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DIAGNOSIS AND TREATMENT OF CANINE APPENDICULAR OSTEOSARCOMA. A CASE REPORT

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Abstract

Canine osteosarcoma is an agressive tumour that has both a locally invasive and highly metastatic biologic behavior. Osteosarcoma is the most important primary bone tumour in dogs, being the most common. Usually, it's occurrence is in the appendicular skeleton and the most frequently involved are large and giant breeds, being the cancer of elderly, large dogs. The aim of this case report is to describe the diagnostic methods, the therapeutic targets and the evolution of a canine osteosarcoma. This case highlights that the diagnosis is made by corroborating the results of the blood tests, the imaging methods (radiographs, CT scans) and the cytological evaluation. Multimodal therapy should be considerd to provide patients with maximum survival time and to improve the quality of life. The therapeutic management for a canine osteosarcoma case should include surgery, adjuvant chemotherapy and palliative care. Despite these therapies, the prognosis is, for the most part, negative with a great metastatic occurrence, mostly to the lungs. This report is an example of how diagnostics and therapeutics can be used in the management of a canine appendicular osteosarcoma.

Key words*: canine osteosarcoma, cancer, chemotherapy, palliative treatment.*

INTRODUCTION

Osteosarcoma (OSA) is a malignant mesenchymal tumour of primitive anaplastic bone cells, these cells being characterized by an extracellular production of osteoid (matrix) (North and Banks, 2009). Osteosarcoma is by far the most frequent primary bone tumour in dogs, accounting for approximately 85% of all bone tumours and 5 % of all malignant tumours in dogs (Dobson and Lascelles, 2019). It mostly affects the limbs (appendicular skeleton) but it can also develop in the skull, spine and the ribs (axial skeleton). Approximately 75% of osteosarcomas affects the appendicular skeleton with the remaining of 25% affecting the axial skeleton. The most common locations for the appendicular osteosarcomas are the distal radius or proximal humerus followed by the proximal and distal femur and tibia (Klopfleisch, 2016).

Canine osteosarcoma can occur in dogs of all ages but it is most common in 7-9 year old dogs. It usually develops in older, large and giant breeds, and there is no gender predisposition confirmed. Osteosarcomas appear to affect large breed dogs more commonly than the small breeds (Klopfleisch, 2016; Tuohy et al., 2019). Reported predisposed breeds include Great Danes, Saint Bernards, Rottweilers, Doberman Pinschers, Golden Retrievers, German Shepherd Dogs, Greyhounds, Irish Setters, Labrador Retrievers (Szewezyk et al., 2015). Nevertheless, higher weight and larger size are reported to be a stronger predisposition factor than breed (Klopfleisch, 2016).

Osteosarcoma is a highly aggressive and metastatic tumour, therefore an early diagnosis is desired. Diagnosis is based on clinical history, clinical and paraclinical examination including imaging methods of investigation (X-rays, MRI, CT), and the confirmation is made by cytology, histopathology. At the time of diagnosis, usually, the cancer cells have already spread in the body even though they are not detectable (about 90-95% of dogs have micrometastasis) (Liptak et al., 2004; Morello et al., 2011). Prognosis is based on many factors like age, large tumour volume, tumour location, elevated alkaline phosphatase (ALKP), high tumour grade, and presence of

metastasis (Boerman et al., 2012). The prognosis is not a favorable one, usually the median survival times (MST) is between 6 and 12 months, depending on the treatment received (Dobson and Lascelles, 2019).
The most effective management of canine appendicular osteosarcoma involves multimodal therapy, to address both the primary tumour and metastatic disease (Tsuji et al., 2019). Surgery (amputation, limb-sparing surgery) with adjuvant chemotherapy is the main treatment option for canine osteosarcomas (Davis et. al., 2013; Kozicki et al., 2015). Even if the the primary goal is local tumour and metastatic control, a very important objective that should not be ignored, is represented by the alleviation of pain and improving the quality of life - the palliative treatment (Duffy et al., 2018; North and Banks, 2009).
In the presented case we described the clinical signs, the diagnostic methods, the treatment but also the evolution of a classic case of canine appendicular osteosarcoma.

