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Clinical Reports

A rare bone metastasis of mammary carcinoma in a female dog: case report

Metástase óssea rara de carcinoma mamário em cadela: relato de caso

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Mammary gland tumors are the most frequent neoplasm in dogs and are mostly malignant. Metastases ordinarily occur firstly at the pulmonary level, and subsequently in the lymph nodes, liver and kidneys. Less frequently, they appear at the bone. Therefore, the present study report a case of bone metastasis in a seven-year-old female boxer dog, consisting of poorly differentiated carcinoma that probably originated from mammary carcinoma. For the diagnosis, the bone biopsy was performed and the tissue fragments obtained were sent for histopathological examination. The positive immunohistochemical stain for cytokeratin 7 performed later reinforced the hypothesis that mammary carcinoma was the primary site of metastasis. The occurrences of bone metastases arising from the mammary gland are rare among dogs, possibly because metastasis is underdiagnosed and the animals do not reach the final stage of the disease. Thereby, there is a need to investigate the entire skeleton more accurately, in order to make an early diagnosis of bone metastasis and increase these animals' survival.

Palavras-chave:
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R E S U M O

Os tumores de glândula mamária são as neoplasias mais frequentes em cães e são principalmente malignos. As metástases geralmente ocorrem primeiro no nível pulmonar e, posteriormente, nos gânglios linfáticos, fígado e rins. Com menos frequência, eles aparecem no osso. Portanto, o presente estudo relata um caso de metástase óssea em uma cadela boxer de sete anos, consistindo de carcinoma pouco diferenciado, provavelmente originado de carcinoma mamário. Para o diagnóstico, foi realizada biópsia óssea e os fragmentos de tecido obtidos foram encaminhados para exame histopatológico. A coloração imunohistoquímica positiva para citoqueratina 7 realizada posteriormente reforçou a hipótese de que o carcinoma mamário era o sítio primário de metástase. A ocorrência de metástases ósseas oriundas da glândula mamária é rara em cães, possivelmente porque a metástase é subdiagnosticada e os animais não atingem o estágio final da doença. Desse modo, há a necessidade de investigar todo o esqueleto com mais precisão, a fim de fazer um diagnóstico precoce de metástase óssea e aumentar a sobrevida desses animais.

INTRODUCTION

Tumors or neoplasms are abnormal tissue growths with accelerated development that involve alterations to cellular DNA and result in dysfunctions that control cell growth and differentiation (ANDRADE, 2008). The prevalence of these neoplastic processes in dogs and cats has been increasing significantly, due to population growth and increased longevity among these animals, achieved through better sanitary conditions and management. Moreover, people's awareness about suffering caused by cancer has increasing (DALECK et al., 2009; MAITI et al., 2014; WITHROW; VAIL, 2007).

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In Brazil, mammary gland tumors are the most frequent neoplasm in dogs. They are mostly malignant (BIONDI et al., 2014; DIAS et al., 2016; TORÍBIO et al., 2012;) and their prevalence ranges from 26 to 73% (ANDRADE et al., 2010; BIONDI et al., 2014; MUNSON; MORESCO, 2007; OLIVEIRA FILHO et al., 2010; PÉREZ-ALENZA et al., 2000). In developed countries, a prevalence of 50% has been reported (CASSALI et al., 2011).

Secondary bone tumors can be described as unifocal or multifocal. They spread from a primary bone or soft-tissue tumor in another place within the body (GOEDEGEBUURE, 1979). Metastases from mammary gland tumors ordinarily occur firstly at the pulmonary level, and subsequently in the lymph nodes, liver and kidneys. Less frequently, they appear at the bone, heart and skin levels (LANA et al. 2007; RUTTEMAN; KIRPENSTEIJN, 2003).

Unlike humans, canine bone metastases are considered to be less common than primary bone tumors. The dogs that exhibit bones metastases are a heterogeneous old aged and variable-sized animal group, and their metastases occur most frequently in the axial skeleton and appendicular proximal bones. There is a hypothesis that bone metastasis is less frequent in dogs because skeleton radiography examinations and necropsy are only rarely performed (TROST et al., 2014).

