CLINICAL REPORT

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Metastatic giant cell osteosarcoma in a cat

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Abstract

A four-year-old male Persian cat was referred with three weeks history of progressive lameness due to a rigid osseous mass with 3.50×2.50×2.00 cm in dimensions in his left arm. In the histopathological evaluation of bone biopsy, two distinct populations of cells including multinucleated giant cells and oval cells which embedded in a fibro-osseous stroma and surrounded by lamellar bone trabeculae were observed. At necropsy, multiple metastatic nodules with different sizes unveiled in the liver and spleen. Microscopically, those tumor cells which already described in the bone lesion were also infiltrated to the liver and spleen. The neoplastic cells had no immunoreaction to CD68, desmin, alpha smooth muscle actin, S100, CD20, CD3 and pancytokeratin, but only a few cells had reaction to vimentin were similar to fibroblasts.

استئوسارکوم دیو سلولی با وقوع متاستاز در یک قلاده گربه

چکیده

یک قلاده گربه ایرانی نر چهار ساله با تاریخچه سه هفته لنگش پیشرونده ناشی از یک توده استخوانی سفت و سخت با ابعاد ۳/۵۰×۲/۵۰×۲/۰۰ سانتی‌متر در بازوی چپ ارجاع داده شد. در ارزیابی هیستوپاتولوژیک نمونه بیوپسی استخوان، دو جمعیت مجزا از سلول‌ها از جمله دیوسلولهای چند هسته‌ای و سلول‌های بیضوی که در استروما فیبروزی-استخوانی قرار گرفته و توسط ترابکولاهای استخوانی احاطه شده بود مشاهده شد. در کالبدگشایی، ندول‌های متاستاز یافته با ابعاد مختلف در کبد و طحال مشهود بود. از لحاظ میکروسکوپی، سلول‌های توموری که قبلاً در ضایعه استخوان شرح داده‌شد نیز به کبد و طحال نفوذ کرده بودند. سلول‌های نئوپلاستیک هیچ تأثیر ایمنی روی CD68، desmin، actin، S100، CD20، CD3 و پانسیتوکراتین نداشتند، اما فقط چند سلول نسبت به ویمنتین واکنش داشتند.

واژه های کلیدی: استئوسارکوم دیو سلولی، ایمونوهیستوشیمی، گربه نژاد ایرانی، متاستاز

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Introduction

Osteosarcoma, the most common non-hematopoietic primary malignant mesenchymal tumor of bone is characterized by the formation of osteoid tissue and various histological patterns.[1] This lesion is a heterogeneous tumor which in addition to producing an osteoid matrix, it might be displayed as a fibroblastic and/or cartilaginous matrix as well. In dogs, 75.00% of all bone tumors occur mainly in midsize to large male dogs, of all ages, with a higher occurrence between the ages of 7 and 8 years old.[2]

In domestic animals, osteosarcomas can be classified as osteoblastic, chondroblastic, fibroblastic, telangiectatic, and giant cell types depending on their matrix appearance.[3] Giant cell-rich osteosarcoma is a rare type of osteosarcoma with an incidence of 3.00% among all osteosarcoma cases and it was first reported in human. It is defined as an osteosarcoma in which more than 50.00% of the tumor is composed of numerous benign osteoclasts like giant cells admixed with malignant bone forming cells. [4]

Case Description

A four-year-old male Persian cat was presented with a history of three weeks of lameness, anorexia and weight loss. The fast-growing palpable hard mass was originated from the left humerus bone with 3.50 × 2.50 × 2.00 cm in size in the lateral surface of the distal part near to supracondylar crest which developed in seven weeks. Laboratory findings such as CBC, serum electrolyte concentrations and C-reactive protein were within normal limits. There were no peculiar changes in chest or abdominal radiographs.

After disinfection of the surrounding tumor area by using electro surgery, the tumor tissue was excised from the arm region. The bleeding was controlled and coagulated. The tissue close to the bone was removed as much as possible, trying to leave no remnant of the suspected tissues. The tumor bed was cauterized to make sure of no more regrowth of the tumor. Post-operative treatments including intramuscular cefazolin (20 mg kg^{-1}, Afa chemi pharmaceutical Co., Tehran, Iran) for three days and subcutaneous carprofen (0.7 mg kg^{-1}, Mahya Darou Co., Tehran, Iran) for pain relief were administered.

