

Malignant giant-cell tumor of bone with lymph node involvement in a cat

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Abstract: The present study describes giant-cell tumor of bone (GCToB) with lymph node involvement in a 5-year-old crossbred cat. The animal was referred to the surgery clinic with progressive subcutaneous swelling in the left proximal femoral region, severe lameness, constipation, and dysuria. A moderately firm, subcutaneous, palpable mass, 9 cm in diameter, was observed, and biopsy samples were taken. Histopathologically, the mass was constituted by ovoid-shaped mononuclear cells intermixed with many multinucleated giant cells (MGC). Immunohistochemically, the giant cells were positively stained with antivimentin, and the same cells were negative for antidesmin and anti-S100 staining. Tartrate-resistant acid phosphatase (TRAP) activity in tumor cells was evaluated and the tumor was diagnosed as malignant GCToB; the cat was euthanized. Macroscopically, while the regional lymph nodes were intact, giant cells were found in the left popliteal lymph node during microscopy. Although a few cases of GCToB have been reported in cats, the case herein displays, for the first time, evidence of lymph node involvement during the process of metastasis.

Key words: Cat, giant-cell tumor of bone, femur, lymph node involvement, immunohistochemistry

Bir kedide lenf yumrusu metastazlı kemiğin dev hücreli tümörü

Özet: Sunulan bu çalışmada, 5 yaşlı bir kedide rastlanan ve lenf yumrusu metastazına sahip kemiğin dev hücreli tümörü rapor edilmiştir. Hayvan cerrahi kliniğine sol femurun proksimal kısmında deri altı şişkinlik, topallama, kabızlık ve ağrılı idrar şikayeti ile getirilmiştir. Dokuz santimetre çapa ulaşan ve orta sertlikteki kitleden tanı amaçlı biyopsi alınarak patoloji laboratuvarında değerlendirilmiştir. Histopatolojik olarak kitlenin çok sayıdaki dev hücreleri ve ovoid şekilli mononükleer hücrelerden oluştuğu gözlenmiştir. Yapılan immunohistokimyasal boyamalarda bahsi geçen hücrelerin anti-vimentin antikorları ile pozitif, anti-desmin ve S-100 antikorları ile negatif olarak boyandıkları görülmüştür. Hücrelerdeki tartarat dirençli asit fosfataz aktivitesi değerlendirilerek kitle kemiğin dev hücreli tümörü olarak teşhis edilmiştir. Ötenazi sonrası makroskopik muayenede popliteal lenf yumrularında herhangi bir lezyon gözlenmezken, mikroskopik incelemede sol popliteal lenf yumrusunda metastaza rastlanmıştır. Kedilerde kemiğin dev hücreli tümörüne ait raporlar bulunsa da, sunulan olguda lenf yumrusu metastazına rastlanılması, bu tipteki tümörlerin lenfojen metastaz ile yayılabildiklerini gösterir ilk kanıtları içermektedir.

Anahtar sözcükler: Kedi, kemiğin dev hücreli tümörü, femur, popliteal lenf yumrusu, immunohistokimya

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Introduction

Giant-cell tumor of bone (GCToB) is an uncommon primary bone neoplasm that usually occurs in the long bones of both domestic animals and humans (1,2). The most common sites include the distal femur, proximal tibia, and distal radius. GCToB is an enigmatic tumor that is histologically benign but clinically shows local invasion and metastatic potential (1). In some cases, dissemination to the lungs and extraskeletal sites was reported (3,4). Radiologically, GCToB shows typical destructive osteolytic lesions in affected bones (3,5,6). The tumoral mass appears either gray to white or gray to brownish in color up to its vascular stroma (1,4-7).

Histopathologically, the tumor is mainly composed of multinucleated giant cells in a moderately vascularized network of proliferating round, oval, or spindle-shaped stromal cells (1,4-9). Although the exact origin of the tumor remains obscure, it has been suggested that the tumor originates from the stromal cells of the bone marrow (1,4,9-11). There are few reported cases of metastatic GCToB in cats, and the way in which metastasis of tumor cells relates to distant organs is not clear. To the best of the authors' knowledge, the case described in the present study is the first observation of the involvement of the lymph nodes during the metastasis of such a tumor in cats.

Material and methods

Case history

A 5-year-old crossbred cat was referred to the surgery clinic with progressive swelling in the left proximal femoral region, severe lameness, constipation, and dysuria. The cat was unable to bear weight on the left hind leg. In the anamnesis, it was discovered that the cat had been operated on for a left femoral fracture 4 years earlier. Treatment had consisted of an open reduction and internal fixation with an intramedullary pin.

