Pathology in Practice

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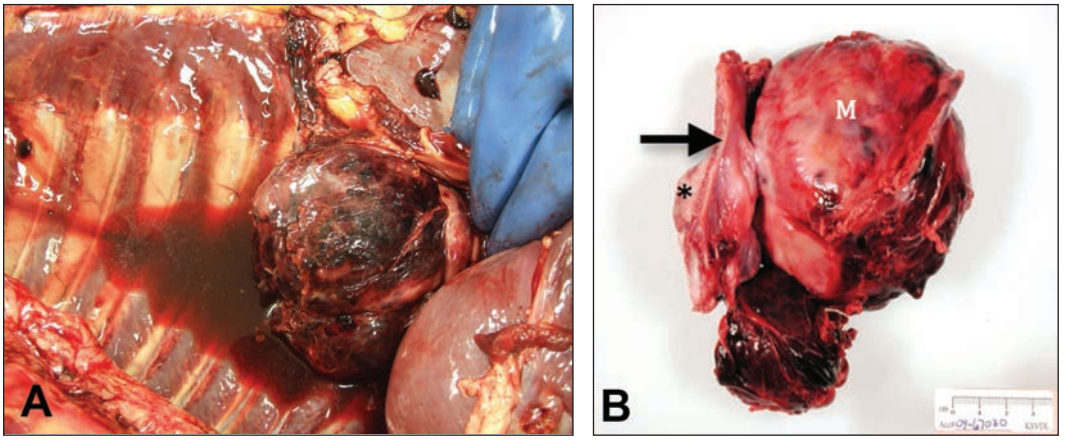

Figure 1—Photographs of a mass in a 7-year-old ovariohysterectomized female Golden Retriever that was evaluated because of sudden-onset respiratory distress and a few-day history of lethargy and was subsequently euthanized. A—Gross image of the mass and associated hemothorax within the thoracic cavity. The diaphragm is to the right, and the mass is exposed with the gloved hand. The mass is associated with the 10th rib and has invaded the surrounding soft tissues. B—Gross image of the excised intrathoracic and extrathoracic components of the mass and the associated 10th rib (arrow). A 15-cm-diameter round, smooth, soft fluctuant mass (M) is attached to the left 10th rib near the costochondral junction. There is a 1-cm-diameter zone of bone lysis in the 10th rib at the costochondral junction. A 4 X 3 X 1-cm soft gray mass (asterisk) was also protruding from the area of lysis in the rib into the subcutaneous tissues of the thoracic wall.

History

A 7-year-old ovariohysterectomized female Golden Retriever was evaluated because of sudden-onset respiratory distress and a history of lethargy of a few days' duration. On physical examination, the dog had pale mucous membranes and dyspnea; decreased lung sounds were auscultated bilaterally.

Clinical and Gross Findings

A CBC revealed normocytic, normochromic anemia (Hct, 29%; reference range, 37% to 55%) and a low platelet count with clumping present. Serum biochemical analyses revealed hypoproteinemia (4.6 g/dL; reference range, 5.4 to 7.6 g/dL) and hypoalbuminemia (2.8 g/dL; reference range, 3.4 to 4.2 g/dL). Coagulation testing was performed; prothrombin time was 17.0 seconds (value obtained from a healthy control dog, 8.2 seconds) and activated partial thromboplastin time was 20.7 seconds (value obtained from a healthy control dog, 9.4 seconds). Thoracic radiography revealed a regionally extensive, soft tissue opacity throughout the ventral aspect of the thorax, which caused border effacement of the heart and diaphragm and caudodorsal displacement of the lung lobes, consistent with pleural effusion. An additional radiographic finding was a 2.2-cm-diameter expansile, lytic, irregularly marginated, round lesion at the costochondral region of the left 10th rib (apparent only in the ventrodorsal view). Also on the ventrodorsal view, there was a 5-cm, oblong, well-demarcated soft tissue mass located lateral to the 10th rib within the tissues of the thoracic wall. Ultrasonography of the thorax was performed, and an 11.6 X 7.5-cm multilobular, complex, mixed echogenic, vascular mass arising from the costal pleura at the level of the costochondral junction of the left 10th rib and extending into the thorax was identified. The mass was bordered by pleural effusion. Multiple smaller complex masses were also seen adjacent to the 10th rib, within the pleural space, at the same location as the large intrathoracic mass. The 10th rib was increased in size (compared with the other ribs), hypoechoic, and irregularly marginated with disruption of the normal smooth, curvilinear, hyperechoic margin.