Although the frequency of mammary tumors is high in dogs, occurrences of bone metastasis is rare (CHUN; LORIMIER, 2003). Therefore, the present study report a case of bone metastasis in a female dog, comprising poorly differentiated carcinoma that probably originated from mammary carcinoma.

CASE REPORT

A seven-year-old female boxer dog weighing 22.1 kg was attended at the Clinical and Surgical Practice Center of the Federal Institute of Santa Catarina, Concórdia campus. The dog had a clinical history of lameness in the right forelimb that began five days earlier. This limb had been increasing in volume for three days and the dog had started to spend more time in decubitus. The animal had already been affected by mammary and vulvar tumors, which had been treated through surgical procedures. However, at that time, no histopathological analysis had been performed on the lesions. Physical examination revealed increased volume at the distal extremity of the right thoracic limb, close to the carpal joint, without any other changes observed.

Laboratory tests were requested. There were no alterations in the blood counts, while in the biochemical profile there was an increased alkaline phosphatase concentration (268 IU/I). A radiographic examination revealed areas of bone lysis and proliferation in the distal third of the radius and ulna (Figure 1).

Figure 1. Areas of bone lysis and proliferation in the distal third of the radius and ulna in the right anterior limb (arrows) (a, b).

Half a 227-mg tablet of firocoxib every 24 hours for 10 days was prescribed, to relieve the animal's discomfort until a bone biopsy could be performed. At the end of this period of time, the bone biopsy was performed and the tissue fragments obtained were sent for histopathological and microbiological examination. The latter was negative for growth of bacteria or fungi. Two bone fragments were collected for histopathological examination: one of them had dimensions of 2.0 x 0.4 x 0.4 cm, with a soft and irregular brownish surface; and the other one had dimensions of 0.8 x 0.4 x 0.4 cm, with a calcified and irregular whitish-brown surface. Under a microscope, the fragments showed malignant neoplasia profusely invading the bone tissue, characterized by papilliferous cordal outlines of cells with oval hyperpigmented nuclei, moderate pleomorphism, evident nucleoli, abundant cytoplasm with distinct borders and presence of numerous mitosis figures (Figure 2, 3 and 4). This was compatible with bone metastasis consisting of poorly differentiated carcinoma that probably originated from mammary carcinoma.

Figure 2. Malignant neoplasm diffusely invading bone tissue, characterized by papilliferous cordal outlines (entire region is shown in image) H&E 10x.

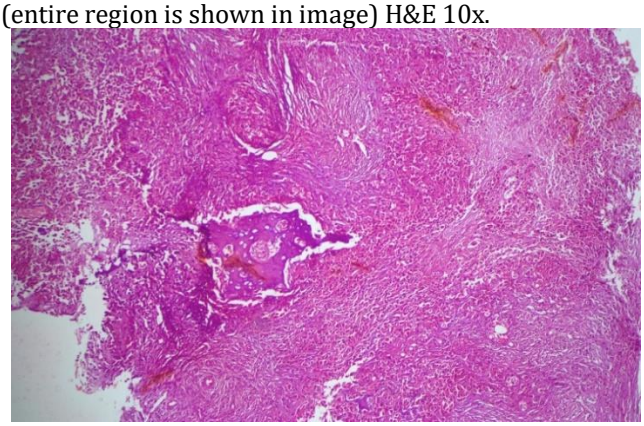


Figure 3. Papilliferous cordal cells outlines with oval hyperpigmented nuclei, moderate pleomorphism, evident nucleoli and abundant cytoplasm with indistinct borders (black arrows). Presence of numerous mitosis figures (white arrows) H&E 40x.