Examination

In the clinical examination, a moderately firm, subcutaneous palpable mass was seen in the left femoral region and biopsy samples were taken. Radiological examination revealed prominent

osteolytic changes in the proximal epiphyseal part of the left femur. In light of the histopathologic examination of the biopsy samples and the results of the radiological examination, the cat was diagnosed with GCToB. Euthanasia followed due to the poor prognosis, including the suspicion of local invasion of the neighboring tissues. At necropsy, a tumoral mass was found in the proximal part of the left femur; it was subcutaneous, grayish to white, and moderately firm, 8 × 9 × 6 cm in size, and it was observed to be compressing adjacent muscles (Figure 1).

The dorsal part of the pelvic cavity was invaded by nodular masses of various sizes compressing the adjacent tissues and organs. Prominent adhesions were noticed between tumoral masses and the serosal surface of the rectum. The large intestines were filled with dry feces, and the urinary bladder was full of dark yellowish urine. Similar tumoral masses also occupied the dorsal left part of the hip.

Macroscopically, no distant lesions or macrometastases were observed in the organs located in the abdominal or thoracic cavity. When the longitudinal section of the left femur was examined, tumoral tissue proliferation was observed from the medullar region to the epiphyseal part of the femur.

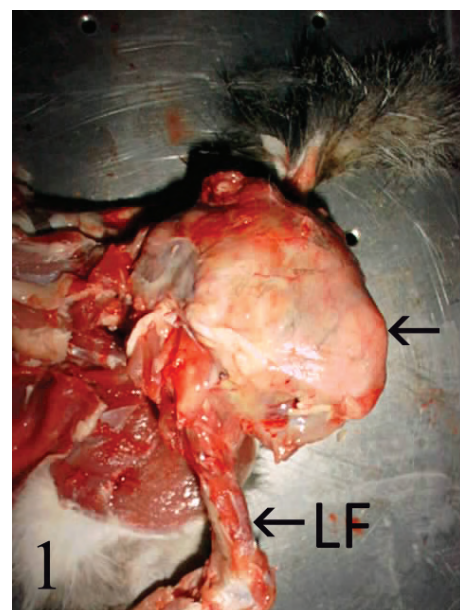


Figure 1. Subcutaneous mass located in the proximal part of the left femur. LF: left femur.

Analysis

Tissue samples taken from the femur, various parts of the subcutaneous mass, rectum, regional skeletal muscles, local lymph nodes, lung, skin, and other major organs were fixed in buffered formalin and processed routinely. Tissues sections of 5 µm were cut from the paraffin-embedded tissue blocks and all slides were then stained with hematoxylin-eosin (H&E). Selected slides were also stained with a standard streptavidin-biotin-peroxidase complex method using 1:500 diluted mouse antihuman antibodies against desmin, vimentin, and S100 (Lab Vision, Fremont, CA, USA), as previously described (12). Tartrate-resistant acid phosphatase (TRAP) activity in tumor cells was evaluated with a commercially available kit (Acid Phosphatase, Leucocyte (TRAP) Kit 387, Sigma-Aldrich Co., St. Louis, MO, USA) (4,13).

Results

Radiological findings

Irregularly margined osteolytic changes were found, including the destruction of the medullary cavity and the adjacent cortex of the left femur (Figure 2). The center was mostly radiolucent with increasing

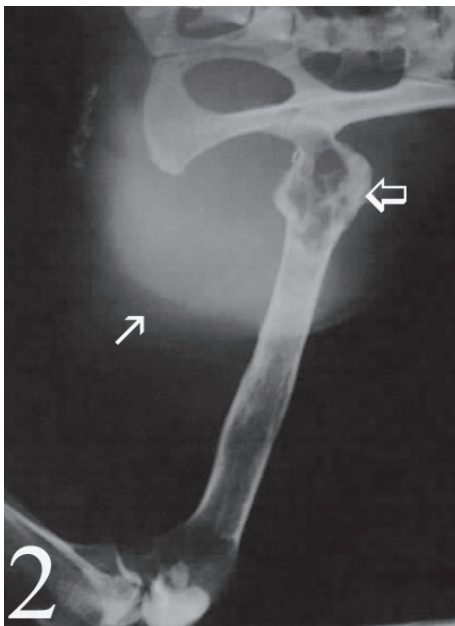


Figure 2. Lateral-medial radiographic view of the mass (arrow), including lytic changes (empty arrow) in the proximal part of left femur.

density toward the periphery. No periosteal response or fracture was found. In the examination of the lungs, metastatic involvement was not observed.

