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Pathology in Practice

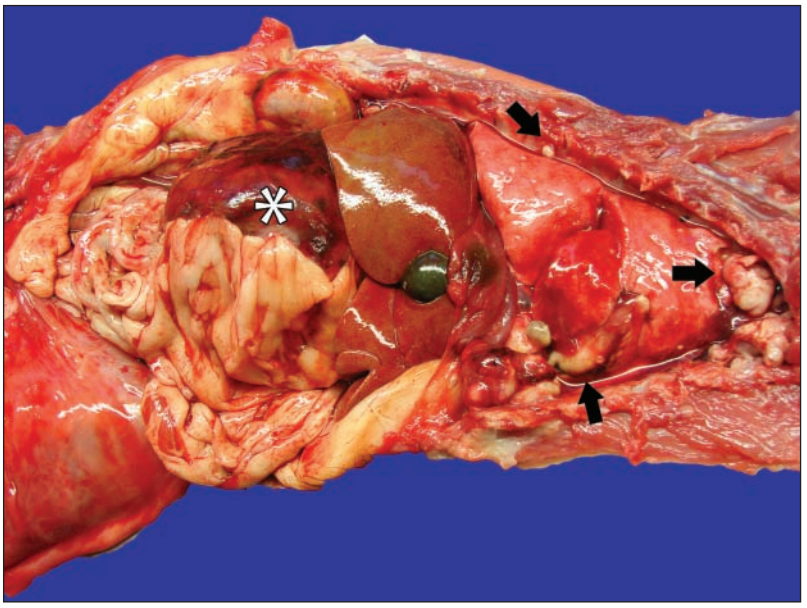

Figure 1—Photograph of the thoracic and abdominal cavities of a domestic shorthair cat that was evaluated because of a rapidly growing, infiltrative, and expansile soft tissue mass in the caudal aspect of the right pelvic limb and was eventually euthanized. Notice that a large mass is effacing the right lateral liver lobe (asterisk), and several smaller nodules (arrows) are present in the thoracic cavity.

History

An 8-year-old 2.8-kg (6.2-lb) spayed female domestic shorthair cat was evaluated at a veterinary hospital because of a rapidly growing, infiltrative, and expansile soft tissue mass in the caudal aspect of the right pelvic limb. The mass was found at the site of a previous rabies vaccination administered 3 years earlier. An incisional biopsy was performed to determine the diagnosis, followed by an excisional biopsy performed 2 weeks later. Both procedures were performed by the referring veterinarian. Specimens obtained during the incisional and excisional biopsies were submitted for histologic examination to the Animal Health Diagnostic Center at Cornell University. Following examination of the incisional biopsy specimen, the patient was evaluated by the oncology service at the Cornell University Hospital for Companion Animals.

Clinical and Gross Findings

Physical examination revealed a focal scar at the previous incision site (surgery performed by the referring veterinarian). No other important abnormalities were detected. Results of a CBC and serum biochemical analysis were within reference ranges. Thoracic radiography revealed the presence of multiple nodules in the thoracic cavity, suggestive of metastatic disease. The owners elected to not pursue additional treatment. Six weeks after the initial consultation at the university hospital, the cat was euthanized because of declining quality of life. A complete necropsy was performed.

On gross examination, the cat was in thin body condition. An area (3.5 × 2 × 1 cm) composed of pale, slightly firm tissue (ie, scar tissue at the previous surgical site) was evident within the caudal aspect of the biceps femoris muscle of the right pelvic limb. Adjacent to this area, there was a 0.6 × 0.7 × 0.3-cm pale tan, soft, nodular mass. A partially encapsulated, 8-cm-diameter, multilobulated, red to tan, soft mass associated with a large hematoma had effaced 95% of the right lateral liver lobe. The omentum was adhered to approximately 30% of the hepatic mass. The remaining hepatic lobes had an enhanced reticular pattern on cut section. A 2-cm-diameter mass of similar consistency that originated from the cortex of the cranial pole of the right kidney and extended along the capsular surface was present; this mass mildly compressed the renal cortex. The capsule of the left kidney was separated from the cortical surface by an extensive hematoma. Another mass (1.3 cm in diameter) of similar appearance and consistency had effaced 90% of the accessory lung lobe. Numerous multifocal to coalescing soft, white to tan nodules ranging from pinpoint to 3 × 2 × 1.3 cm in diameter were present on the pleural surfaces of all lung lobes, the diaphragm, and the pericardium; along the pleural surfaces of the ribs and sternum; and within the thoracic inlet (**Figure 1**).