Thoracocentesis was performed, and the thoracic fluid obtained was hemorrhagic and did not clot after collection. Fluid analysis revealed an Hct of 29%, total protein concentration of 5.0 g/dL, and total nucleated cell count of 11.6 X 10^3 cells/µL. Microscopic analysis of the fluid was consistent with hemorrhagic effusion. Approximately 1 hour after initial peripheral Hct assessment, the value had decreased to 25%. Based on the findings, continued hemorrhage, and suspected mass, euthanasia was elected and necropsy was performed.

Necropsy revealed that the pleural cavity contained approximately 1 L of unclotted blood and that the lungs were diffusely collapsed. Arising from the left 10th rib near the costochondral junction was a mass composed of a 15-cm-diameter, poorly circumscribed, infiltrative, round, smooth, soft, red, fluctuant mass that protruded into the thoracic cavity. On cut surface, the mass contained numerous blood-filled spaces. Lysis of the cortex and medullary bone of the left 10th rib was present (**Figure 1**). Additionally a 4 X 3 X 1-cm, gray, soft mass extended from the 10th rib into the thoracic body wall and subcutaneous tissues. The mediastinum contained a large number of multifocal, 1-cm-diameter, round, soft, red nodules.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →

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Histopathologic Findings

During necropsy, samples of tissues of particular interest were collected for histologic examination. Both of the large soft tissue masses arising from the 10th rib were composed of an infiltrative, unencapsulated, highly cellular neoplasm consisting of spindle cells forming solid bundles and streams with frequent blood-filled channels and cystic spaces lined by neoplastic cells (**Figure 2**). Neoplastic cells had distinct cell borders and moderate amounts of eosinophilic cytoplasm. Nuclei were oval with coarse chromatin and large central nucleoli and were frequently eccentrically located. There were rare islands of osteoid separated by neoplastic cells. Multifocal giant cells with large atypical nuclei were scattered throughout the neoplasm. Mitotic figures were rare. One blood vessel was occluded by a small number of cohesive neoplastic spindle cells. Lysis of the cortex of the 10th rib was evident.

The subcapsular and medullary sinuses of a draining lymph node contained moderate numbers of neoplastic polygonal to round cells with abundant eosinophilic cytoplasm and round to oval nuclei with coarse chromatin and large central nucleoli. There were frequent binucleate and trinucleate cells.

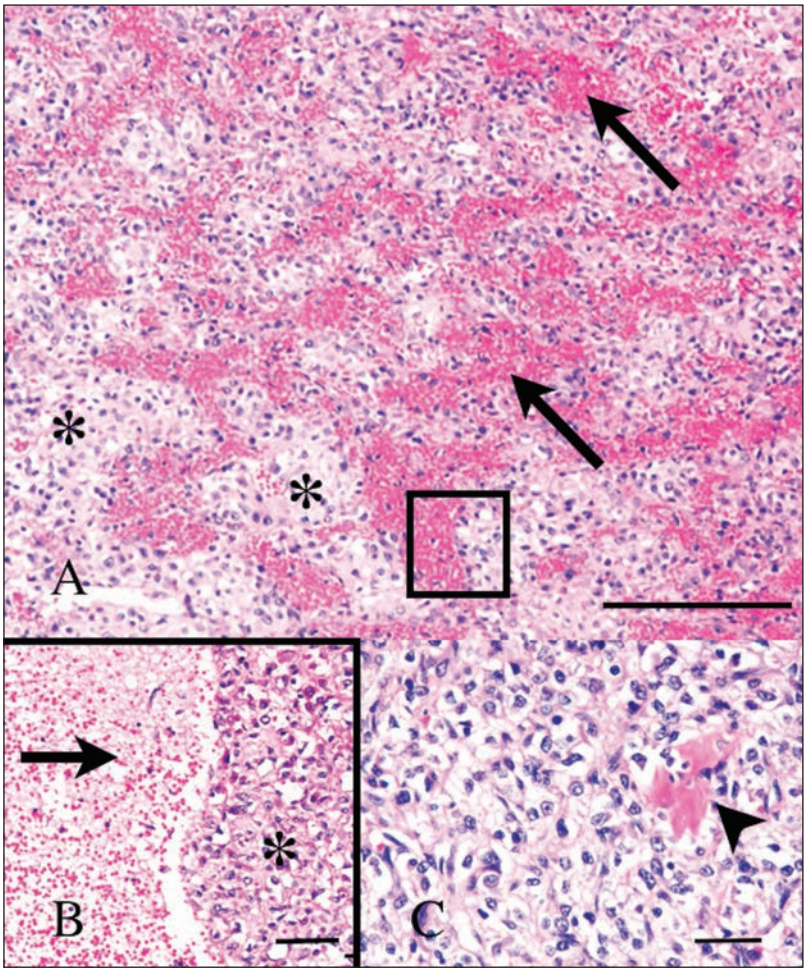

Figure 2—Photomicrographs of sections of the intrathoracic mass in the dog in Figure 1. A—Neoplastic cells (asterisks) surround several small vascular channels (arrows). H&E stain; bar = 100 µm. B—Higher magnification image of a portion of panel A. The vascular channels (arrow) are not lined with endothelium, but rather with the neoplastic cells (asterisk), a defining characteristic of telangiectatic osteosarcomas. H&E stain; bar = 50 µm. C—Higher magnification image of a portion of panel A. In addition to the neoplastic cells, a small amount of osteoid (arrowhead) is present associated with the tumor cells, defining this as a type of osteosarcoma. H&E stain; bar = 50 µm.

