PESQUISA VETERINÁRIA BRASILEIRA
Brazilian Journal of Veterinary Research
ISSN 0100-736X (Print)
ISSN 1678-5150 (Online)

Pesq. Vet. Bras. 43:e07186, 2023
DOI: 10.1590/1678-5150-PVB-7186

Original Article
Small Animal Diseases

A comparative analysis of anatomopathological features and COX-2 expression of mammary neoplasms with malignant mesenchymal components in female dogs[1]

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ABSTRACT.- Prates K.S., Oliveira P.L., Bueno T.S., Damasceno K.A., Driemeier D., Sonne L., Pavarini S.P. & Bertagnolli A.C. 2023. **A comparative analysis of anatomopathological features and COX-2 expression of mammary neoplasms with malignant mesenchymal components in female dogs.** *Pesquisa Veterinária Brasileira 43:e07186, 2023.* Laboratório de Histopatologia, Centro Estadual de Diagnóstico e Pesquisa em Saúde Animal Desidério Finamor,, Departamento de Diagnóstico e Pesquisa Agropecuária, Secretaria da Agricultura, Pecuária e Desenvolvimento Rural, Estrada Municipal do Conde, 6000, Eldorado do Sul, RS 92990-000, Brazil. E-mail: angelbertagnolli@gmail.com

Canine mammary neoplasms with malignant mesenchymal components, such as carcinosarcomas and sarcomas, belong to an uncommon and histologically heterogeneous group. Little is known about the biological behavior of these histogenic variants. This study aimed to compare the clinicopathological characteristics and the COX-2 immunohistochemical expression of different histologic subtypes of carcinosarcomas and sarcomas. Samples of 23 carcinosarcomas and 15 sarcomas from the mammary glands of female dogs were studied. Medical records were reviewed to obtain clinical data. Subsequently, histology microscope slides were analyzed to assess for mesenchymal subtypes, necrosis, vascular invasion, histologic grades, and lymph node metastasis. Immunohistochemistry was used to assess the COX-2 expression. The malignant mesenchymal proliferation was categorized into osteosarcomas (23/40), fibrosarcomas (5/40), liposarcomas (6/40) and chondrosarcomas (4/40). The osteosarcomatous differentiation was the most predominant type among the sarcomas and carcinosarcomas and was associated with vascular invasion (P=0.010) and lymph node metastases (P=0.014). High COX-2 expression was detected in 14.3% of the carcinosarcomas (carcinoma and/or sarcoma cells) and 27.3% of the sarcomas. The carcinosarcomas and sarcomas had similar clinical and pathological characteristics and developed as large tumors, with intratumoral necrosis and a predominance of high histologic grades, although the frequency of vascular invasion and lymph node metastasis was low. Osteosarcoma subtypes presented more aggressive characteristics than non-osteosarcoma subtypes.

INDEX TERMS: Canine, carcinosarcoma, COX-2, mammary, mesenchymal, sarcoma, tumor.

RESUMO.- [**Análise comparativa das características anatomopatológicas e expressão de COX2 em neoplasias mamárias com componentes mesenquimais malignos em cadelas.**] Neoplasias mamárias caninas com componentes mesenquimais malignos, como carcinossarcomas e sarcomas, são um grupo de neoplasias pouco frequentes e histologicamente heterogêneas e pouco se sabe sobre o comportamento biológico das variantes histogênicas. O objetivo desse estudo é comparar as características anatomopatológicas e a expressão imunoistoquímica de COX-2 de diferentes subtipos histológicos de carcinossarcomas e sarcomas.

[1] Received on November 10, 2022.
Accepted for publication on March 11, 2023.

