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Canine periosteal osteosarcoma

Osteosarcoma periosteal en perro

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ABSTRACT:

Osteosarcoma is the most common bone tumor in dogs. The periosteal osteosarcoma is a subtype of osteosarcoma, and is considered rare in the canine species. The purpose of the present study was to describe a 14-year-old female dog with an ulcerated mass located in the right tibia and 30-days of evolution. The patient was submitted to complementary exams (blood count analysis, dosage of biochemical enzymes - creatinine and alanine aminotransferase, thoracic radiographs, and abdominal ultrasonography) to perform complete staging of the disease. Radiography of the right tibia revealed proliferative and lytic periosteal reaction. The cytological analysis of the mass suggested a round cell tumor. The clinical and the radiological findings indicated the presence of a bone tumor. Pelvic limb amputation was the initial surgical treatment suggested to the client. The histopathological examination revealed the presence of periosteal osteosarcoma with free margins and lymph nodes without evidence of tumor cells. Clinical follow-up was performed through imaging exams without evidence of metastatic disease. The dog had a nine-month survival free time from diagnosis.

KEYWORDS: Bone tumor, dog, neoplasia, periosteum, veterinary pathology.

RESUMEN:

El osteosarcoma es el tumor óseo más común en los perros. Osteosarcoma periosteal es un subtipo de osteosarcoma y se considera raro en la especie canina. El objetivo del presente estudio fue describir un caso de una perra mestiza de 14 años de edad con una masa ulcerada y localizada en la tibia derecha y 30 días de evolución. El paciente se sometió a exámenes adicionales (análisis de sangre, dosis de enzimas bioquímicas - creatinina y alanina aminotransferasa, radiografías torácicas y ultrasonografía abdominal) para la estadificación completa de la enfermedad. La radiografía de la tibia derecha reveló reacción perióstica proliferativa y lítica. El examen citológico de la masa sugirió un tumor de células redondas. La evaluación clínica y hallazgos radiológicos sugieren la presencia de una neoplasia ósea. La amputación de la extremidad pélvica derecha fue el tratamiento quirúrgico inicial sugerido al cliente. El examen histopatológico reveló la presencia de osteosarcoma periosteal con márgenes libres y ganglios linfáticos sin

evidencia de células tumorales. El seguimiento clínico se realizó a través de exámenes de imágenes sin evidencia de enfermedad metastásica. El perra tenía un tiempo de sobrevida de nueve meses desde el diagnóstico.

PALABRAS CLAVE: Tumor óseo, perro, neoplasia, periostio, patología veterinaria.

INTRODUCTION

Osteosarcoma is a malignant mesenchymal tumor that corresponds the most common primary bone tumor in dogs. Due to the implantation ability of the distant tumor cells from the original tumor, the animals affected by this tumor die because of lung metastasis. Regarding all the aspects given, the treatment becomes challenging for Veterinary Oncologists (1).

The periosteal osteosarcoma was described together with other types of osteosarcoma in 1976 (2,3). This malignant bone tumor has low incidence and is a variant of osteosarcoma. The main lesion of the periosteal osteosarcoma is surface lesion without evidence of medullary involvement. However, some reports have described periosteal osteosarcoma involving the bone marrow (3,4).

Other types of osteosarcoma (parosteal, central and high-grade) develop in the periosteal region but the periosteal osteosarcoma shows distinct anatomical distribution, clinical symptoms, radiographic features and prognostic pattern (5,6).

Periosteal osteosarcoma shows variable imaging appearances at the site of the diaphyseal lesion of the tibia and femur. Several imaging techniques, such as radiography, computed tomography, and magnetic resonance imaging can be used to gather information about periosteal osteosarcoma. All these techniques allow observing changes at the tumor site, tumor size, cortical alterations, spinal involvement and other tumor characteristics (7).

In humans, periosteal osteosarcoma is an intermediate grade chondroblastic osteosarcoma, representing less than 2% of all osteosarcomas (6). As high-grade osteosarcoma, periosteal osteosarcoma affects young patients and the most frequent locations are tibia (40%) and femur (38%), followed by humerus (10%) and ulna (5%) (7). In dogs, the number of cases reported is insufficient to determine the place of incidence (8).