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

This report was submitted by Anh N. Diep, VMD, DACVP, and Rebekah I. Fleis, DVM, DACVP; from the Department of Biomedical Sciences, College of Veterinary Medicine, Cornell University, Ithaca, NY 14853. Dr. Fleis' present address is Department of Pathobiology, Veterinary Faculty, Utrecht University, 3584 CL Utrecht, The Netherlands.

Address correspondence to Dr. Diep (anhdiep@stanford.edu).

Histopathologic Findings

Sections of the masses and surrounding tissues in the right biceps femoris muscle, liver, right kidney, pleural cavity, lungs, and pericardium were routinely processed and examined microscopically. All of the masses were composed of neoplastic polygonal cells arranged in haphazard sheets. The cells had variably distinct borders and abundant eosinophilic cytoplasm with micro- and macrovesicular clear, round, sharp-bordered, lipid-like droplets (**Figure 2**). Nuclei of the neoplastic cells were round to oval and had vesiculated to finely dispersed chromatin with a single large central nucleolus. The degree of anisokaryosis and extent of anisocytosis were marked, and numerous karyomegalic and occasional multinucleated cells were present. The mitotic index ranged from 2 to 8/hpf. Within the large hepatic mass, there were large areas of liquefactive and coagulative necrosis with hemorrhage. In the remaining liver lobes, there was a moderate degree of centrilobular necrosis and hepatic lipidosis. The cytoplasmic droplets within the neoplastic cells from the right pelvic limb and hepatic masses were confirmed to contain lipid by use of oil red O staining of formalin-fixed, frozen tissue sections.

Morphologic Diagnosis

Widespread, metastatic liposarcoma and moderate, acute, diffuse centrilobular hepatic necrosis.

