**B**) Osteoid irregular islands are surrounded by malignant and spindle-shaped osteoblasts, some of them entrapped by the osteoid matrix. HE, obj.20x. (**C**) Abundant amount of osteoid in a productive type osteoblastic osteosarcoma. HE, obj.10x. (**D**) Moderately productive osteoblastic osteosarcoma characterized by a mantle of malignant osteoblasts with only minimal osteoid production. HE, obj.40x.

Hart 1979, Ru et al. 1998, Morello et al. 2010). There are indications that in certain dog breeds, such as Saint Bernard, the number of affected females exceeds the males (Brodey & Riser 1969).

Most (60%) dogs of this study were between 6 and 10-years-old with a peak at 8 and 9-years-old (24 cases). The age pattern of OS in dogs can be bimodal, with a small peak of cases between 18 and 24 months (only six cases in this series) and most of them are concentrated between 7 and 9-years-old (Brodey & Riser 1969, Brodey 1979, Dernell et al. 2001, Morello et al. 2010). In dogs less than 1-year-old OS is considered rare (Brodey 1979).

Some breeds are described as having an increased risk of developing OS. Among them are Doberman Pinscher, Saint Bernard, German Shepherd, Golden Retriever, Great Dane and Irish Setter (McNeill et al. 2007, Morello et al. 2010). The discussion about prevalence of the breeds more affected by OS in this retrospective study is hampered because the breed prevalence in the general population of dogs in the area covered by the LPV-UFSM is unknown. However, it is noteworthy that Rottweiler was the most affected (43%) breed in this study. This breed has been described as susceptible to the development of various tumors, including OS (Michell, 1999). In addition, one study attributed a more aggressive behavior of OS in Rottweilers, when compared to OS in other dog breeds (McNeill et al. 2007).

Breed predisposition appears to be more linked to the size of the dog than to the breed itself (Brodey 1979, Ru et al. 1998). Osteosarcoma is classically a tumor of large and giant breeds (Ru et al. 1998) and the high percentage of large and giant breeds represented in this case series (90% of all dogs with specified breed) corroborates with this information. Some studies indicate that giant and large dogs are more prone to develop OS and have, respectively, 60.9 and 7.9 times more chances to develop primary bone tumors, especially when compared to small dogs (Thompson & Pool 2002). In this case series, small size dogs were not affected. It is reported that only 5% of OS occurs in dogs less than 15 kg (Dernell et al. 2001). The OS tend to occur in bones suffering greater weight burden and in adjacent regions of the epiphyseal plates with later closure. In these areas, heavy dogs are more susceptible to suffer multiple and minor traumas that can damage sensitive cells and induce the formation of mutant cell lines in these regions (Ru et al. 1998, Dernell et al. 2001).

The appendicular skeleton was about five times more

affected by OS than the axial skeleton in this study. Appendicular location has been cited as the most common site of OS. The axial skeleton is involved in about one quarter of the cases (Brodey 1979, Dernell et al. 2001, Thompson & Pool 2002, Selvarajah & Kirpensteijn 2010), although in small breeds more than 50% of OS can be diagnosed in flat bones (Coley & Waters 1997).

The prevalence of OS in the forelimbs is considered to be double that of the prevalence of OS in the hind limbs (Brodey 1979). However, forelimb OS were 3.5 times more prevalent than hind limb OS in this case series. The higher prevalence of OS in the forelimbs may be related to the fact they support 60% of body weight and would therefore be subjected to multiple and repeated microtrauma (Ru et al. 1998).

Several studies indicate that there are places of strong predilection for the development of appendicular OS. The main appendicular bones affected individually or in combinations in this study were humerus, radius and ulna, femur, scapula and humerus, scapula, and tibia, in descending order of prevalence. These results differ from other studies were OS occurred mostly in the radius and ulna (distal metaphysis), in the humerus (proximal metaphysis), tibia (distal metaphysis), and femur (proximal metaphysis), in descending order of prevalence (Brodey 1979, Dernell et al. 2001, Pool & Thompson 2002, Morello et al. 2010). In dogs OS distal to the carpal and tarsal joints is a relatively rare occurrence (Dernell et al. 2001, Thompson & Pool 2002).