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Foram estudados 23 carcinosarcomas e 17 sarcomas da glândula mamária de cadelas. Os prontuários médicos foram revisados para obtenção de dados clínicos. Posteriormente, as lâminas histológicas foram avaliadas para acessar os subtipos mesenquimais, necrose, invasão vascular, grau histológico, metástase linfonodal. A imunoistoquímica foi realizada para avaliar a expressão de COX-2. Os tipos encontrados de proliferação mesenquimal maligna foram osteossarcoma (23/40), fibrossarcoma (7/40), lipossarcoma (6/40) e condrossarcoma (4/40). A diferenciação osteossarcomatosa foi predominante entre os sarcomas e carcinossarcomas e foi associado com invasão vascular (*P*=0,006) e metástase linfonodal (*P*=0,014). Uma expressão alta de COX-2 foi detectada em 14,3% dos carcinossarcomas (células carcinomatosas e/ou sarcomatosas) e 27,3% dos sarcomas. Os carcinossarcomas e sarcomas apresentaram características clínicas e patológicas semelhantes e se desenvolveram como tumores grandes, com necrose intratumoral e predomínio de alto grau histológico, mas com baixa frequência de invasão vascular e metástase distante. Os subtipos osteossarcomatosos apresentaram características mais agressivas quando comparados com subtipos não osteossarcomatosos.

TERMOS DE INDEXAÇÃO: Canino, carcinossarcoma, COX-2, mama, mesenquimal, sarcoma, tumor.

INTRODUCTION

Canine mammary sarcomas belong to a rare and diverse group (Lorenzová et al. 2010, Dolka et al. 2013, Nunes et al. 2018) consisting of malignant mesenchymal tissue neoplasms in mammary glands (Cassali et al. 2014, Zappulli et al. 2019). The most common subtypes of primary mammary sarcomas are chondrosarcomas, fibrosarcomas, hemangiosarcomas, and osteosarcomas (Misdorp et al. 1971, Dolka et al. 2013, Nunes et al. 2018).

However, canine mammary carcinosarcomas are uncommon (Lorenzová et al. 2010, Dolka et al. 2013, Nunes et al. 2018). Carcinosarcomas are composed of a malignant luminal epithelium and a malignant mesenchymal component. In addition, myoepithelial cell proliferation may occur (Misdorp et al. 1973, Cassali et al. 2014, Zappulli et al. 2019).

Tumor sizes, lymph node involvement, distant metastasis, histologic grades, and the expression of immunohistochemical markers like cyclooxygenase-2 (COX-2) have been used to assess female dogs with mammary carcinomas and establish their prognosis (Queiroga et al. 2007, Rasotto et al. 2017, Canadas et al. 2019).

COX-2 is an inducible enzyme involved in inflammation, neoplastic transformation, and tumor progression (Méric et al. 2006, Hayes 2007). COX-2 overexpression is associated with disease progression, angiogenesis, and poor prognosis in canine mammary tumors (Lavalle et al. 2009, Queiroga et al. 2010, Carvalho et al. 2016, Pastor et al. 2020). Furthermore, selective COX-2 inhibitors have been used as therapeutic tools for canine mammary carcinomas (Souza et al. 2009, Lavalle et al. 2012). Although the expression and function of COX-2 in canine mammary carcinomas have been studied, little is known about COX-2 expression in canine mammary non-epithelial tumors.

Sarcomas and carcinosarcomas generally display aggressive biologic behavior with a tendency toward local recurrence and metastasis (Misdorp et al. 1971, 1973, Hellmen et al. 1993, Langenbach et al. 1998). Although most studies about canine mammary sarcomas and carcinosarcomas have focused on histologic types, little is known about the biological value of histogenic variations (Misdorp et al. 1971, 1973, Dolka et al. 2013). This limited knowledge justifies further research regarding the prognostic value of different clinical and pathological parameters for mesenchymal subtypes. As such, this study aimed to compare the clinical and pathological characteristics and the COX-2 immunohistochemical expression of different histologic subtypes of sarcomas and carcinosarcomas.

MATERIALS AND METHODS

Case selection. Thirty-eight tissue samples of mammary tumors with malignant mesenchymal components from female dogs (23 carcinosarcomas and 15 sarcomas) were selected for the study. All samples were obtained from the pathological archives of the "Setor de Patologia Veterinária" of the "Universidade Federal do Rio Grande do Sul" (UFRGS). These cases were registered from 2014 to 2018. The inclusion criteria were: I) a histologic confirmation of sarcoma or carcinosarcoma, II) no prior history of surgical correction of mammary issues, III) no simultaneous malignant neoplasms other than carcinosarcoma or sarcoma and IV) available tissue in paraffin block storage.