In veterinary medicine, two types of periosteal osteosarcoma have been described in dogs. One form is an aggressive tumor with the same histological characteristics and biological behavior of central osteosarcoma (tumors with central or medullary origin) (8). It may present as asymmetric central osteosarcomas that arise in the spongiosa outer layer of the long bones metaphysis. The second type of periosteal osteosarcoma in dogs is similar to the description found in humans (8).

The definition of periosteal osteosarcoma is challenging. An accurate diagnosis requires correlation of the clinical, radiographic, and histopathologic evaluation. It is essential to exclude periosteal osteosarcoma from central osteosarcoma with periosteal extension, high-grade surface osteosarcoma and parosteal osteosarcoma (1).

The histopathological pattern of the central osteosarcoma includes the production of osteoid or immature bone by malignant osteoblasts. However, both the amount and quality of the osteoid matrix can vary highly between tumors (8). The basic characteristic of the high-grade surface osteosarcoma is the fast-growing sarcoma arising from the periosteal tissue (3,6). Histopathologically, parosteal osteosarcoma arises from the outer fibrous layer of the periosteum and reveals characteristics of grade I or II osteoblastic osteosarcoma, resembling fibrous dysplasia (4).

In all types of osteosarcoma, adjuvant chemotherapy may be prescribed to provide pharmacological support after surgical procedures (7). At the same time, the value of adjuvant treatments for periosteal osteosarcoma is unclear (9,10). Consequently, several studies have been performed to assess if the free survival time of dogs with osteosarcoma can be prolonged by adjuvant chemotherapy (1,4,9,11). However, because of the rarity of the tumor, insufficient data are available to support such treatment (9,12). Latest reports showed the efficacy of few cytostatic drugs, such as carboplatin, cisplatin, and doxorubicin (1).

In veterinary oncology, the periosteal osteosarcoma in dogs is poorly described. Equally important, the number of reported cases describing the histopathological findings and survival time is restricted. A descriptive report showing the clinical appearance and diagnosis of this rare tumor in dogs in order to stimulate an accurate investigation was the purpose of this report.

Anamnesis. At the Veterinary Hospital of School of Agrarian and Veterinary Sciences, São Paulo State University (UNESP/FCAV Jaboticabal, São Paulo, Brazil), a female dog of 14-year-old, 6 kg, was admitted showing 15 days of right pelvic limb lameness.

Clinical Exam Findings. On the first appointment day, the client reported as main complaint pelvic limb lameness and a lump located in the right tibia. The mass was adhered, alopecic and ulcerated, measured by a pachymeter 8.8x6.8 x 6.3 cm (Figure 1).