Morphologic Diagnosis and Case Summary

Morphologic diagnosis: telangiectatic osteosarcoma originating from the left 10th rib with invasion of the thoracic body wall and secondary hemothorax with vascular invasion and lymph node metastasis.

Case summary: telangiectatic osteosarcoma of a rib in a dog.

Comments

In dogs, the primary bone tumors most commonly diagnosed are osteosarcomas, accounting for > 80% of malignant bone tumors.[1] These tumors are characterized by the production of osteoid and immature bone by malignant osteoblasts.[1] Classifications of these tumors based on nature of the matrix produced by the malignant cells have been proposed. Telangiectatic osteosarcoma is a subtype characterized by blood-filled, cystic spaces that are lined by neoplastic cells rather than by endothelial cells. Radiographically, these tumors generally appear as aggressive, osteolytic lesions and grossly cannot be distinguished from primary or metastatic hemangiosarcoma of bone or from aneurysmal bone cysts.[1,2] Sites for development of telangiectatic osteosarcoma are similar to those for conventional osteosarcoma, but telangiectatic osteosarcoma can also uncommonly develop in the pelvis, scapulae, vertebral column, ribs, skull, and mesentery.[3,4] Rib osteosarcomas in dogs have a particularly high degree of necrosis.[5]

Radiographic findings consistent with osteosarcoma include a predominantly lytic bone mass that is expansile and lacking intralesional sclerosis. Telangiectatic osteosarcoma can also appear radiographically similar to aneurysmal bone cysts, but via cross-sectional CT or MRI, specific differences are apparent. Telangiectatic osteosarcomas have a viable rim of tumor cells around cystic areas and septa that appear as solid tumor tissue; in images obtained after administration of contrast medium, these rims of cells are contrast enhanced.[3] Osteoid, which defines the telangiectatic osteosarcoma, is often detectable via CT as subtle foci of globular ill-defined matrix mineralization or less often identified via MRI as a region of low signal intensity but is not associated with aneurysmal bone cysts.[3] These advanced imaging techniques can thus help distinguish these 2 radiographically similar lesions (which have vastly different prognoses and treatments) prior to invasive biopsy.[3]

Treatment recommendations for telangiectatic osteosarcoma are similar to those for other subtypes of osteosarcoma, including radical amputation, if possible, and chemotherapy. Telangiectatic osteosarcoma was previously considered fatal with poor response to chemotherapy and was considered to have a less favorable prognosis than other forms of osteosarcoma for people and dogs.[1,2] However, current research suggests that this osteosarcoma subtype may be more sensitive to newer chemotherapy drugs than is conventional osteosarcoma, with a higher response rate to current combination chemotherapeutic regimens and greater 5-year survival rate in humans, compared with findings for osteoblastic or chondroblastic subtypes.[6–8] Detection of specific oncoreceptors and gene expressions that are considered of prognostic value for humans with osteosarcomas have been receiving attention with regard to prognosis for dogs with osteosarcoma. c-Met is a proto-oncogenic receptor that has been implicated in growth, invasion, and metastasis of cancers in humans. A study[9] evaluating c-Met expression in dogs with osteosarcoma revealed that c-Met expression did not correlate with patient outcome; however, there was an association between the presence of c-Met and lymph node metastasis. Vascular endothelial growth factor mediates tumor growth, neovascularization, and metastasis, and a study[10] evaluating expression of that factor in dogs with various spontaneous tumors revealed high levels of vascular endothelial growth factor expression in patients with sarcomas. Gene expression profiling has also been previously evaluated in humans with cancer to help identify prognostic biomarkers. When evaluating patterns of gene expressions in dogs with osteosarcoma, differences were found between dogs that survived > 6 months and those that did not.[11] This may provide prognostic information for clients unsure of whether they want their pet to undergo surgery or chemotherapy at the time of initial diagnosis, which may also be of particular importance for tumors in locations where tumor removal with adequate surgical margins cannot be guaranteed. With the advent of new therapeutic and genetic markers, an accurate diagnosis of this subtype of osteosarcoma becomes more important with regard to treatment recommendations and prognosis.

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