Microscopic findings

Light microscopic examination of the H&E-stained slides showed the presence of ovoid-shaped mononuclear cells intermixed with multinucleated giant cells (up to 105 nucleuses) with irregular round-to-ovoid nuclei and small, centrally located nucleoli in a vascularized stroma (Figure 3). Multinucleated giant cells (MGCs) were uniformly scattered throughout the sections. In some areas, pinkish collagen fibers, disseminated small hemorrhagic foci, siderocytes, and coagulation necrosis were noticed. Mitotic figures were not common and no metastasis was observed in the lungs or other major organs. In the left popliteal lymph node, however, MGCs with a similar morphology to that of the primary tumoral site were found in the cortical sinuses (Figure 4). The invasion of regional muscles, the serosal wall of the rectum, and the dermal tissue of the skin by tumor cells revealed that the tumor was locally aggressive and destructive. Osteoid tissue production was noted as a pinkish, homogenous material located in the peripheral parts of the tumoral mass.

Almost all of the tumoral cells gave a strong positive reaction to the vimentin antibody, and no staining was observed with the desmin or S100 antibodies. While the regional muscle tissues were

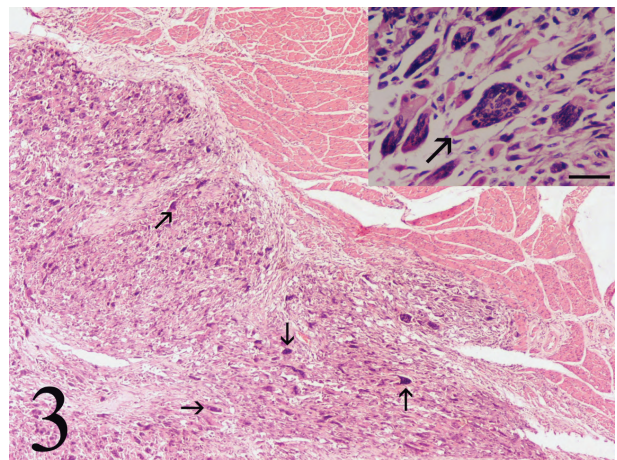


Figure 3. Local invasion of regional muscles by tumoral cells and giant cells (arrows) via hematoxylin & eosin staining; bar = 120 µm.

positively stained with desmin antibody, the tumoral cells did not react. Almost all MGCs showed a strong positive reaction to the TRAP test (Figure 5). The staining was cytoplasmic and positively stained cells displayed a pinkish, granular appearance.

Discussion

When compared with other reports on GCToB in cats, the present case had both typical and atypical features, but the cardinal macroscopic and microscopic findings observed in this case were found to be similar to those of previous studies (1,4,8,9).

Although the exact origin of the tumor is not known, the stromal cells of bone marrow are thought to be the primary point of origin (1,4,10,11). Parallel to this interpretation, in the present case, the authors think that the tumor most probably originated from bone marrow stromal cells. This conclusion is based on the whitish tissue proliferation observed in the medullar region of the longitudinal section of the femoral bone. The authors also used immunohistochemistry to determine the histological origin of the tumoral cells and performed antidesmin, vimentin, and S100 staining, as well as the TRAP test. The positive reaction for vimentin was seen in almost all of the mononuclear and multinucleated tumoral cells, leading the authors to conclude that the tumor

was of mesenchymal origin. TRAP activity has been used in previous studies for the determination of the origin of giant cells (4,8). While the giant cells originating from soft tissue tumors are not sensitive to the TRAP test (4,11), the giant cells from GCToB react positively, a feature that reflects their osteoclastic origins (4,11).

MGCs are also seen in other kinds of skeletal and extraskeletal tumors, such as giant-cell osteosarcoma and giant-cell tumors of soft tissues (1,4,14). The existence of lesions in the left femoral bone in the submitted case was used to distinguish GCToB from the similar giant-cell tumor of soft tissues. The distribution of the MGCs can be used for the differential diagnosis of these kinds of tumors from the giant-cell-type osteosarcomas. For instance, while MGCs are uniformly dispersed in the tumoral mass in GCToB, they are selectively found in the neoplastic areas in giant-cell-type osteosarcomas. In the submitted case, MGCs were dispersed uniformly throughout the tissue sections. The formation of bony material and osteoid tissue is the significant feature of giant-cell-type osteosarcomas (1). Osteoid material is not usually seen in GCToB unless the tumor is associated with a pathologic fracture (1,4); in the submitted case, osteoid tissue was observed sparsely in some areas, and it should be noted that the cat had a history of left femur fracture.