Exam request records were searched to collect the following information: age, affected mammary glands, and radiographic evidence of distant metastasis at the initial diagnosis. Tumor diameter was determined using pathologic reports (measurement at the trimming time).

Histologic assessment. The selected cases were histologically reviewed using hematoxylin and eosin-stained (HE) sections. Standard criteria were followed for classifying neoplasms such as sarcomas and carcinosarcomas (Cassali et al. 2014, Zappulli et al. 2019). The mammary origin of the neoplasms was determined by identifying mammary acini in the histologic sections. The histologic parameters were the type of sarcoma proliferation, intratumoral necrosis, vascular invasion, lymph node metastasis, and histologic grade. Vascular invasion was defined as neoplastic cells in spaces with a clear-cut endothelial lining.

We followed the established criteria for grading mammary sarcomas in female dogs (Trojani et al. 1984, Dolka et al. 2013). The most representative areas of sarcomatous proliferation were used to assess histologic grades. The number of mitotic cells in 10 high-power fields (HPFs) was counted under a 40x objective lens. An Olympus CX31 microscope (Olympus, Tokyo, Japan) with a field diameter of 0.51mm and an HPF of 0.2mm^2 was used to perform the mitotic counts. The mean number of mitoses (the number of mitoses divided by the number of fields) was adjusted to ensure equivalence among the assessments conducted by Dolka et al. (2013).

Sarcomatous proliferation was classified into low-grade malignancy (grades I and II) and high-grade malignancy (grade III) (Dolka et al. 2013). Samples of surgically resected neoplastic lymph nodes (24 cases) were reviewed to assess for neoplastic cells and the type of metastatic proliferation (epithelial, mesenchymal, or both). Lymph nodes were considered positive for metastasis when isolated cells or groups of non-lymphoid neoplastic cells were detected in the subcapsular sinus or lymph node parenchyma.

Immunohistochemistry (IHC). The immunoreactivity for cytokeratin (AE1/AE3) and vimentin was used in tumor samples and lymph nodes to confirm epithelial and mesenchymal proliferation. Neoplasms with spindle cell proliferation (fibrosarcomas and

carcinosarcomas with fibrosarcomatous components) were also immunohistochemically evaluated for the presence of p63. All tumor samples were analyzed for COX-2 immunoreactivity.

For the immunohistochemical analysis, tissue sections of 3µm thickness were prepared and mounted on gelatin-coated slides. Deparaffinized tissue sections were subjected to heat-induced antigen retrieval (cytokeratin AE1/AE3, vimentin and COX-2) or pressurized heat (125°C/2 min) (p63). Endogenous peroxidase activity was blocked with a 10% hydrogen peroxide (H_2O_2) solution in methyl alcohol. Next, the sections were incubated with the following antibodies, known for their reactivity with canine tissues (Vascellari et al. 2012, Vieira et al. 2022): Novocastra™ Liquid Mouse Monoclonal Anti-Multi-Cytokeratin, NCL-L-AE1/AE3, Leica Biosystems; United Kingdom (1:150); Novocastra™ Liquid Mouse Monoclonal Antibody Vimentin, NCL-L – VIM-V9; Leica Biosystems; United Kingdom (1:800); Monoclonal Mouse Anti-Human p63 Protein, Clone Dak p63, Dako Denmark; Denmark (1:100) and rabbit anti- COX2 Monoclonal Antibody, Clone SP21, MA5-14568, Thermo Scientific, Invitrogen, USA (1:80). The antibodies were incubated for one hour (cytokeratin, vimentin, and COX-2) or 14-16h/4C (p63) in a humid chamber. Subsequently, a Novolink™ Polymer Detection System (Leica Biosystems, United Kingdom) was used for incubation in compliance with the manufacturer's instructions. Chromogen 3.3-diaminobenzidine was used to visualize immunoreactivity, followed by Harris hematoxylin to counterstain. Sections of canine mammary tumors that had previously tested positive for vimentin, cytokeratin AE1/AE3 and p63 were used as positive controls. Sections of canine kidney tissue that had previously tested positive were used as a positive control. For a negative control, PBS was used to omit the primary antibody in the three markers.