The OS can be classified into central and peripheral. Periosteal OS biological behavior is similar to central OS and may progress to the point of invading the adjacent cortical bone and extend into the marrow cavity (Thompson & Pool 2002, Thompson 2007). The radiographic and macroscopic appearance of the central OS varies depending on the behavior of neoplastic cells and the type of matrix produced by them (Thompson 2007). Some types are predominantly lytic, some are productive, while others are a mixture of proliferative and destructive elements (Pool & Thompson 2002, Thompson 2007). However, not all studies of OS in dogs examined the tumors from a central-peripheral perspective so information is limited.

Osteosarcomas are dynamic lesions and may demonstrate dramatic changes in the radiographic appearance in a few days. There seems to be little correlation between radiographic patterns (i.e., osteolytic, mixed and productive) and the development or degree of malignancy of the tumor (Thompson & Pool 2002). Lytic or radiolucent tumors are usually hemorrhagic and soft and often contain light yellow areas of necrosis. Lytic tumors tend to infiltrate adjacent soft tissues and pathological fractures may be associated with cortical bone erosion (Thompson 2007). Although OS invariably leads to erosion of cortical bone, these tumors are more likely to spread toward the epiphysis than to the shaft and rarely invade the adjacent articular cartilage (Thompson 2007).

Sixty percent of the 43 necropsy cases had metastases and the lungs were mostly affected in this study. In many cases, lung metastases were present even before the primary tumor was diagnosed (Loukopoulos & Robinson 2007). Metastases occur mainly by the hematogenous route to the lungs, as well as to other bones and to other visceral organs, brain, skin and subcutaneous tissue (Cooley & Waters 1997, Morello et al. 2010). Seven out of the 43 necropsy cases had metastases to the regional lymph nodes. Generally, lymph nodes are involved with low frequency (Morello et al. 2010, Selvarajah & Kirpensteijn 2010). As seen in one case of osteoblastic osteosarcoma in this case series, which was part of another previously published article (Trost et al. 2012), hypertrophic osteopathy is described as a potential consequence of OS in dogs (Brodey & Riser 1969)

Different histological features can be observed in OS. In all cases the diagnosis is based on the production of some amount of osteoid and/or malignant bone by osteoblasts (Pool & Thompson 2002, Thompson 2007). Due to the nature of pluripotent mesenchymal cells, the tumor matrix may contain varying amounts of cartilage, collagen, and osteoid (Thompson & Pool 2002). The histological subtypes are: poorly differentiated, osteoblastic, chondroblastic, fibroblastic, telangiectatic, and giant cell type (Thompson & Pool 2002). About 45% of the cases were osteoblastic OS in this case series. The osteoblastic OS can also be subclassified according to the amount of osteoid matrix produced in non-productive, moderately productive and fruitful. The moderately productive osteoblastic OS is the most common subtype of OS in the dog (Thompson & Pool 2002).

Metastases were detected in 60.5% of the necropsy cases; most of them were to the lungs. The biological behavior of appendicular OS is aggressive and most dogs die a few months after diagnosis. Some factors associated with poor prognosis for dogs with OS include: lung metastasis, metastasis to lymph nodes, large tumors (which are directly associated with lung metastases), invasion of adjacent soft tissues, a large percentage of areas of necrosis in the tumor, and vascular invasion (Selvarajah & Kirpensteijn 2010). Dogs with fibrosarcomatous type of OS have a better prognosis than those with telangiectasic OS (Misdorp & Hart 1979, Thompson & Pool 2002, Selvarajah & Kirpensteijn 2010).

The results obtained in this study lead to the following conclusions: (1) malignant bone neoplasms in dogs were much more prevalent than the benign ones, (2); OS were the most prevalent bone neoplasms, (3) most affected dogs had between six and 10 years of age, (4) the appendicular skeleton was affected more than the axial, and the majority of cases occurred in the forelimbs, especially in the humerus (5), the histological subtype most commonly diagnosed was the osteoblastic OS, and (6) most necropsied dogs had metastases, which occurred mainly to the lungs.

Acknowledgments.- M.E. Trost and M.A. Inkelmann have a scholarship from the Coordenacão de Aperfeiçoamento de Pessoal de Nível Superior (CAPES). G.D. Kommers has a fellowship from Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

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