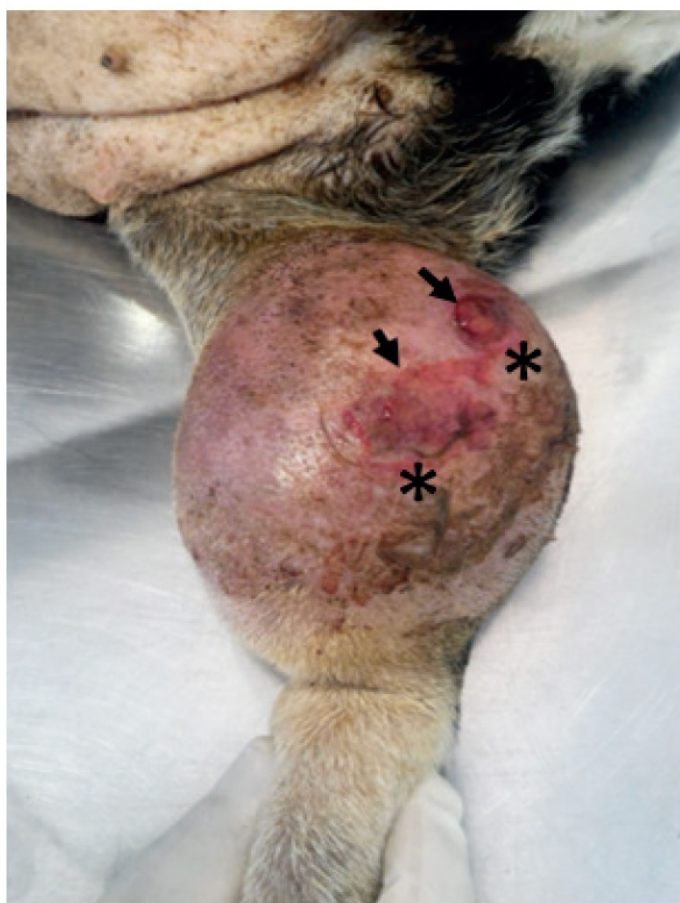


Figure 1. Periosteal osteosarcoma of the right tibia in a 14 year old female, mongrel dog. The tumor shows areas of ulceration (arrows) and a large erythematous area (*). Notice two small-ulcerated areas. The photo was taken on the first appointment day.

FIGURE 1

Figure 1

During the physical examination, a heart murmur (4/6) was observed. Thereafter, the dog was referred to the Veterinary Cardiology Service at the same hospital. The diagnosis was mitral valve endocardiosis and cardiac insufficiency (II) and the appropriate treatment started with client's agreement.

Diagnostic aids used. Further examinations were performed to rule out other systemic alterations. The patient was submitted for blood count analysis, dosage of biochemical enzymes (creatinine and alanine

aminotransferase – ALT) and abdominal ultrasonography, without alterations. The cytological examination of the mass located in the right pelvic limb suggested round cell tumor.

The dog did not show any other changes related to the skeletal system. During the orthopedic examination, the dog demonstrated moderate pain in the right pelvic limb. Neurological examination revealed no changes.

The dog was referred for Diagnostic Imaging Service at the same hospital. Thoracic radiographs in three views (right and left lateral, ventrodorsal) were performed and the findings were consistent with the age of the dog.

The lateral view of the right tibia showed proliferative and lytic periosteal reaction, predominantly proliferative in the distal third of the tibia and right talus, exceeding the articular line. Beyond an increased area of soft tissue mass, with homogeneous appearance adjacent to the distal third of the tibia and right tarsus and loss of bone trabeculation was observed (Figure 2).



Figure 2. Lateral radiograph of periosteal osteosarcoma involving the canine right tibia. The tumor displays an active periosteal reaction and homogeneous soft tissue mass adjacent on the distal third of the tibia and is consistent with an aggressive bone lesion. tumor shows areas of ulceration (arrows) and a large erythematous area (*). Notice two small-ulcerated areas. The photo was taken on the first appointment day.

FIGURE 2
Figure 2

Based on the clinical signs, cytological analysis, and radiographic examinations the presumptive diagnosis was osteosarcoma. The histopathological diagnosis was periosteal osteosarcoma with free margins. It was not found tumor cells in the respective popliteal and inguinal lymph node of the affected limb.

The measure of the mass was 8.8 x 6.8 x 6.3 cm . The samples were fixed in 10% neutral buffered formalin and transferred to a formic acid solution for decalcification. After three days of decalcification, the tissue samples were processed, paraffin embedded, sectioned at five μm (micrometer) and stained with Haematoxylin and Eosin (HE) for histologic evaluation by the responsible professor of the Veterinary Pathology Department.

Histopathological evaluation revealed tissue showing neoplastic proliferation of mesenchymal cells originated from the periosteum that extended to adjacent soft tissue, with high cellularity, poorly demarcated, unencapsulated and infiltrative growth pattern. Through histopathological analysis, the tumor cells were between an amorphous material. The presence of areas of mineralization was also observed (poorly differentiated osteoid matrix). Singly, the cells had distinct borders, the cytoplasm was elongated and rounded, moderately and discretely acidophilic. The nuclei were elongated, hyperchromatic, with densely clustered chromatin with the single and evident nucleolus. Nuclear alterations (anisokaryosis, anisocytosis, and karyomegaly) were described. The mitotic figures were common (18 in 10 field of great increase). Few multinucleated cells (osteoclasts) were also noticed (Figure 3).