The expression of COX-2 in the sarcomatous and carcinomatous components was evaluated using a semi-quantitative calculation of the percentage of positive cells in 5 HPFs and their intensity. Scores were distributed by percentage, in which 0 = no staining, 1 = fewer than 10% stained cells, 2 = between 10 and 30%, 3 = 31% to 60%, and 4 = more than 61%. Regarding intensity, 0 = no intensity, 1 = weak, 2 = moderate, and 3 = strong. These values were multiplied, and the total score, which ranged from 0 to 12, was then divided into groups of low (0-5) and high (6-12) scores (Lavalle et al. 2012).

Statistical analysis. Associations between mesenchymal subtypes (osteosarcomatous versus non-osteosarcomatous), osteosarcomatous pattern (osteoblastic versus non-osteoblastic), histologic types (sarcomas versus carcinosarcomas), and clinical and pathological variables (tumor size, intratumoral necrosis, mesenchymal vascular invasion, lymph node metastasis, histologic grade, and COX-2 immunohistochemical expression) were tested. All associations were analyzed using Fisher's exact test (more than 25% of the cells had an expected value of less than 5) (P<0.05) and STATA 14.0 software (Stata Corp LP).

RESULTS AND DISCUSSION

The sarcomas presented malignant mesenchymal differentiation of the following types: osteosarcoma 62.7% (11/17), fibrosarcoma 20.0% (3/15), and liposarcoma 5.9% (1/17). Among the carcinosarcomas, 52.2% (12/23) showed a malignant mesenchymal component of the osteosarcoma type, 21.7% (5/23) of the liposarcoma type, 17.4% (4/23) of the chondrosarcoma type, and 8.7% (2/23) of the fibrosarcoma type.

For all the cases in our study, we performed an immunohistochemical analysis of the expression of intermediate vimentin and cytokeratin AE1/AE3 filaments. This made it possible to confirm epithelial and mesenchymal proliferation, which is important in distinguishing sarcomas from carcinosarcomas (Kandukuri et al. 2017). Besides this, in some cases, immunohistochemistry made it possible to detect small foci of sarcoma and carcinoma proliferation in lymph nodes.

For neoplasms with a monomorphic proliferation of fusiform or spindle cells (based on the HE stain), cytokeratin AE1/AE3, vimentin and p63 expression allowed the researchers to distinguish between fibrosarcomas and malignant myoepitheliomas. Fibrosarcomas were differentiated from malignant myoepithelioma by positive vimentin staining (myoepithelial/mesenchymal marker) and negative cytokeratin AE1/AE3 (epithelial/myoepithelial marker) and p63 (myoepithelial marker) staining (Alonso-Diez et al. 2019).

For biphasic neoplasms, consisting of a population of columnar cells arranged in tubules and a second population of oval-to-fusiform cells, immunohistochemistry was used to distinguish between carcinosarcomas and carcinoma and malignant myoepithelioma. The oval-to-fusiform cells showed positive staining for vimentin and negative staining for p63 and cytokeratin AE1/AE3, facilitating a diagnosis of carcinosarcoma (Canadas et al. 2019).

Lymph node mesenchymal metastasis and vascular invasion were more frequent for sarcomas and carcinosarcomas with osteosarcomatous proliferation (P<0.005) (Table 1). Compared with other mesenchymal proliferation types, these findings demonstrate the more aggressive proliferation of osteosarcomatous cells and their propensity to invade lymph vessels.

Table 1. Clinical and histologic aspects according to mesenchymal proliferation (n=40)

	Osteosarcomatous n (%)	Non-osteosarcomatous n (%)	*P*-value
Tumor diameter			
< 5.0 cm	5 (21.7)	2 (13.3)	0.419
>5.0 cm	18 (78.3)	13 (86.7)	
Lymph node metastasis*			
Absent	6 (54.5)	12 (100.0)	0.014
Present	5 (45.4)	0 (0)	
Distant metastasis			
Absent	10 (100.0)	10 (90.9)	0.524
Present	0 (0)	1 (9.09)	
Necrosis			
<50.0%	14 (60.9)	12 (80.0)	0.190
>50.0%	9 (39.1)	3 (20.0)	
Vascular invasion*			
Absent	15 (65.2)	15 (100.0)	0.010
Present	8 (34.8)	0 (0)	
Histologic grade			
Low and intermediate	5 (21.7)	3 (20.0)	0.615
High	18 (78.3)	12 (80.0)	
COX-2*			
0-5	14 (73.7)	9 (90.0)	0.302
6-12	5 (26.3)	1 (10.0)	

* Mesenchymal cells.

