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Case Report

Fibroblastic osteosarcoma in a guinea pig (*Cavia porcellus*)

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Abstract

The article describes the case of a 3 year 6 months old Guinea Pig (*Cavia porcellus*) that was assisted at the Wildlife and Exotic Animal Practice of the Faculty of Veterinary Sciences, National University of Asunción. The patient presented a hard mass in the right hind limb extending from the proximal portion of the femur, projecting caudally to the proximal tuberosity of the calcaneus, with an increase in temperature, and a marked increase in sensitivity. Radiographic diagnosis refers to a mass with amorphous areas of mineral density. Fine needle aspiration puncture revealed an undifferentiated malignant proliferative process, requiring histopathological analysis to characterize the process. Disarticulation was performed and subsequent histopathologic diagnosis under hematoxylin-eosin and Masson's trichrome stain revealed fibroblastic osteosarcoma.

Key words: *Cavia porcellus*, neoplasm, bone, Paraguay,

Introduction

Fibroblastic osteosarcomas are a type of malignant neoplasm with proliferation of spindle cells and formation of osteoid or bone by neoplastic osteoblasts. Bone spicules may be sparse, especially in early lesions, and it is not uncommon for such tumors to be initially diagnosed as fibrosarcomas and later reclassified as osteosarcomas after examination of additional biopsies (6).

Osteosarcomas can be sub classified according to the predominant histological pattern. The sub classification of osteosarcomas can be justified because it can lead to the identification of correlations of osteosarcoma subtype with prognosis and susceptibility to therapy. Classification into one of the 6 categories is determined by the predominant pattern in representative sections of the tumor. The categories are as follows: poorly differentiated osteosarcoma; osteoblastic osteosarcoma; chondroblastic osteosarcoma; fibroblastic osteosarcoma; telangiectatic osteosarcoma; giant cell-rich osteosarcoma (6, 31).

The histologic appearance of osteosarcomas varies markedly, but the production of osteoid and/or tumor bone by malignant osteoblasts is a common factor. The tumor matrix may also contain variable amounts of cartilage and collagen. Bone formation also occurs in some chondrosarcomas, but indirectly through endochondral ossification of tumor cartilage, and should not be misconstrued as tumor bone. Similarly, bone metaplasia of mesenchymal cells in tumors of non-bone origin, such as mammary carcinomas, can be confusing (6).

Neoplasms occur in guinea pigs, especially those older than 3 years; but reports are rare and therefore the impression given by a single report may belie real incidences in the long run (11). Among the most described neoplasms in guinea pigs are skin tumors (trichofolliculomas; lipomas), mammary gland tumors (adenomas and adenocarcinomas), tumors of the reproductive system (uterine leiomyomas), tumors of the endocrine system (thyroid carcinomas), tumors of the respiratory system (bronchogenic papillary adenoma), and tumors of the hematopoietic system (lymphoma; leukemia) (11, 13).

Bone neoplasms described in guinea pigs included: osteosarcoma, osteogenic sarcomas, and a single case of iliac chondrosarcoma (20). Osteosarcomas in guinea pigs are apparently uncommon, occurring in approximately 1% of reported neoplastic lesions, and presenting as painful enlargements in guinea pigs older than 1 year of age (26).

The objective of this work is to report a case of skeletal fibroblastic osteosarcoma in a guinea pig, with emphasis on diagnosis and resolution.

Case description

A male guinea pig (*Cavia porcellus*), approximately 3 years 6 months old, weighing 905 g, and body condition 3/5 (ideal) (23), was taken to the Wildlife and Exotic Animal Practice at the Faculty of Veterinary Sciences in the National University of Asunción. Physical inspection revealed a mass in the right hind limb extending from the proximal portion of the femur, projecting caudally to the proximal tuberosity of the calcaneus. On palpation, a hard mass is perceived, with an increase in temperature, and a marked increase in sensitivity.

Radiographs of the right tibia were obtained in orthogonal projections (Fig. 1). In the caudal and medial region of the right tibia, a significant increase in soft tissue volume with amorphous areas of mineral radiodensity was observed; apparent mild proliferative bone reaction adjacent to the right patella, femoral condyles, and femorotibiopatellar joint. Radiolucent, poorly defined areas in the distal epiphysis of the right tibia and calcaneus with mild bone proliferation.

The radiographic diagnosis refers to a mass with amorphous areas of mineral density in the medial region of the right pelvic limb. The proposed differential diagnosis was primary osteosarcoma, soft tissue metastatic osteosarcoma, soft tissue bone metaplasia as well as other mineralized soft tissue neoplasms. Bone proliferation adjacent to the patellofemoral joint was suggestive of degenerative joint disease. A presumptive area of lysis was also observed in the right tarsus, which may have been overestimated by the radiographic technique.