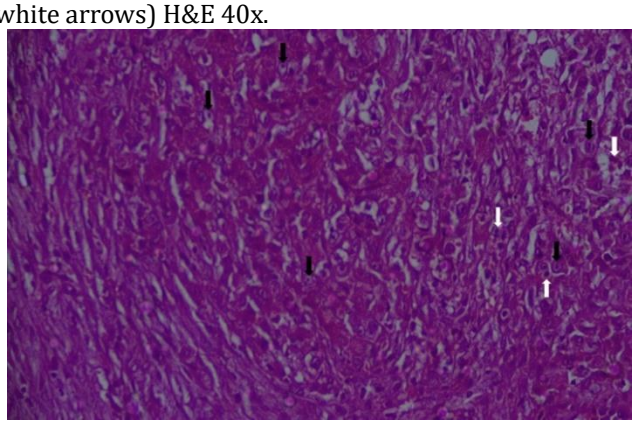
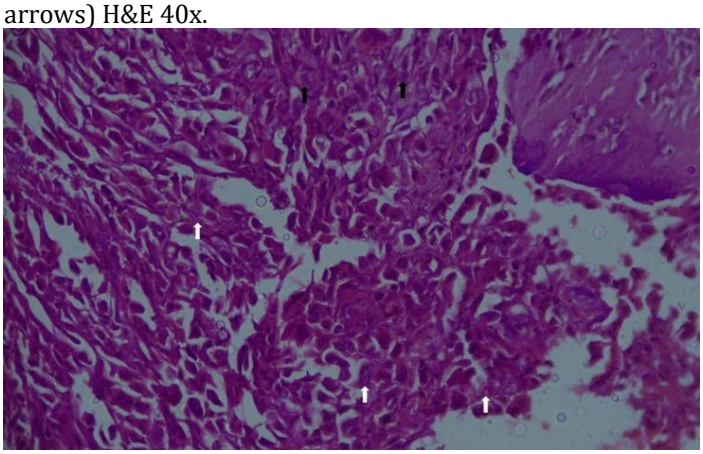
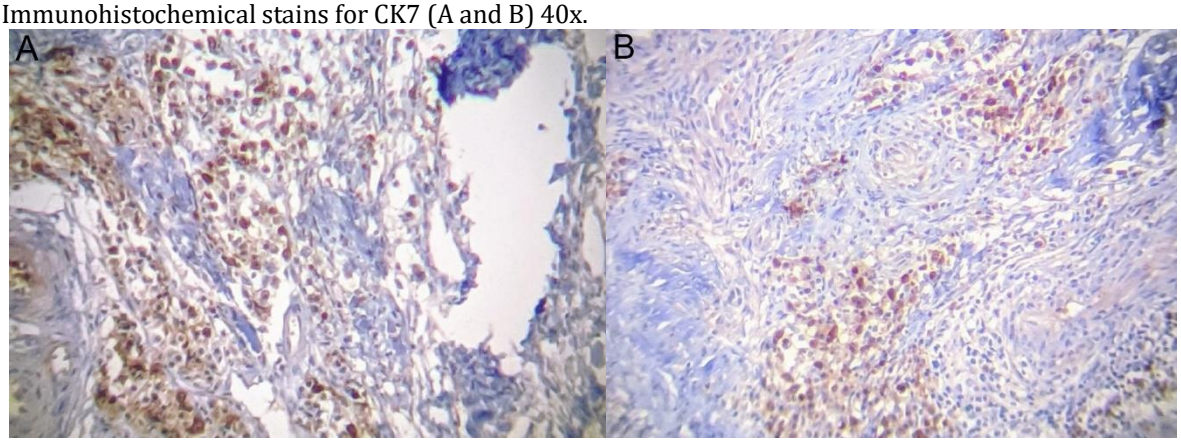


Figure 4. Oval hyperpigmented nuclei, moderate pleomorphism, evident nucleoli, abundant cytoplasm with indistinct borders (black arrows) and mitosis figures (white arrows) H&E 40x.



Subsequently, the material was subjected to immunohistochemical stains for cytokeratins (CK) 7 and 20, as well as for the marking of estrogen (ER) and progesterone (RP) receptors, to delimit the primary site of metastasis. After analysis, the material was positive only for CK 7 (Figure 5).

Figure 5. Immunohistochemical stains for CK7 (A and B) 40x.



Chemotherapy treatment was proposed, but the dog's keeper did not authorize the treatment. Thus, the prescription of firocoxib was maintained, with the addition of tramadol (3 mg/kg every 8 hours) and dipyrone (25 mg/kg every 12 hours). At this time, no pulmonary metastasis was observed. Fifteen days after the diagnosis had been made, the animal was brought back for revaluation due to of lack of appetite and apathy. A physical examination showed that the lameness was still present, with significant growth of the bone lesion and growth of the left prescapular lymph node. The dog's keeper only wanted palliative care and therefore maintenance of pain control was recommended. Twenty days later, the animal died at home. It was not possible to perform a necropsy.