MATERIALS AND METHODS

In October 2019, a 10 years old, female, Presa Canario was presented at the clinic for evaluation, with signs of generally lameness and swelling of the left posterior limb. After the anamnesis, it was found that there was no trauma before the onset of clinical symptoms. The owner noticed the swelling of the leg four months ago and treated the dog, at the recommendation of a veterinarian from another clinic, with non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics. Initially, an improvement was observed after one month of Meloxicam (orally administered for one month with an initial dose of 0.2 mg/kg followed by a maintenance dose of 0.1 mg/kg q 24 h). But, in the last month, the patient presented a lack of appetite and severe lameness. Also, the owner noticed that the swelling of the posterior limb is no longer localized but the entire limb is swollen (Figure 1). As the lameness worsens, there was no noticeable response to rest and non-steroidal anti-inflammatory drugs. Following the clinical examination, the visible symptoms such as limping or swelling were observed, and also the palpation revealed that the left posterior limb was mildly painful. No changes were detected at the level of the regional lymph nodes. In order to make a diagnosis, it was necessary to perform blood tests (complete blood count - CBC and serum chemistry), radiographs of the affected limb, chest and abdominal radiographs (in order to detect possible metastases). After the radiographs evaluation, it was recommended to perform a CT scan and a fine-needle aspiration for cytological evaluation. Also, a specialized cardiological consultation was recommended, after which the patient was diagnosed with dirofilariosis and a therapeutic scheme was performed.

Figure 1. Swollen posterior limb

RESULTS AND DISCUSSIONS

The complete blood count (CBC) was normal but there were changes in the biochemical parameters as shown in table 1. Although most blood tests were within normal limits, increasing alkaline phosphatase was a cause for concern. In patients with osteosarcoma, routine blood work like haematology, biochemistry and urinalysis are often normal. However, an evaluation of alkaline phosphatase may appear, which is a negative prognostic factor (North and Banks, 2009).

Table 1. Biochemical parameters of the dog presented in this paper

Parameter	Value	Reference range
TP	7.9	5.2-8.2 g/dL
ALB	3.5	2.2-3.9 g/dL
GLOB	4.2	2.5-4.5 g/dL
CRE	0.8	0.5-1.8 mg/dL
UREA	11	7-27 mg/dL
ALKP	295 ↑	23-212 UI/L
ALT	78	10-125 UI/L
GLU	88.5	70-143 mg/dL

TP: Total protein, ALB: Albumin, GLOB: Globulin, CRE: Creatinine, ALKP: Alkaline Phosphatase, ALT: Alanine aminotransferase, GLU: Glucose

Radiographs of the affected limb revealed an osteolytic and proliferative lesion of the femur. Radiographic features displayed that both the diaphysis and the epiphysis of the femur were afected.

Cortical lysis and perpendicular radiating new bone formation from the cortical bone into the surrounding soft tissue (sunburst pattern) were observed.

Even if at the clinical examination it was observed that the tibia region was swollen, there were no changes of the tibia visibile on x-ray. Radiographs of the affected bones are of particular revelance for the diagnosis of canine osteosarcomas.

Usually, the radiographic appearance in osteosarcoms is variable, it presents either loss of bone structure (lysis), or proliferative lesions, or a mixture of both patterns (Klopfleisch, 2016).

Three view thoracic radiographs revealed no pulmonary pattern consistent with lung metastasis. Even if less than 15% of dogs have clinically detectable metastasis at the time of initial diagnosis, approximately 90% will die with metastatic disease, usually to the lungs.

Metastasis occurs primarily through hematogenous routes, particularly to the lungs, but on rare occasions extension to regional lymph nodes may occur (Dobson and Lascelles, 2019).

The CT scan revealed the appearance of lysis, cortical erosion and bone proliferation of the proximal femur.

The CT scans allowed a better evaluation, and were essential to improve visualization of tumour margins (Figures 2, 3, 4).

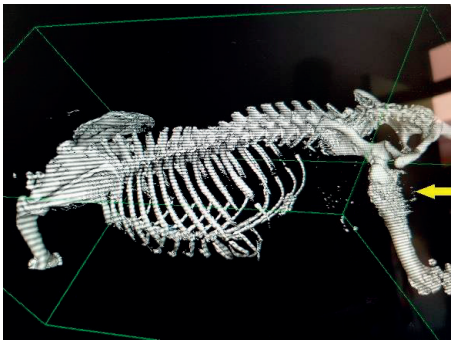

Figure 2. A 3-D reconstruction of the proximal femur with osteosarcoma of the dog presented in this paper, the yellow arrow indicates both lysis and bone proliferation

Figure 3. Transverse view of a dorsal 2-D reconstructed CT scan with contrast, yellow arrow shows the extension of the appendicular osteosarcoma of the dog presented in this paper

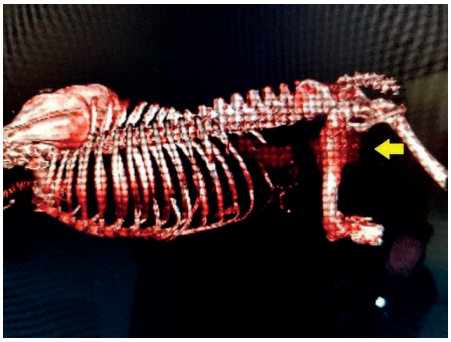

Figure 4. A 3-D reconstruction of the appendicular osteosarcoma of the dog presented in this paper, the yellow arrow shows the vast vascularisation of the tumour