No other factors showed significant association with mesenchymal histologic subtypes, including tumor size, intratumoral necrosis, histologic grade, high COX-2 scores, and distant metastasis.

Concerning the carcinoma component, we observed a simple papillary pattern in 60.8% (14/23) of cases, 26.1% (6/23) tubular patterns, 8.7% (2/23) solid patterns, and 4.3% (1/23) comedocarcinoma patterns.

Skeletal osteosarcomas can be classified into diverse types due to the heterogeneity of their cellular populations and diverse extracellular matrix formation (Thompson & Dittmer 2017). In our study, the osteosarcoma proliferation presented osteoblastic 47.8% (11/23), 4.3% (1/23) chondroblastic, 21.7% (5/23) fibroblastic, 8.7% (2/23) telangiectatic, and 17.4% (4/23) giant cell-rich patterns (Fig.1-4). Skeletal fibroblastic osteosarcomas have been associated with better prognoses, while the opposite has been reported for the telangiectatic type (Thompson & Dittmer 2017). Similarly, we found no correlation between histologic subtypes and other clinical or pathological variables (Table 2).

Sarcomas and carcinosarcomas showed similar clinical and pathological characteristics (Table 3). Tumor sizes varied between 2.0cm and 20.0cm, with an average of 10.6cm as the largest dimension. A prevalence of carcinosarcomas and sarcomas larger than 5.0cm is consistent with the unfavorable prognoses usually attributed to these tumors (Rasotto et al. 2017). Since survival rates are lower among female dogs with larger-diameter tumors, tumor size is an important prognostic factor for female dogs with mammary neoplasms (Ferreira et al. 2009).

Adjacent lymph node samples were available for 60.5% (23/38) of the cases. The frequency of lymph node metastases for sarcomas was 37.5% (3/8), while 13.3% (2/15) of carcinosarcomas presented mesenchymal metastasis. There was lymph node metastasis with carcinoma components for 6.6% (1/15) of the carcinosarcomas. This component was of