A fine-needle aspiration puncture (FNA) of the mass was performed on the inner side of the thigh, followed by a Giemsa-stained smear. It was possible to evaluate a high cellularity of cells forming solid aggregates and others dispersed. A cell population made up of round to slightly polygonal cells, approximately 15 microns in size, with a 3:1 (high) nucleus-to-cytoplasmic (N:C) ratio, anisocytosis, anisokaryosis, marked cellular and nuclear pleomorphism, with a central to eccentric nucleus, punctate chromatin and pale basophil cytoplasm was observed, and scattered neutrophils. The background of the smears was observed to be pale eosinophilic, interpreted as a matrix. Cytologically, the result was compatible with an undifferentiated malignant proliferative process, requiring histopathological analysis to characterize the process.

Disarticulation of the affected limb was decided. The anesthetic protocol consisted of Dexmedetomidine 3 µg/kg and Fentanyl 2 µg/kg intramuscularly (IM) (19). Anesthesia was induced and maintained with Isoflurane, 1.5% to 2.5% respectively, in oxygen administered by mask using a Bain anesthesia system and a 0.5 L reservoir bag. The oxygen flow rate was maintained at 2 L/min. Regional blocks with Bupivacaine 0.5% were used. Heart rate remained at 180 beats/min, on average, with systolic pressure of 80 mmHg and diastolic pressure of 63 mmHg, measured with a SunTech Vet30 multiparametric device. Anesthesia was monitored with

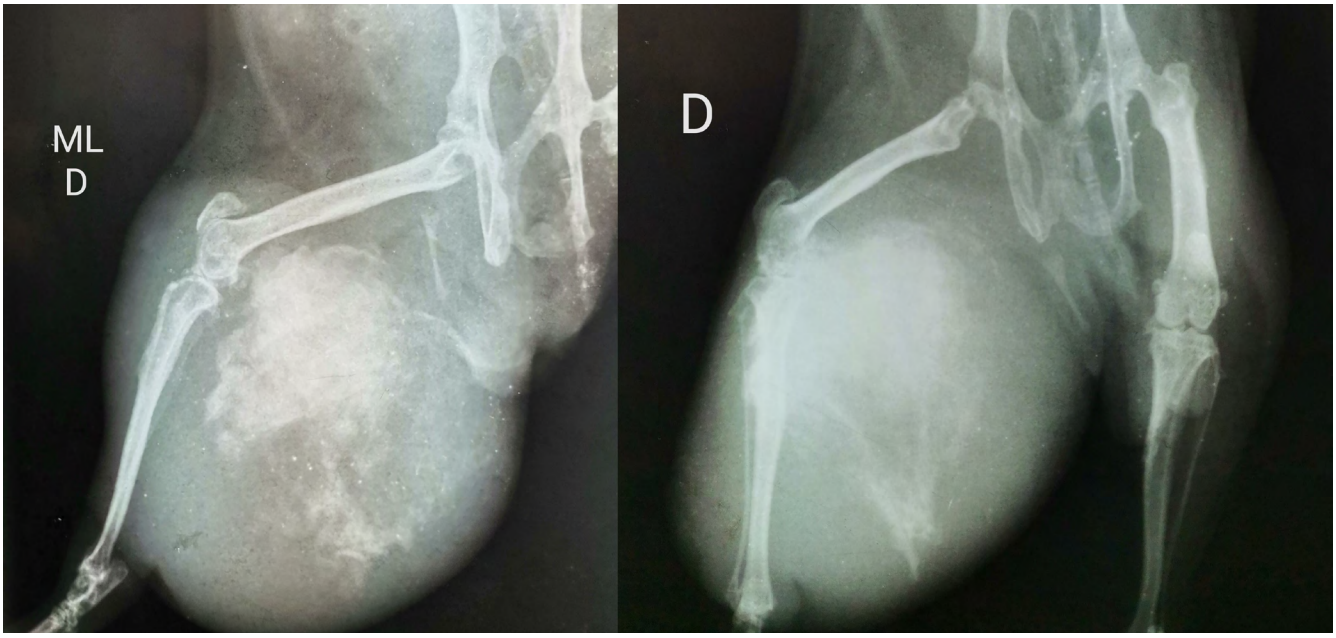

Figure 1. Right hind limb, mediolateral (A) and craniocaudal (B) incidence. A significant increase in the volume of soft tissues with amorphous areas of mineral radiodensity.

the help of pulse oximetry and Doppler. Manual intermittent positive pressure ventilation was administered as needed.

