

Primary extraskeletal hepatic osteosarcoma in a cat

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- ▶ Extraskeletal osteosarcoma is a rare malignancy in cats.
- ▶ En bloc excision may improve survival for extraskeletal osteosarcoma.

A 13-year-old 4.5-kg (9.9-lb) spayed female domestic shorthair cat was evaluated by the referring veterinarian because of a 3-day history of change in personality and lethargy. On physical examination, a low-grade (II/VI) systolic murmur and a firm palpable mass in the left cranial quadrant of the abdomen were detected. The cat's past medical history did not include any major illnesses. Initial diagnostic testing included a CBC, serum biochemical analyses, urinalysis, and thoracic and abdominal radiography. Hemoconcentration (Hct, 54%; reference range, 29 to 48%) was detected via CBC; results of the serum biochemical profile were within reference ranges. Urinalysis revealed urine specific gravity of 1.034 with a trace amount of protein and an acellular sediment. The cat was euthyroid and seronegative for feline retroviruses. Differential diagnosis for increased Hct included dehydration masked by hypoproteinemia and primary or relative polycythemia. However, results of further CBCs indicated complete resolution of hemoconcentration.

Abdominal radiography revealed a large (approx $7 \times 5 \times 4$ cm), ill-defined radiopaque mass in the right cranioventral region of the abdomen causing dorsocranial displacement of the stomach and transverse colon (Fig 1). Differential diagnosis for this finding included a neoplastic or granulomatous mass involving the pancreas, ventral portion of a liver lobe, tail of the spleen, or mesentery. Three radiographic views of the thorax failed to reveal any evidence of pulmonary nodules.

The owners were counseled on the need to perform an exploratory celiotomy to excise the mass and establish a diagnosis. With the owner's consent, a large firm mineralized mass involving the left lateral lobe of the liver was excised en bloc. No evidence of hepatic or mesenteric lymphadenopathy was noted. The cat recovered from anesthesia without complication. Histologically, the mass was expansile and infiltrative and had effaced the normal hepatic architecture. The neoplasm was composed of spindle-shaped to polygo-

nal, occasionally multinucleated, pleomorphic cells with high mitotic activity. The neoplastic cells produced irregular islands and trabeculae of well-developed osteoid. Histopathologic diagnosis of hepatic osteosarcoma was made on the basis of the microscopic features (Fig 2). Only a portion of the biopsy specimen was submitted for histologic examination; therefore, the microscopic margins could not be evaluated. Grossly, the margins had appeared unaffected when the entire left lateral hepatic lobe was excised. Because whole-body skeletal radiography was not performed, a tentative diagnosis of an extraskeletal hepatic osteosarcoma was made on the basis of the initial clinical, laboratory, and radiographic findings. A covert primary skeletal lesion involving the skull or an extremity could not be ruled out.

Four weeks after the initial surgery, the cat was referred for further evaluation of hepatic osteosarcoma. The owner reported that the clinical signs of lethargy were alleviated. On physical examination, the cat was active, bright, and alert; signs of tenderness were observed on palpation of the abdomen, but no other physical abnormalities were noted. At this time, a CBC, serum biochemical analyses, urinalysis, thoracic radiography, and abdominal ultrasonography were performed to rule out any local recurrence or distant metastasis of the neoplasm. Thoracic radiography revealed a bronchointerstitial pattern with no evidence of pulmonary nodules. Mildly hyperechoic liver parenchyma and slight splenomegaly were detected ultrasonographically. Differential diagnosis for these changes included mild fatty liver disease, cholangitis, and nonspecific splenic changes that were probably inflammatory. Results of initial postoperative staging in this cat were negative, with no evidence of gross residual disease or metastasis.

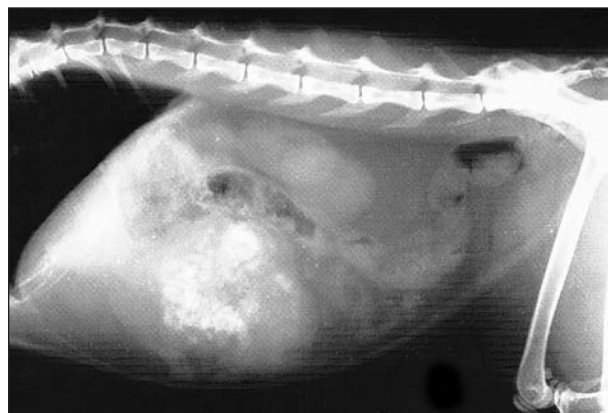


Figure 1—Lateral radiographic view of the abdomen of a cat with primary extraskeletal hepatic osteosarcoma. Notice an ill-defined radiopaque mass in the cranioventral region of the abdomen causing displacement of the stomach and transverse colon.