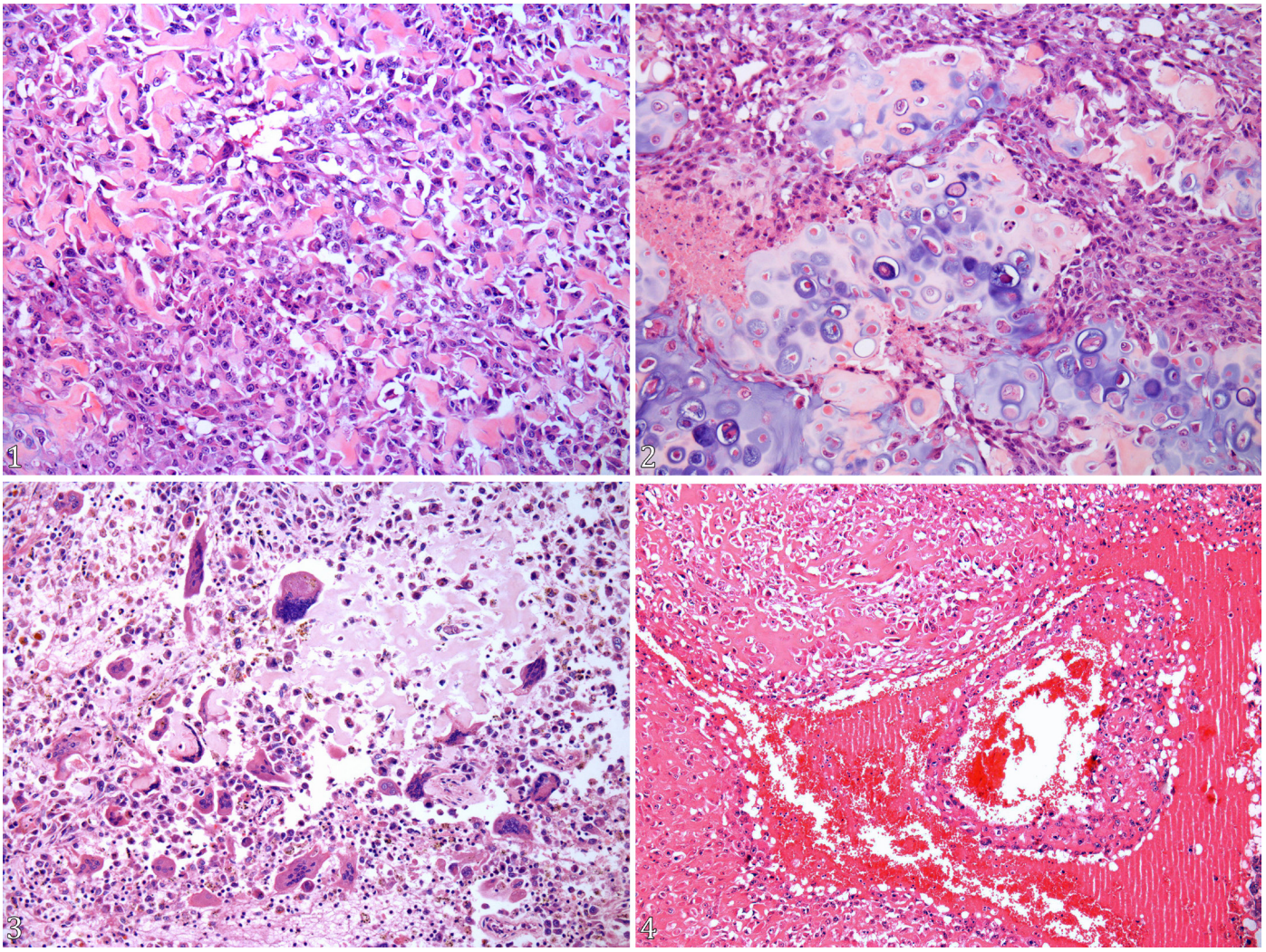

Fig.1-4. Osteosarcomatous subtypes in the mammary glands of the female dogs. (**1**) Osteoblastic pattern. Proliferation of osteoblasts intermixed with a large quantity of amorphous eosinophilic material (osteoid matrix). HE, obj.40x. (**2**) Chondroblastic pattern. Proliferation of osteoblasts intermixed with an osteoid matrix, as well as multifocal pre-chondroid forms and focal areas of necrosis. HE, obj.40x. (**3**) Giant cell-rich pattern. Proliferation of osteoblasts intermixed with a large quantity of osteoid matrix, in addition to numerous multinucleated giant cells and a focally extensive area of necrosis. HE, obj.40x. (**4**) Telangiectatic pattern. Proliferation of osteoblasts surrounded by an osteoid matrix and intermixed with large vascular spaces containing large quantities of red blood cells. HE, obj. 40x.

Table 2. Clinical and histologic aspects according to osteosarcomatous pattern (n=23)