DISCUSSION

The type of neoplasm most commonly diagnosed in female dogs is mammary gland tumors (SABA et al., 2007) and this is one of the main types of tumor that cause bone metastases (BRODEY; REID; SAUER, 1966; MISDORP; DEN HERDER, 1966; MORGAN, 1972). Bone metastases in dogs are uncommon and less frequent than primary neoplasms (CHUN; LORIMIER, 2003). The present report corroborates the data in the literature, given that the bone metastasis found here probably originated from mammary carcinoma.

Immunohistochemical stain positive for CK 7 favors breast carcinoma as the primary site of bone metastasis. In a study by Espinosa de Los Monteros et al. (1999), fortify this affirmation, since, among the epithelial tumors used by them, only canine and feline breast carcinomas and canine cholangiocarcinomas were the only with CK7 positive and CK 20 negative immunophenotype.

In veterinary medicine, information about bone metastasis and bone involvement in multicenter tumors is limited to descriptions of individual cases, in a small number of studies that are very old (TROST, 2014). In a study by Misdorp et al. (1972), two animals with mammary gland tumors developed skeletal metastases: one in the femur and the other in a vertebra. In another study by the same author in 1966, 10 animals out of 114

that were affected by mammary tumor metastasis had secondary bone involvement; in six of these cases, the main initial symptom was lameness, as in the case reported in the present study.

One of the most recent studies published on this subject was conducted by Trost (2014). In this study, the skeletons of 110 animals were analyzed and 21 of them were found to contain metastatic bone involvement. Most of these animals were female, aged 4 to 16 years. In eight of these animals with bone metastases, the initial tumor location was the mammary gland: seven had simple carcinoma and one had osteochondrosarcoma. Furthermore, dogs with tumors originating in the mammary glands were the most prevalent cases in that study. In the present report, the animal studied was a female and was within the age range of most of the animals reported by Trost (2014).

Cooley; Waters (1998) found that bone metastasis was the initial manifestation of metastatic carcinoma in 79% of the animals that they studied. The most preferred site for metastasis was the axial skeleton and only 4 of the 36 animals developed bone carcinoma that was distant from the elbow/knee, and all of these affected the ulna. These data denote the rarity of the present report, since the animal developed the metastatic tumor in the carpal region.

The lumbar vertebrae, femur, humerus, ribs and pelvis are common sites for dissemination of bone metastases, possibly because these are the preferred sites for metastases from common urogenital malignancies such as prostate, bladder, urethra and breast cancer (EHRHART et al., 2013). As in humans, bone metastases distal to the knee and elbow joints are uncommon (ADLER, 2000; COOLEY; WATERS, 1998; THOMPSON; POOL, 2002).

Breast tumors in women have been a subject of intense study for years, and the frequency of bone metastasis is probably equal to, if not exceeding, the frequencies of lung and liver metastases (HAAGENSEN, 1956). Among these women, bone metastases due to breast cancer are common. These are responsible for much of the morbidity and mortality, and approximately 80% of the patients affected die, which thus emphasizes the importance of metastases in disease progression (SIMMONS et al., 2015). In dogs, bone metastases are considered uncommon, or their frequency is considered underestimated because it is rare for the skeleton to be fully examined through radiography and necropsy (BRODEY et al., 1966; MISDORP; DEN HERDER, 1966; OWEN, 1967; THOMPSON; POOL, 2002). Moreover, it needs to be borne in mind that female dogs with mammary neoplasms are often destroyed before the terminal stage of the disease is reached, which means that bone metastasis may not have been completed (MISDORP; DEN HERDER, 1966; OWEN, 1967; TROST, 2014).

CONCLUSIONS

From the bibliographic investigation conducted here, occurrences of bone metastases originating from the mammary gland are rare among dogs, possibly because metastasis is underdiagnosed and the animals do not reach the final stage of the disease. Moreover, this location for metastases is uncommon, in relation to the cases already reported. In this light, there is a need to investigate the entire skeleton more accurately, in order to make an early diagnosis of bone metastasis and increase these animals' survival.

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