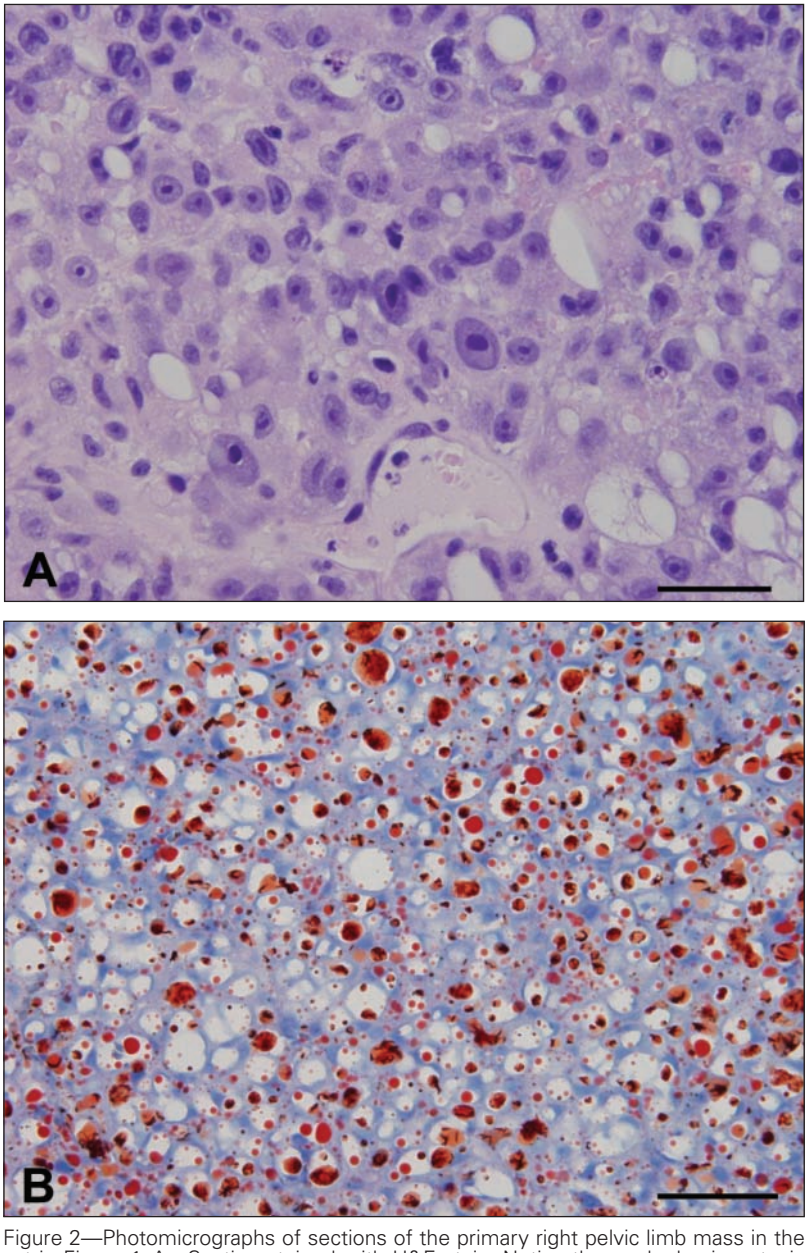

Figure 2—Photomicrographs of sections of the primary right pelvic limb mass in the cat in Figure 1. A—Section stained with H&E stain. Notice the marked anisocytosis and anisokaryosis of the neoplastic cells and the presence of round, cytoplasmic, well-demarcated, clear droplets. Bar = 100 µm. B—Formalin-fixed, frozen tissue section stained with oil red O stain and hematoxylin counterstain. Lipid within the cytoplasmic droplets in the neoplastic cells appears bright red. Bar = 100 µm.

Comments

In the cat of this report, a mass was first noticed at the site of a rabies vaccination administered 3 years earlier. Therefore, the initial differential diagnosis by the referring veterinarian was a vaccine-associated sarcoma, most likely a fibrosarcoma. At necropsy, a pale tan, soft, nodular mass was detected in that region. In general, differential diagnoses for white to pale tan, soft subcutaneous masses in cats should include round cell tumors (lymphoma, histiocytoma, plasmacytoma, and mast cell tumors) and mesenchymal tumors (lipoma, liposarcoma, myxoma, and myxosarcoma). Nonneoplastic lesions such as granulomas or abscesses can often be ruled out on the basis of the gross appearance of the lesion and results of cytologic examination of fine-needle aspirates of the tissue.

In cats, other reported vaccine-associated sarcomas include malignant fibrous histiocytomas, osteosarcomas, chondrosarcomas, and rhabdomyosarcomas.[1,2] Vaccine-associated sarcomas develop at vaccination sites in the neck, thoracic and lumbar regions, flank areas, and limbs.[3] It is thought that most killed virus vaccines contain adjuvants that enhance the immune response, resulting in granulomatous inflammation that progresses to sarcomatous transformation.[4] Development of fibrosarcomas at sites of microchip implantation in a cat and a dog has also been reported.[5,6] Postinjection or vaccination-associated sarcomas have also been identified in dogs and ferrets.[7] Most typically, a firm, white, rapidly growing and infiltrative mass is detected in the subcutis or skeletal muscle; however, in the cat of this report, the noticeable mass in the right pelvic limb was soft. Histologically, vaccine-associated sarcomas have features of high-grade sarcomas (high mitotic index, marked or severe degrees of anisocytosis and anisokaryosis, and extensive necrosis) and the presence

of foamy macrophages with gray-blue pale cytoplasm, presumably containing engulfed adjuvant. Often, there are prominent perivascular lymphoid aggregates at the periphery of the mass.