	Osteoblastic (n=11)	Non-osteoblastic (n=12)				*P*-value
		CH (n=1)	FS (n=5)	RGC (n=4)	TA (n=2)	
	n (%)	n (%)	n (%)	n (%)	n (%)	
Tumor diameter						
<5.0 cm	3 (27.3)	0 (0)	0 (0)	2 (50.0)	0 (0)	0.455
>5.0 cm	8 (72.7)	1 (100.0)	5 (100.0)	2 (50.0)	2 (100.0)	
Lymph node metastasis*						
Absent	3 (60.0)	-	1 (50.0)	2 (66.7)	0 (0)	0.608
Present	2 (40.0)	-	1 (50.0)	1 (33.3)	1 (100.0)	
Distant metastasis						
Absent	5 (100.0)	1 (100.0)	2 (100.0)	2 (100.0)	1 (100.0)	-
Present	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Necrosis						
<50.0%	8 (72.7)	0 (0)	2 (40.0)	3 (75.0)	1 (50.0)	0.247
>50.0%	3 (27.3)	1 (100.0)	3 (60.0)	1 (25.0)	1 (50.0)	
Vascular invasion*						
Absent	6 (54.5.0)	0 (0)	4 (80.0)	3 (75.0)	2 (100.0)	0.278
Present	5 (45.4.0)	1 (100.0)	1 (20.0)	1 (25.0)	0 (0)	
Histologic grade*						
Low and intermediate	4 (36.4)	0 (0)	1 (20.0)	0 (0)	0 (0)	0.131
High	7 (63.6)	1 (100.0)	4 (80.0)	4 (100.0)	2 (100.0)	
COX-2*						
0-5	6 (60.0)	0 (0)	2 (100.0)	3 (100.0)	1 (100.0)	0.184
6-12	4 (40.0)	1 (100.0)	0 (0)	0 (0)	0 (0)	

CH = chondrosarcomatous, FS = fibrosarcomatous, RGC = rich with giant cells, TA = telangiectatic; * Mesenchymal cells.

Table 3. Clinical and pathological characteristics of neoplasms with malignant mesenchymal components (n=40)

	Carcinosarcoma n (%)	Sarcoma n (%)	*P*-value
Tumor diameter			
<5.0 cm	5 (21.7)	2 (13.3)	0.419
>5.0 cm	18 (78.2)	13 (86.7)	
Lymph node metastasis*			
Absent	12 (80.0)	5 (62.5)	0.334
Present	3 (20.0)	3 (37.5)	
Distant metastasis			
Absent	14 (93.3)	7 (100.0)	0.682
Present	1 (6.7)	0 (0)	
Necrosis			
<50%	16 (69.5)	10 (66.7)	0.563
>50%	7 (30.4)	5 (33.3)	
Vascular invasion *			
Absent	16 (69.6)	10 (66.7)	0.563
Present	7 (30.4)	5 (33.3)	
Histologic grade**			
Low or intermediate	6 (26.0)	2 (13.3)	
High	17 (74.0)	13 (86.7)	0.302
COX-2*			
0-5	14 (77.8)	8 (72.7)	0.547
6-12	4 (22.2)	3 (27.3)	

* Epithelial and/or mesenchymal cells, ** mesenchymal cells.

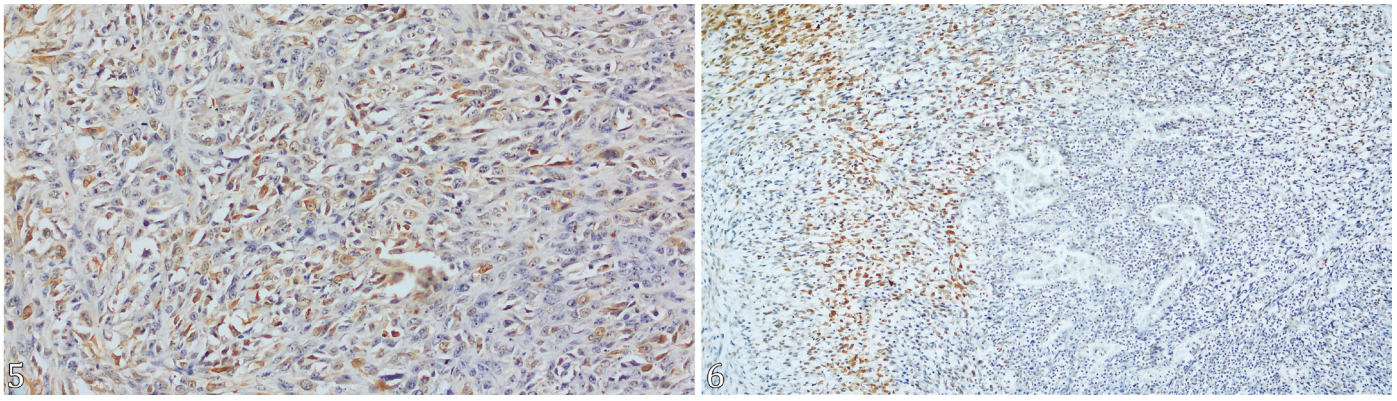

Fig.5-6. COX-2 immunohistochemical staining in canine mammary sarcomas. (**1**) Osteosarcoma showing diffuse immunoreactivity for COX-2 in the cytoplasm of neoplastic fusiform, stellate and ovoid cells. IHC, obj.40x. (**2**) Fibrosarcoma showing intense immunoreactivity for COX-2 in tumor cells surrounding areas of tumor necrosis. IHC, obj.20x.