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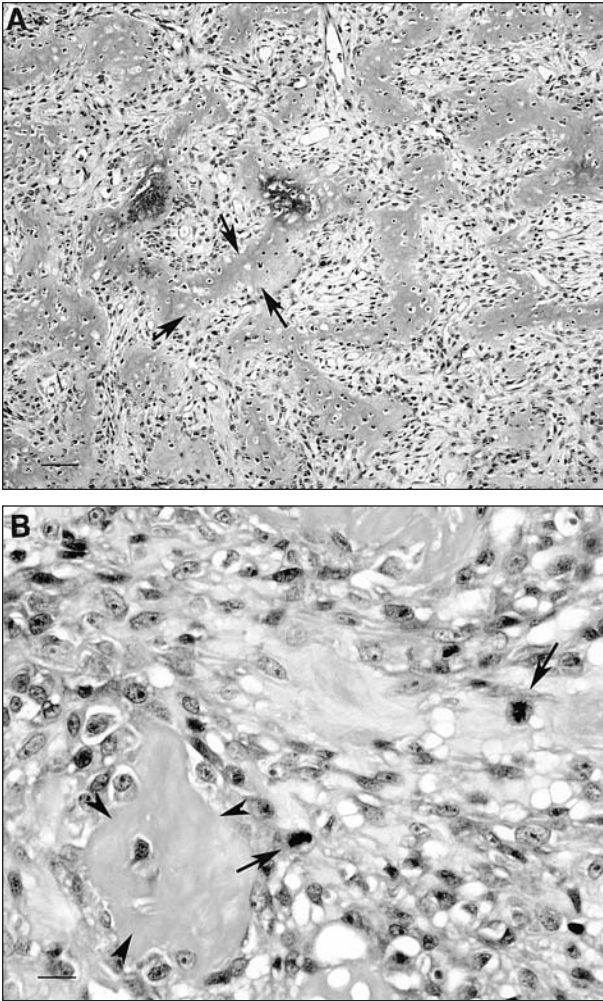


Figure 2—Photomicrographs of sections of a primary extraskeletal hepatic osteosarcoma in a cat. A—Notice spindle-shaped to polygonal neoplastic cells producing trabeculae of osteoid (arrows) that is multifocally mineralized. H&E stain; bar = 100 μ m. B—Nuclear pleomorphism and high mitotic activity (arrows) are evident; neoplastic cells surround and are embedded in islands of well-developed osteoid (arrowheads). H&E stain; bar = 25 μ m.

The cat was treated with 6 cycles of the chemotherapeutic agent carboplatin⁹ every 3 to 4 weeks. Initially, the dosage of carboplatin was 180 mg/m², administered IV. Mild myelosuppression with evidence of neutropenia was noted via a CBC performed 7 days after the second chemotherapeutic treatment. Neutropenia resolved during prophylactic oral administration of amoxicillin-clavulanate potassium (62.5 mg, PO, q 12 h). Hospitalization or more aggressive medical management was not required. At the third cycle, the dosage of carboplatin was decreased by approximately 25% to 130 mg/m² for this and subsequent treatments. Eleven months later, thoracic radiographs were obtained at the referring hospital; a mild bronchial lung pattern was observed with no evidence of pulmonary metastasis. Forty-two months after surgical treatment, telephone interview with the owners revealed that the cat had no clinical signs of metastatic or hepatic disease and appeared to be doing well. The last clinical staging of the neoplasm was performed 11 months from the date of initial diagnosis.