Interestingly, in the cat of this report, the mass in the right pelvic limb was a liposarcoma, and there was evidence of widespread metastatic disease. Histologic examination of the incisional biopsy specimen from the right pelvic limb mass did not reveal clusters of foamy macrophages suggestive of a vaccine-associated sarcoma; however, there were prominent lymphoid aggregates within the mass and at the periphery. For the cat of this report, it was difficult to definitively establish that the vaccination was the primary cause of the neoplastic growth, although the location of the mass was strongly suggestive of such an association. To our knowledge, there has been 1 other report[8] of a vaccine-associated liposarcoma in a cat that resulted in metastasis to the liver and spleen. In the cat of this report, the original mass was presumed to be that located within the subcutis of the proximal aspect of the right pelvic limb, yet at necropsy, the largest detected mass was within the liver. However, the mass in the limb had been excised prior to necropsy and may have been larger if it had remained in situ. Therefore, it was impossible to determine whether the mass in the limb was a metastatic lesion or the primary neoplasm.

Liposarcomas are rare malignant tumors that are derived of adipocytes and lipoblasts. In animals, liposarcomas can be subclassified as well-differentiated, anaplastic-pleomorphic, and myxoid variants. The myxoid variant is composed of scattered neoplastic lipocytes and lipoblasts loosely arranged in an Alcian blue–positive mucoid stroma and often has to be differentiated from a myxosarcoma. Prognosis for people with liposarcomas is dependent on the tumor subclassification, and anaplastic-pleomorphic variants are the most malignant. In the cat of this report, the liposarcoma was an anaplastic-pleomorphic variant, as determined on the basis of the highly variable morphology and multinucleation of the neoplastic cells. The gross appearance of liposarcomas depends on the amount of lipid produced.[3] In the cat of this report, the masses were uniformly soft and contained variable amounts of lipid. Other liposarcomas can produce little lipid and be firm, gray-white infiltrative masses, which have to be differentiated from other types of sarcomas.

Results of cytologic examination of the limb mass were not available for the cat of this report; however, cytologic examination of fine-needle aspirates of solid tumors may be useful for evaluating the morphologic features of the neoplastic cells. Oil red O stain, which is commonly used to detect lipid in frozen tissue, may be used to stain air-dried fine-needle aspirate specimens of liposarcomas.[9] The presence of lipid within the cytoplasm of the cells allows a clinician to consider liposarcoma as a differential diagnosis. Most veterinary practices do not have oil red O stain or hematoxylin counterstains readily available to perform this diagnostic test. In addition, there are other neoplasms that can contain lipid, such as lipid-rich rhabdomyosarcomas or lipid-rich mammary carcinomas. Therefore, histologic examination of a mass is essential for diagnosis. Lipoblasts express S-100 antigen; therefore, results of immunolabeling of neoplastic cells for the presence of S-100 antigen can be helpful but are generally not needed for definitive diagnosis. The ultrastructural appearance of liposarcomas in people and dogs has been described.[10,11] Ultrastructurally, neoplastic lipocytes contain strongly osmiophilic substances and larger droplets appear to be membrane bound.

As with other types of soft tissue sarcomas, treatment of liposarcomas typically involves wide surgical resection with evaluation of the excised tissue margins to ensure complete excision. Radiation therapy may induce remission of incompletely excised liposarcomas in small animals.[12] In veterinary species, prognosis is determined by grade and histologic subtype of the liposarcoma. If the size and location of the tumor preclude wide excision, then prognosis is guarded. Widespread metastatic disease may also compromise organ function when the masses are of substantial size or compress vital structures. In the cat of this report, there were masses within the right kidney and lungs which may have altered renal and pulmonary functions. Interestingly, moderate acute diffuse centrilobular hepatic necrosis was detected via histologic examination of sections of several liver lobes. Acute centrilobular necrosis can be due to anemia, hypoperfusion resulting in hypoxic injury, or indirect-acting toxins. Toxin-induced hepatic necrosis is often accompanied by biliary hyperplasia,[13] which was not evident in the cat of this report. Results of a CBC were within reference ranges, and anemia was ruled out. Therefore, the necrosis was most likely due to hypoperfusion and hypoxia.

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