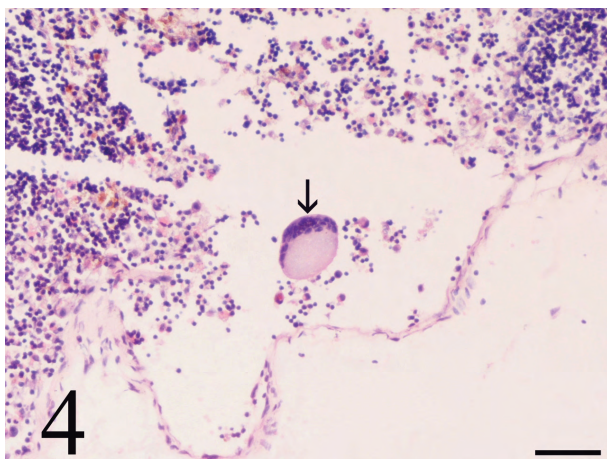


Figure 4. Metastatic giant cell (arrow) in the cortical sinuses of the popliteal lymph node via hematoxylin & eosin staining; bar = 100 μ m.

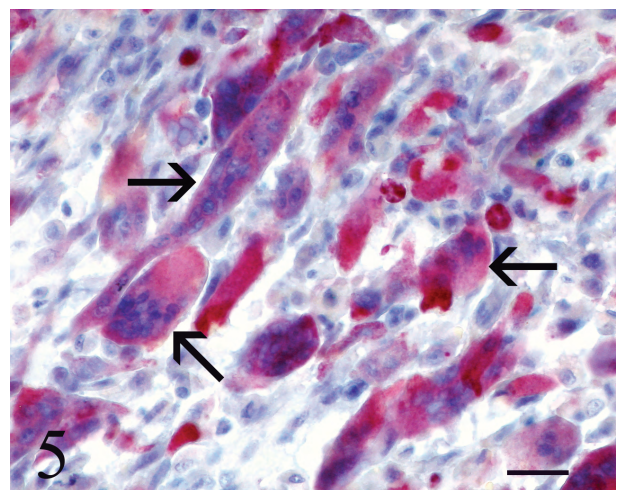


Figure 5. Tartrate-resistant acid phosphatase activity in the cytoplasm of giant cells (arrows) via TRAP kit, counterstained with hematoxylin; bar = 100 μ m.

Classically, GCToB is known to have a benign nature, even though the existence of metastatic cases in cats has been observed (3,4,11). Distant metastases to the lung or other organs are rare (<10%) in humans (2,3), but the rate is not clear in cats, as the number of the cases is quite limited. In the present case study, the tumor prominently displayed locally aggressive and invasive features. Even though macroscopic metastasis was not seen in the organs, MGCs were found microscopically in the cortical sinuses in the left popliteal lymph node.

In humans, after surgical removal of the tumoral masses, the estimated recurrence rate is about 40%-60% because of the deep dermal infiltration (2,3,14). Such infiltration may explain why this tumor often demonstrates local recurrence even after surgical removal. In the present case, tumoral cells also infiltrated the dermis. Information about the recurrence rate in cats after surgical removals is scarce due to the limited number of studies.

In the present case, the subject experienced constipation and dysuria. The authors connected these 2 complaints with the local mechanical and

invasive effects of tumoral masses, which often cause difficulties in the passages of both the intestine and the urethra. Veterinary practitioners should be aware of this condition.

In humans, the prognosis associated with the treatment of malignant giant-cell tumors is dependent upon the degree of cellular differentiation, the number of mitotic figures, the location of the tumor, the degree of involvement of surrounding tissues, the involvement of local lymph nodes, and the success of surgical excision. Due to the fact that there have been very few reports on GCToB in cats, the present study is the first to provide valuable information on the route of metastasis in cats afflicted with GCToB. The authors hope that this report will be helpful for cat practitioners during the examination and sampling of suspected cases of giant-cell tumor of bone in cats.

Information on the incidence, age, sex, site, and breed predisposition for GCToB tumors in cats is inadequate. This causes difficulties in predicting the behavior of these kinds of tumors after surgical excision and therapy. For this reason, surgeons often choose euthanasia.

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