the anaplastic subtype, but the primary tumor exhibited a simple papillary pattern. None of the lymph nodes we assessed presented metastasis of both components.

In canine mammary sarcomas and carcinosarcomas, metastases through the lymphatic and hematogenous routes to the lungs have been reported (Hellmen 2014, Nunes et al. 2019). The frequency of distant metastasis was lower than previously reported for sarcomas (Hellmen et al. 1993) and carcinosarcomas (Rasotto et al. 2017, Nunes et al. 2019). A lack of radiographic exam results weakens knowledge regarding tumor behavior from the moment of the first diagnosis. This limitation was probably due to problems accessing the results of pre-surgical radiographic exams and those conducted throughout the clinical history.

Histologic grades might help predict survival time in female dogs with mammary carcinomas (Karayannopoulou et al. 2005, Nguyen et al. 2018). A previous study used a grading system to assess mammary sarcomas in female dogs, and 88.9% of the sarcomas demonstrated a high histologic grade (Dolka et al. 2013). The authors also observed that sarcomas with a higher histologic grade were associated with more proliferative activity (Ki67 index). We used the same grading system and observed a remarkably similar percentage of high grades among the sarcomas and carcinosarcomas.

There are rare, published reports regarding COX-2 expression in canine mammary sarcomas. One study found intense expression in one mammary fibrosarcoma (Arenas et al. 2016). In our series, high COX-2 scores were detected in 50.0% (1/2) fibrosarcomas and 25% (2/8) osteosarcomas.

Positive staining was observed in 16.7% (3/18) of the sarcomatous component in carcinosarcoma. All of these were osteosarcomas.

The expression was cytoplasmatic and multifocal and was detected in osteoblasts, fibroblasts, chondroblasts, and, occasionally, in multinucleated giant cells (Fig.5). Immunoreactivity was detected mainly in tumor cells surrounding areas of tumor necrosis in 66.7% of the positive cases (Fig.6). One possible explanation for this finding is induction of COX2 expression in tumor cells by regional hypoxia or inflammatory response (Herceg et al. 2009). One in 18 carcinosarcomas presented high COX-2 expression in the carcinomatous and sarcomatous components. Another case of carcinosarcoma showed high expression in the carcinomatous component.

The percentage of carcinosarcomas with a high COX-2 score was lower than the one previously described elsewhere (Queiroga et al. 2010, Carvalho et al. 2016). Possible justifications for these differences in results include the use of dissimilar antibodies or inherent variations in immunohistochemical exams.

CONCLUSIONS

Sarcomas and carcinosarcomas had similar clinical and pathological characteristics. They developed as large tumors, with intratumoral necrosis and a predominance of high histologic grades, although there was a low frequency of vascular invasion and nodal metastasis.

Compared with non-osteosarcomatous subtypes, osteosarcomas presented more aggressive characteristics, such as vascular invasion and lymph node metastasis.

COX-2 was overexpressed in similar ratios of sarcomas and carcinosarcomas. However, the prognostic value of COX-2 expression and the usefulness of COX-2 inhibitors in treating these neoplasms remain to be further investigated.

Acknowledgments.- The authors are grateful to the Brazilian research council "Conselho Nacional de Desenvolvimento Científico e Tecnológico" (CNPq) for financing this study (Proc. 454297/2014-9) and for providing undergraduate researcher scholarships. The authors would like to thank Dr. Geovanni Dantas Cassali and Fernanda Freitas Miranda, who contributed to the immunohistochemical study.

Conflict of interest statement.- The authors declare that there are no conflicts of interest.

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