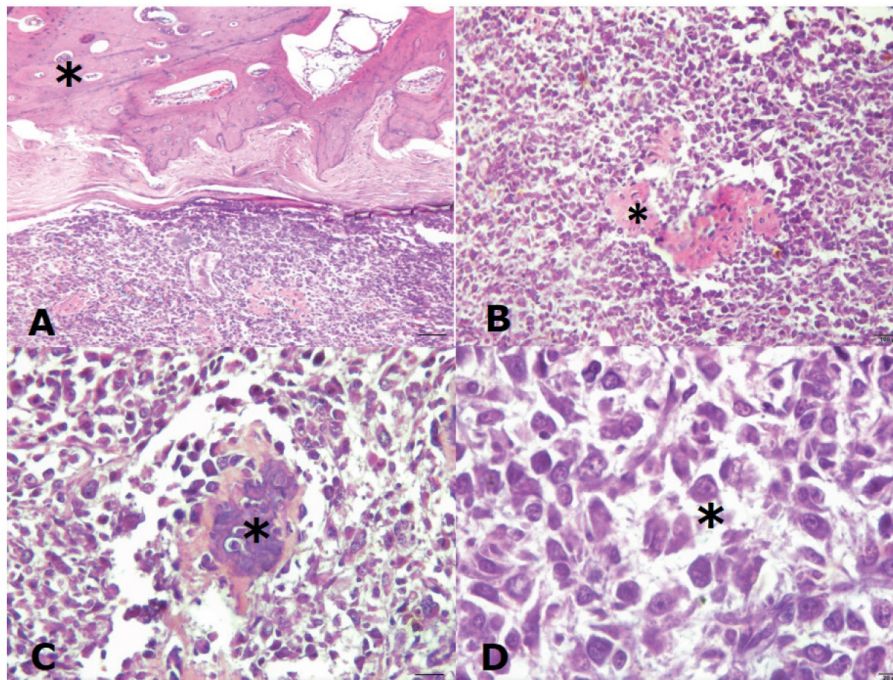


Figure 3. Photomicrography of a sample of canine bone tissue showing neoplastic mesenchymal proliferation, originated in bone cells of a 14-year-old female, mongrel dog. **3 A:** Periosteal array of tumor cells. Histopathology showing areas of cartilage with eosinophilic deposits of osteoid (*), bar 50 μm . **3 B:** Detail of area with bone matrix production by tumor cells, note the island of osteoid mineralization (*), bar 200 μm . **3 C:** Area showing differentiation of young bone tissue (*), bar 100 μm . **3 D:** Higher magnification of the same tumor. Morphology of tumor bone cells, notice evident polymorphism cell (*), bar 400 μm , HE.

FIGURE 3
Figure 3

Treatment approach. Due to these findings, surgery was the first method of treatment and pelvic limb amputation was suggested to the client. The surgery was performed with no complications and the entire pelvic limb was sent to the Department of Veterinary Pathology of the School of Agrarian and Veterinary Sciences (FCAV/UNESP).

After the explanation of histopathological report, the client declined to the adjuvant chemotherapy and the follow-up examinations. The client has chosen for palliative care based on medication for pain relief.

Thoracic radiographs and ultrasonography were performed during the time of clinical follow-up without evidence of metastatic disease or new lumps. The dog had a nine-month survival free time from diagnosis.

DISCUSSION

Considering the mass appearance, size, evolution time, the age of the dog, the anatomical position and the physical examination, osteosarcoma was suspected initially. Furthermore, in this case, the radiographic findings suggested the presence of an inflammatory process or a bone tumor, especially due to the presence of periosteal reaction seen in this type of tumor.

In humans, the radiographic findings were classified in five parameters (tumor matrix, periosteal response, cortex underlying the lesion, presence of soft tissue component, and integrity of the medullary cavity (13). In the present case report, the parameters described above were also evaluated and only the medullary cavity revealed no alterations. Our findings were in line to those described by other authors.

Periosteal osteosarcoma is an uncommon bone tumor with insufficient data on long-term follow-up. In humans, a large study with periosteal osteosarcoma described patients with a free survival time of 83% over than 10 years (4, 12). The survival rate of the dog described in this case report was nine months after diagnosis, which is considered satisfactory in this species. However, the number of cases reported, and follow-up information were minimal to determine a rate of survival time in dogs. The present case added the follow up information on this type of tumor, as we consider this information relevant. In the future, new cases would be compiled with the aim of evaluating this parameter, isolated or in association with others.