The fine-needle aspiration from the mass and the cytological examination were performed, being less invasive than a bone biopsy. Fine needle aspiration entails using a very thin needle to collect a sample of a lesion for microscopic examination. In order to perform the microscopic evaluation, the aspirate smear was stained using the DiffQuik staining procedure. The Diff-Quick stain consists of a fixative agent (methanol), solution I (eosinophilic) and solution II (basophilic). The smear was dipped sequentially into each solution 5 times, followed by a water rinse and drying. The cytological evaluation revealed a group of osteoblasts, anisocytosis, anisokaryosis, binucleated cells and osteoid extracellular protein matrix among the cells (Figure 5). Based on these findings and taking into account the rest of the results (radiographs, CT scans, biochemestry analysis) the certainty diagnosis of osteosarcoma was made.

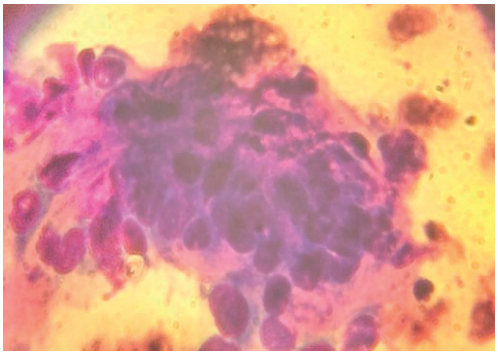

Figure 5. Cytology of fine needle aspirate of the osteosarcoma of the dog presented in this paper. Diff-Quik ×100

The patient's prognosis and treatment options were discussed in detail with the owner. A multimodal therapy was recommended, including both the treatment of the local disease (primary tumour) and systemic disease (micrometastasis). The therapy was primarily focused on local tumour control, so amputation of the affected limb was recommended. Surgery is the standard treatment for canine appendicular osteosarcoma, even large and giant breed dogs can function well after limb amputation (Dobson and Lascelles, 2019). In order to control the micrometastasis adjuvant chemotherapy was recommended (even if metastasis were not detected, canine osteosarcoma is a very agresive and metastatic tumour, so we assumed it already spread in the body).

The owner refused the surgery, considering that the pacient is a very large and old dog that will not adapt to the loss of a limb, but he agreed with the administration of the systemic treatment.

Subsequently, carboplatin chemotherapy was initiated and given IV (300 mg/m^2) once every 3 weeks for a total of four seassions.

During the administration of chemotherapy the patient was constantly monitored and also blood tests were performed. Adverse reactions following therapy were in the gastrointestinal system, clinically represented by vomiting and diarrhea. To reduce side effects, when needed, the patient was treated with antiemetics, antidiarrheal drugs.

Considering the aggressiveness of the tumour and the patient's condition, palliative treatment was recommended to maintain the patient comfort. It was administred Meloxicam in a dose of 0.1 mg/kg daily with a gastrointestinal protector (omeprazol). The goal of palliative treatment is to alleviate pain and improve quality of life.

The patient was monthly evaluated, and unfortunately, after 5 months pulmonary metastases were detected on radiographs. The patient's condition worsened, became dyspneic, lethargic and had inappetence. Because the quality of life of the animal decreased euthanasia was recommended.

Canine osteosarcoma represents a challenge for veterinarians being a highly malignant and metastatic tumour, as reported in this case.

The prognosis is often negative, with frequent euthanasia in patients due to the extension of the neoplastic lesion and the appearance of metastases. Being able to make an early diagnosis and starting a multimodal treatment as soon as posible, contributes to providing a longer median survival time.

Radiographs and cytologic examination were essential to diagnose, but CT images contributed to the assessment of the tumour extension and the blood tests contributed to the assessment of the patient's health.

In order to obtain the best result, the owners' compliance is required. In the present case, we consider that if the owner had accepted the

amputation of the affected limb, the patient's survival time would have been extended.
If a patient diagnosed with osteosarcoma is treated only with analgesics and non-steroidal anti-inflammatory drugs the survival time rarely increase beyond 3 months.
When treated only surgically, MST is increased, but when surgery is associated with adjuvant chemotherapy MST is considerably increased with a 12 month survival rate (North and Banks, 2009).
In the present case, in which the treatment consisted only of chemotherapy, the survival time after diagnosis was 5 months, being obtained a longer interval than if no treatment had been received at all, but less than if the amputation had been performed.

CONCLUSIONS

The diagnosis of osteosarcoma is based on the corroboration of anamnetic data, clinical data, and mainly on the results obtained in the imaging methods and on the cytological evaluation.
In the treatment of canine osteosarcoma is recommended both a local approach for tumour (surgery) and a systemic approach (chemotherapy) to control or prevent metastasis. The palliative treatment is essential in any type of cancer, in order to provide comfort to the patient.

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