The removed mass was fixed in 10.00% neutral buffered formalin for five days and decalcified in 3.00% nitric acid for six days, then the tumor mass was processed according to the routine histopathological procedure and stained with hematoxylin and eosin (H & E). A panel of immunomarkers including CD68 (Dako, Glostrup, Denmark), CD3 (DakoCytomation, Zug, Switzerland), CD20 (Dako, Carpinteria, USA), alpha smooth muscle actin (Dako, Glostrup, Denmark), desmin (Bio-Science, Emmenbrücke, Switzerland), pan-cytokeratin (AE1/AE3; Biogenex, Fremont, USA), S100 (Dako, Glostrup, Denmark), and vimentin (Clone V9; Dako) were applied in order to differentiate the mass and identify its histogenesis and origin.

Microscopically, the mass composed of two distinct cell populations (large and small cell populations) among bone spicules and occasionally osteoid matrix. The large population of the cells consisted of polygonal mono-nucleated cells were various in morphology and size, with sharply demarcated borders, with variable amounts of pale to deep eosinophilic cytoplasm from scant to abundant. The rounds to oval vesicular nuclei were often eccentric with one or two prominent nucleoli (Fig. 1). The small population of the cells were composed of extremely pleomorphic multinucleated giant cells with intense eosinophilic cytoplasm, from few to numerous small nuclei (Fig. 2). Bizarre mitotic figures were 5-7 in high power field.

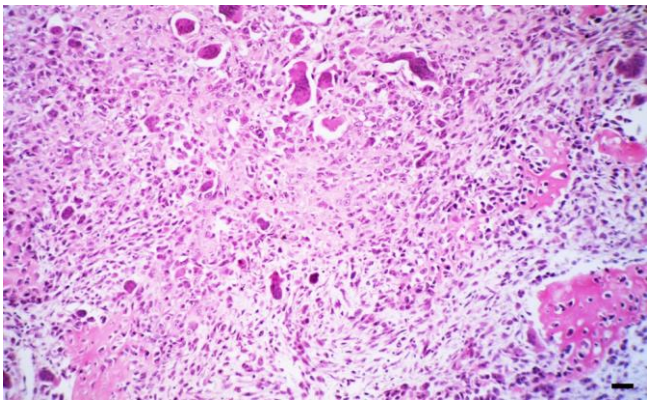

Fig. 1. Giant cell osteosarcoma. The tumor consists of polygonal mononucleated cells and numerous multinucleated giant cells apposed amounts of osteoid matrix (H & E, Bar = 100 µm).

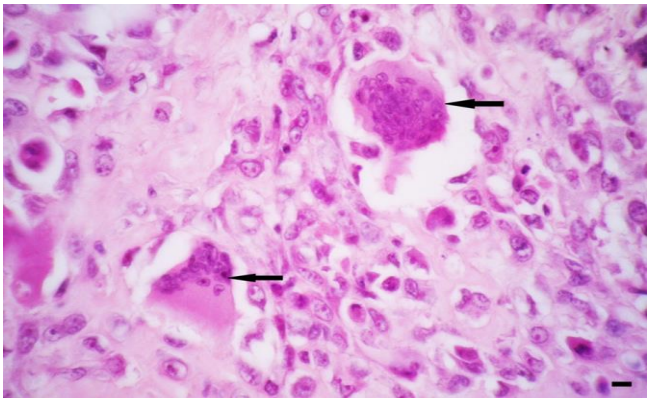

Fig. 2. Giant cell osteosarcoma. Pleomorphic multinucleated giant cells (arrows) are surrounded by mononucleated polygonal cells (H & E, Bar = 25 µm).

All neoplastic cells were negative in reactions with immunomarkers except for the small populations of mesenchymal cells resemble to fibroblasts and microcapillaries which were immunostained with vimentin and also a few cells stained with CD3 or CD20.

Two weeks after tumor diagnosis, as it was requested, the cat was referred to the hospital. Chemotherapy was performed using cisplatin (Sigma-Aldrich, St. Louis, USA) IV at 60 mg m^{-2} for six doses at three week intervals and to avoid nephrotoxicity, chemotherapy was combined with concurrent 4 hr saline (Samen Pharmaceutical Co., Mashhad, Iran) diuresis. In addition, 0.02 mg kg^{-1} buprenorphine (Farachemi Co., Isfahan, Iran) was administered to control pain.

The patient was only alive for two months after treatment. In postmortem examination, multifocal metastatic tumor nodules ranging from 0.50 to 2.00 cm in their greatest dimensions were found in the liver and spleen. No other significant gross lesions and no microscopic evidence of metastasis in the other organs were observed. The target tissues and other organs like lung, kidney, stomach and intestines were fixed in formalin for more histopathologic evaluation. In liver and spleen, the neoplastic cells were arranged in large lobules, separated either with fibrous connective tissue stroma or remnant parenchymal cells which existed exclusively in liver.