Osteosarcomas are highly aggressive tumors characterized by local invasion and destruction of normal tissue and distant metastasis. Osteosarcoma in cats is uncommon, and extraskeletal osteosarcoma is a rare malignancy in dogs, cats, and humans.¹⁻⁴ As reported by Patnaik et al,¹ 3,145 feline necropsies performed during an 11-year period revealed 289 tumors of non-hematopoietic origin in 264 cats; pulmonary carcinomas and osteosarcomas were more frequent in domestic shorthair cats than in other breeds. In a study⁵ by Heldmann et al, 62% of osteosarcomas in cats originated from the skeleton, and 38% developed from extraskeletal sites. In that study, cats with either appendicular or extraskeletal osteosarcoma survived longer (mean, 11.8 months or 12.7 months, respectively) than those with axial osteosarcoma (mean, 6.1 months). The shorter survival times of cats with axial skeletal osteosarcoma, compared with those with appendicular osteosarcoma, have been confirmed in other studies.⁶⁻⁸ In cats, extraskeletal osteosarcoma has been reported to occur at sites of vaccine administration.^{5,7,8} Approximately 25% of vaccine-associated soft-tissue sarcomas in cats have distant metastases, and cats with these neoplasms also have shorter survival times.⁵⁻⁸

The etiology of extraskeletal osteosarcomas is largely unknown, and in the cat of this report, there was no history of chronic hepatic disease or other primary malignancy. Furthermore, we were unable to find any other evidence of primary or metastatic lesions via routine thoracic and abdominal survey radiography, and thus a tentative diagnosis of primary extraskeletal hepatic osteosarcoma was made. The cat was alive 42 months after surgical treatment, which strongly supports the diagnosis of an extraskeletal hepatic osteosarcoma.

In dogs, extraskeletal osteosarcoma appears to have worse prognosis for survival and metastasis than skeletal osteosarcoma^{3,4,9,10}; metastases were reported in 7 of 11 dogs in 1 study,³ and regional lymph nodes were the most frequent site of metastasis. In a retrospective study⁴ of 169 dogs with extraskeletal osteosarcomas that originated in various soft-tissue sites, reported median survival time was 26 days; however, median survival time for dogs with extraskeletal mammary gland osteosarcomas was 90 days. The common causes of death are related to local recurrence in dogs with extraskeletal osteosarcomas and pulmonary metastasis in dogs with mammary gland osteosarcomas. Systemic administration of chemotherapeutic agents is recommended as follow-up treatment for dogs with appendicular osteosarcoma. Unfortunately, chemotherapeutic treatment is unlikely to cure most dogs with osteosarcoma, but it may prolong survival time with a good quality of life.

In cats, it has been suggested that, regardless of location of osteosarcoma, aggressive excision of the tumor appears to be the most effective form of treatment.⁵ The role of adjunctive chemotherapy in the treatment of osteosarcoma in cats has yet to be fully explored. For the cat of this report, adjunctive treatment with carboplatin was administered; the decision to treat was made on the basis of the large size and high mitotic activity of the primary mass. In human and veterinary oncology, histologic grade is a critical prognostic factor for most tumor types.¹¹ A histologic grade was

not assigned in this case. Carboplatin appears to be well tolerated by cats at a dosage range of 150 to 260 mg/m², IV, every 21 days. Dose escalation is presently being investigated in cats at several institutions, and we have administered doses as high as 225 mg/m² with minimal adverse effects. In our experience, the maximum recommended dosage of carboplatin (260 mg/m², IV) causes severe myelosuppression in cats and can potentially cause death. It is difficult to determine the role of adjunctive treatment with carboplatin in the cat's prolonged disease-free survival; the partial hepatectomy alone may have been curative, as has been reported in cats with appendicular osteosarcoma.

Although rare, osteosarcoma is the most common skeletal neoplasm in dogs and cats. Interestingly, appendicular osteosarcoma has a more favorable prognosis in cats than in dogs.^{6,12,13} In our experience, long-term survival can be anticipated in cats with appendicular osteosarcoma treated with limb amputation alone. Median survival of 49 months for cats with appendicular osteosarcoma has been reported, compared with a shorter median survival time of only 5.5 months for cats with axial skeletal osteosarcoma.¹³

In general, extraskelatal osteosarcomas are highly malignant tumors and are associated with a 5-year survival rate of 37% in humans.² In human medicine, classification of a neoplasm as an extraskelatal osteosarcoma requires that the tumor originates in soft tissue and is not attached to bone or periosteum, has a uniform sarcomatous pattern identified histologically (to exclude the possibility of a mixed malignant mesenchymal tumor), has a high mitotic index, and produces osteoid or cartilage matrix.^{2,14} To our knowledge, the veterinary literature lacks a comprehensive review of feline extraskelatal osteosarcomas. Our findings in this cat agree with a report¹⁵ that suggests surgery and neoadjuvant treatment with carboplatin may yield a good prognosis in cats with extraskelatal osteosarcomas.

^aCarboplatin, Bristol-Meyers Squibb, Princeton, NJ.

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