An incision was made at the level of the distal half-third of the femur, which initially covered the skin and the connective tissue. Due to the volume of the mass, a delicate dissection of the femoral vessels was performed, double arterial and simple venous ligation with polyamide 3-0 type material, the nerves were sectioned. Subsequently, the muscles were sectioned, performing hemostasis by ligation, using the same material. The disarticulation was performed at the coxo-femoral level. Washing was carried out with 0.9% NaCl saline solution. The muscle stump was made with a Ford suture pattern using 4-0 polyamide, and at the cutaneous level, mattress stitches were made with 5-0 polyamide.

Post-surgical treatment consisted of meloxicam at 0.2 mg/kg PO, every 12 hours for 4 days; tramadol 10 mg/kg PO every 24 hours for 7 days; and Enrofloxacin 5 mg/kg SC, every 12 hours for 7 days (18).

The disarticulated limb was sent for histopathological study. Macroscopic findings reported femur with a white, mineralized, firm, non-encapsulated irregular mass of approximately 4 cm X 7 cm, with focal hemorrhagic necrosis. In serial decalcified sections, proliferation of densely organized spindle/mesenchymal cells with formation of areas of mineralized osteoid matrix was evaluated. The cells showed moderate cellular and nuclear pleomorphism, anisocytosis and anisokaryosis. Mitotic figures were not evaluated. Neoplastic cells were not identified in blood and lymphatic vessels present in the sections. The histopathological diagnosis was fibroblastic osteosarcoma (Figs. 2 and 3). Masson´s Trichrome slides showed marked fibroblastic proliferation (Fig. 4).

In conversation with the owner, the animal showed a good response to treatment, behaving normally. Approximately 6 months after the procedure, the animal was found dead. No post-mortem examination was performed.

Discussion

Osteosarcomas in small mammals are rare findings but have already been described in mice (1), African pygmy hedgehog (25), rabbits (12, 31), as well as in large animals like horses (24). Instead, reports in canines and felines (7), and young humans (29) are more frequent.

Although reports of osteosarcomas in guinea pigs are scarce, there are reports in different anatomical regions such as: humerus (10), tibia (3, 16), femur (17), lumbar vertebrae (14), middle ear (4), and even intraocular (9). There is a record of extra skeletal osteogenic sarcoma in guinea pigs (5).

In order to establish an interspecies comparison; in dogs affected by appendicular tumors, lameness is often the primary symptom, and there may be a history of minor trauma prior to the lameness (7). Some dogs may have muscular atrophy of the affected limb caused by persistent lameness (7). Appendicular osteosarcoma causes pain and lameness, which is usually gradual in onset with an acute or chronic course with the limb clamped (7). Systemic signs (eg, fever, anorexia, and weight loss) are rare in the acute stages of the disease (27). Axial skeletal tumors are often palpable as firm swellings (27).

Radiographic evaluations are important in analyzing the extent of bone involvement and distinguishing bone neoplasms from other non-neoplastic conditions, such as fractures, osteomyelitis, and metabolic bone diseases (7). Radiography of a suspected primary malignant bone tumor in canines demonstrates cortical lysis, poor margins between normal and abnormal tissues, and active periosteal bone proliferation and reaction that characterize an aggressive bone lesion (7). Bone neoplasia in exotic pets is usually characterized by osteolysis with minimal periosteal changes; however, an osteoblastic neoplasm with a marked periosteal reaction can occur (30). Bone lysis, mineralization and periosteal spicules, and reactive periosteal reaction can generally be observed, with cortical lysis being the most frequent finding, which promotes areas of discontinuity in

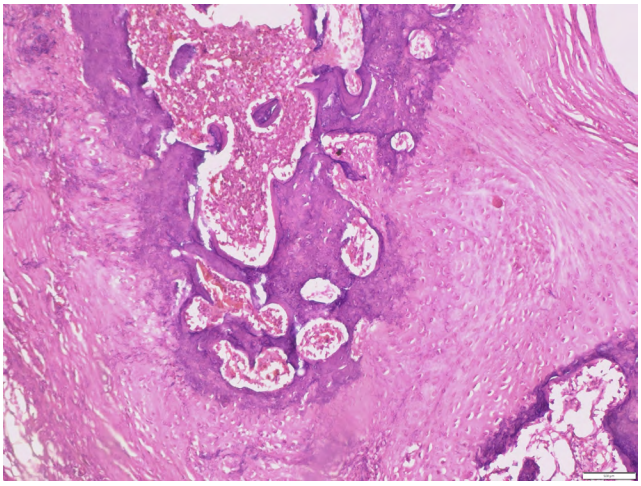

Figure 2. Focal osteoid matrix surrounded by fibroblastic neoplastic cells. H-E. 40x.