Metastatic tumor harvested from liver and spleen was characterized by moderate cell density and it composed of numerous scattered nests of multinucleated giant cells. The nests were separated by small bundles of pleomorphic, spindle shaped cells resembling fibroblasts which were various in morphology and size (Fig. 3).

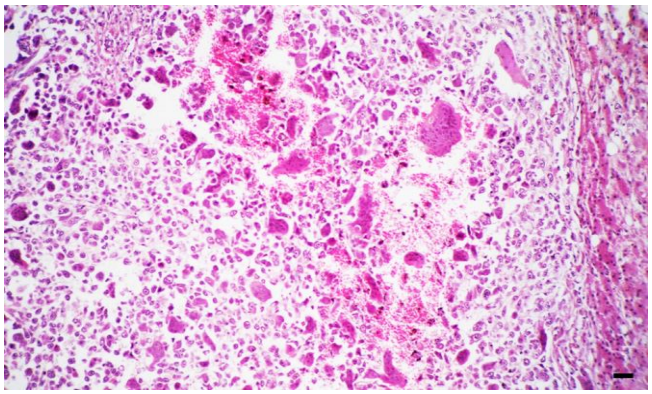

Fig. 3. Metastatic tumor in the liver. Numerous scattered nests of pleomorphic multinucleated giant cells separated by polygonal mononucleated cells (H & E, Bar =100 µm).

Discussion

Osteosarcomas are malignant tumors of the bony tissues with a higher degree of metastasis.[5] After the first description of giant cell osteosarcoma, only few reports of this type of osteosarcoma in human have been published. Moreover, there is very rare reports regarding this type of tumor in veterinary and wildlife literature.[6] However, feline osteosarcomas occur most commonly in the appendicular skeleton and hind limbs.[7]

Giant cell osteosarcoma is identified by the presence of osteoclast-like giant cells, while producing scant amounts of osteoid, however osteoid production in some giant cell osteosarcomas are undetectable, and hetero-morphism of mononuclear tumor cells is not conspicuous.[8] Different types of malignant osteoid fragments were appeared throughout the lesion in the present animal.

Histologically, atypical tumor cells with osteoid formation and multinucleated giant cells are the key features in identification and differential diagnosis of this tumor. The origin of multinucleated giant cells in osteosarcoma is poorly understood in human and veterinary medicine. Furthermore, the origination of osteoclasts and osteoblasts has been postulated. A number of researchers believed that the multinucleated giant cells could arise by fusion of osteoclasts, whereas, others consider an osteoblastic origin is more likely.[9]

In addition to specific antibodies which are the most reliable procedures for the diagnosis of giant cell tumors, with macrophage-histiocyte lineage, they are morphologically very similar to giant cell osteosarcomas, which osteoid production by latter could also be an appropriate indicator for discriminating them from each other.[10] Although, C-reactive protein (CRP) level and CBC count in our patient were in normal range and also no infection was found in blood or wound culture, however it was difficult to differentiate osteomyelitis and bone tumor from each other, since both lesions show similar features in radiopraphy,[11] therefore, next proceeding was absolutely related to histopathological results.

The treatment protocols for this neoplasm include radical surgery and chemotherapy, however, despite the treatment, the amputation might be as the choice treatment for pain relief and for effective removal of the primary tumor, but post-amputation survival times are short, on average three to four months.[12,13] Osteosarcoma is a highly metastatic neoplastic disease, mainly towards the lungs, which metastasis is developed in 90.00% of the animals within one year after limb amputation.[14]

A retrospective study of extraskeletal osteosarcoma in 169 dogs and a comparative evaluation of osteosarcoma in dogs and humans described metastasis in lymph nodes, lungs, kidneys, spleen, bone marrow, tegument, but did not mention the liver. [15] The occurrence of pulmonary metastases has been detected in 5.00 to 11.00% of cases at the time of diagnosis.[16] In the present study, liver and spleen were affected by original bone tumor, without pulmonary metastasis in a two months period after limb amputation.

Osteosarcomas are consistently immunoreactive for vimentin.[17] In the present report, immunohistochemical staining of tumor tissue with antibodies against vimentin implicated that this tumor originated from mesanchymal cells. Histological finding and negativity for desmin (intermediate filament in the muscle cells) identified that this tumor is not originated from myoblasts.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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