Periosteal osteosarcoma and other bone tumors were diagnosed based on the radiographic and histopathologic analysis with no medullary involvement of the tumor (3). Other authors have described periosteal osteosarcoma with microscopic or gross medullary involvement (3,4). Although the radiographic and histopathologic features of this tumor were consistent, they cannot be diagnosed alone. When medullary involvement is present, it is not possible to distinguish periosteal osteosarcoma from classic chondroblastic osteosarcoma, which has broken through the cortex and shows a surface mass, primarily (12).

In humans, three typical radiographic and histopathological features of periosteal osteosarcoma were pointed. The first one is a periosteal mass attached to the cortex of the affected diaphysis of long bones. The second one is the presence of Codman's Triangle formations in the cortex of bone tumor. The Codman's triangle is a triangular area of new subperiosteal bone that occurs when an injury (often a tumor) raises the periosteum from the bone. The third one is the size of the main tumor at the periosteal lesion that is larger than the intramedullary lesion. The observation of chondroblastic matrix with the osteoid formation and histopathological grade II or III were considered the foremost lesions on histopathological examination in the patient of the case (3).

Previously in humans' studies, it was suggested that the anatomic position of the tumor might influence the survival time; proximal femoral lesions might show lateness through the course of disease with poorer outcomes (12). However, similar survival rates for patients with tumors located proximally or distally and in patients with femoral and non-femoral tumors were reported (12, 14). In one study, the anatomic position (proximal versus distal or femoral versus non-femoral) did not influence the survival time (12). The most frequent sites of periosteal osteosarcoma was tibia, nearly 40% (7). The anatomic position seen in this case report was distal diaphysis of the right tibia and our results agreed with the previous authors. Most of the cases seen in dogs are descriptive and do not allow a study comparing the tumor anatomical position and the survival rate.

In a veterinary report, periosteal osteosarcoma had histopathologic appearance characterized by low or medium histopathologic grade, usually with ossification areas (8). Only two reports have been described this tumor in the metaphyseal surface of long bones rather than the diaphyseal surface in humans (5). In dogs, the tumor usually is in the diaphyseal region, produces dense bone matrix, and no pulmonary metastases were detected at the time of amputation (8). Additionally, there is one case report of periosteal osteosarcoma described in the scapula of an eight-year-old Arabian horse. The neoplastic proliferation of the periosteum was disseminated, starting at the distal neck of the scapula and extending distally to the metaphyseal region of

the humerus (15). Considering the anatomic position and the histopathological changes, these events were identical to that observed by previous authors. The exception was the absence of the Codman's triangle and the metaphyseal location of the tumor in the horse.

Surgical treatment is the best option in cases of osteosarcomas, including the periosteal osteosarcoma (12). Surgery (either limb amputation or limb-sparing surgery) is the first method of treatment. (10). Limb-sparing surgery is an alternative method to limb amputation (2). Moreover, tumor recurrence appears in 15–25 % of cases. As a result, this technique is recommended for dogs with compromising neurologic or orthopedic problems (11). In the present study, pelvic limb amputation was performed with free margins and lymph nodes without evidence of tumor cells and these results were confirmed in the histopathological evaluation. Nine months after diagnosis there was no evidence of metastasis or new lumps. Thoracic radiographs and ultrasound follow-up were performed every 2 months. It was not possible to establish if there was a recurrence of the tumor since the patient had an advanced age and died due to natural causes. The client has chosen for palliative care based on medication for pain relief and metronomic chemotherapy (cyclophosphamide 12.5 mg/m²), and the follow-up examinations.

In conclusion, the clinical evidence suggested that periosteal osteosarcoma in dogs must be treated surgically. The unusual occurrence of periosteal osteosarcoma in canine patients, the histopathological description and the free survival time were highlighted in this report. Studies involving a greater number of reported cases must be analyzed to compile additional data such as age, sex, breed, biological behavior, prognosis and free survival time on this rare tumor in dogs.

CONFLICTS OF INTEREST.

The authors declare that they have no conflict of interest.

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