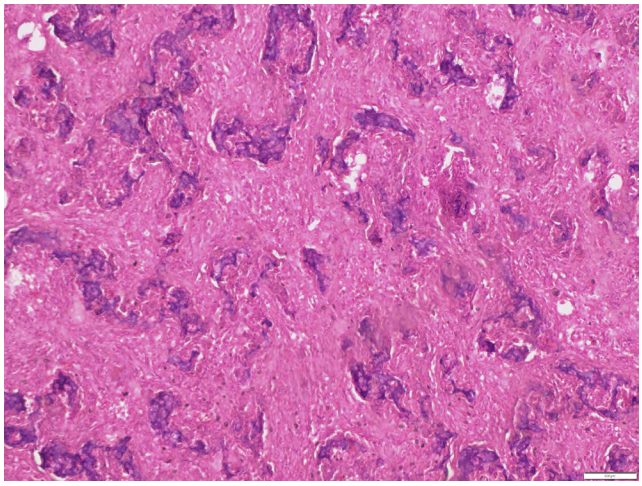

Figure 3. Multifocal osteoid matrix formation surrounded by fibroblastic neoplastic cells. H-E. 40x

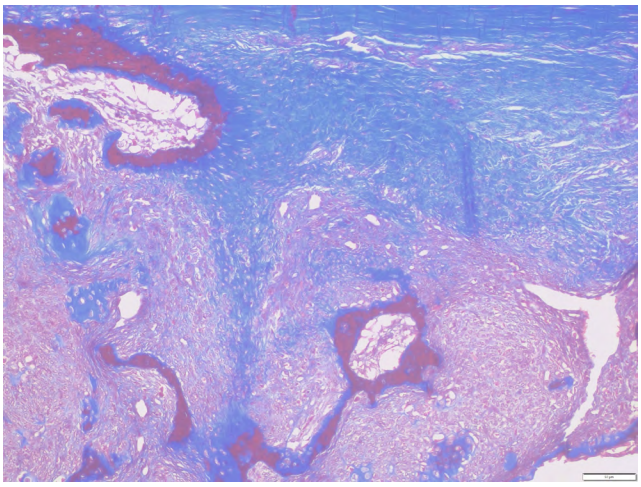

Figure 4. Mesenchymal neoplastic cells (blue), associated to osteoid matrix (red). Masson's Trichrome. 20x.

the cortex, causing spontaneous fractures (7, 30). They can be lytic, productive, or mixed, with calcification extending to adjacent soft tissues (7), although soft tissue neoplasia can also affect bone and be a cause of lameness (30).

Definitive diagnosis of osteosarcoma is made by identifying neoplastic cells on cytology and histopathology (15). Fine-needle aspiration has the advantage of being inexpensive and minimally invasive and has been shown to be up to 97% accurate in identifying lesions in human bone (2). In cases where cytology is not definitive, the larger the size of the biopsy sample obtained, the more useful it will be in diagnosing osteosarcoma and arriving at a subtype (8).

Chemotherapy is considered a coadjuvant therapy in domestic animals, and treatments with carboplatin, cisplatin, doxorubicin, and their combinations are described, but it should not be performed in isolation, that is, without amputation of the affected limb (7). Pain control using a combination of non-steroidal anti-inflammatory drugs in conventional doses and tramadol is important, not only because of the analgesic effect, but also because of the high expression of the COX-2 enzyme in advanced osteosarcomas (21), which turns out to be a new therapeutic strategy. It should also be considered that postoperative pain can induce mutilation of the amputation site (33).

Studies suggest that the use of Fluoroquinolones (Enrofloxacin and Ciprofloxacin) contribute to the outcome of canine patients with osteosarcoma, by inhibiting survival and proliferation of canine osteosarcoma cells (28), as well as protecting normal tissues from cytotoxic damage in canine osteosarcoma patients currently undergoing chemotherapy (32). These studies were performed in-vitro, and may be specific to canine cells, so further research must be performed on the potential benefits of fluoroquinolone use in osteosarcoma patients. Also, the responsible use of antimicrobials must be prioritized, as patient microbiome and antimicrobial resistance must be considered.

Small exotic mammals generally tolerate amputation well, although after surgery additional padding should be provided in the cage and the animal should be monitored for leg injuries caused by uneven weight bearing (33). Comparatively, there is evidence that rabbits without concurrent disease can tolerate limb amputation well, making amputation a viable treatment option (22).

The data from the clinical history, as well as the observable signs during the physical examination, the radiographic findings, and the histopathological results, confirmed the diagnosis of fibroblastic osteosarcoma in the right hindlimb of an adult guinea pig (*Cavia porcellus*).

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Conflict of Interest

The authors declare no competing interests.

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