



Pathology in Practice

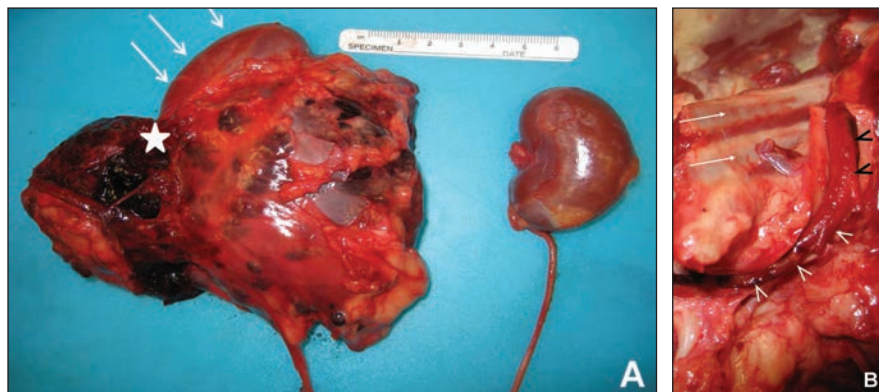


Figure 1—Photographs of a perirenal mass (A) and opened left subclavian and brachial arteries (B) in an 8-year-old spayed female American Cocker Spaniel that was evaluated because of a 6-day history of non-weight-bearing lameness in the left thoracic limb. The photographs were obtained during necropsy. A mass (white star) is attached to the caudal pole of the right kidney (white arrows). The perirenal mass is larger than the kidney itself, dark red to black, and bilobed. In panel B, notice the thrombus that is present in the dissected and opened left subclavian artery (black arrowheads) and extends down into the brachial artery (white arrowheads). The ribs are denoted with white arrows.

History

An 8-year-old spayed female American Cocker Spaniel was evaluated because of a 6-day history of non-weight-bearing lameness in the left thoracic limb.

Clinical and Gross Findings

On physical examination, the dog was dragging its left thoracic limb with knuckling at the carpus. The limb appeared painful, was cold and swollen, and had cyanotic nail beds and absent pulses. The dog's abdomen was tense during abdominal palpation, and cranial abdominal organomegaly was detected.

Hematologic abnormalities included mild normocytic, normochromic minimally regenerative anemia (Hct, 30%; reference range, 39% to 55%) and moderate to marked thrombocytopenia (62,000 platelets/ μ L; reference range, 180,000 to 525,000 platelets/ μ L). Biochemical abnormalities included markedly high aspartate aminotransferase (903 U/L; reference range, 9 to 54 U/L) and creatine kinase (21,978 U/L; reference range, 22 to 422 U/L) activities. The evident venous blood glucose (left thoracic limb, 61 mg/dL; right thoracic limb, 103 mg/dL) and lactate (left thoracic limb, 6 mmol/L; right thoracic limb, 1.7 mmol/L) concentration differentials between thoracic limbs were consistent with arterial embolism. Results of kaolin-activated, citrated whole blood thromboelastography were consistent with a hypocoagulable state. Results of a saline (0.9% NaCl) solu-

tion slide agglutination test were positive, consistent with immune-mediated hemolytic anemia.

Thoracic radiography and CT did not reveal pulmonary metastatic lesions. Following IV injection of iohexol, contrast medium was absent from the left subclavian artery and its branches in CT images. The muscles of the left thoracic limb were thickened, hypoattenuating, and non-contrast enhancing. Abdominal ultrasonography revealed a large, heterogeneous mass in the right dorsal aspect of the abdomen, which was suspected to be peritoneal in location and mesenteric or omental in origin. Small hypoechoic nodules were scattered throughout the mesentery. Exploratory celiotomy revealed a nonresectable, perirenal mass and suspected multifocal metastatic lesions (Figure 1). Euthanasia was elected.

The necropsy was performed after a postmortem interval of 19 hours. Mild subcutaneous edema of the left antebrachium and brisket region was evident. The neck, the right thoracic and pelvic limbs, and the left pelvic limb were in rigor mortis, but the left thoracic limb was completely flaccid. A 10-cm-long, firm, dark pink to red-brown thrombus was completely occluding the left subclavian artery beginning 2 cm proximal to its intercostal segment and extending distally into the left brachial artery (Figure 1). The musculature of the left brachium and antebrachium and scalenus muscle were diffusely pale, soft, and swollen (edematous). A dark red to black, bilobed, ovoid to spherical mass was attached to the caudal pole of the right kidney and invaded extensively into the perirenal adipose tissue. The lobes of the mass measured roughly $8.5 \times 5.5 \times 5.5$ cm and $9.5 \times 9.5 \times 7.5$ cm. On cut surface, the mass was hemorrhagic, with multiple variable-sized cavities, and oozed blood. Numerous dark red to black masses (1 to 10 mm in diameter) were disseminated randomly throughout the mesentery.

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

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Histopathologic Findings

The lumens of the left brachial and subclavian artery were occluded by a moderately to well-organized thrombus, which was adhered to the vessel walls. The presence of lines of Zahn in the thrombus—striations created by pale eosinophilic and proteinaceous material alternating between bright eosinophilic and hemorrhagic material—were indicative of its antemortem development (Figure 2). Additionally, there was evidence of partial recanalization of the thrombus with regular flattened endothelial cells lining the vascular channel.

A loosely cellular, poorly circumscribed, nodular mass expanded from the right renal capsular surface. The mass was composed of moderately cellular neoplastic endothelial cells forming irregularly sized blood-filled vascular channels, often wrapping around

collagen bundles (Figure 2). The cells had variably distinct cell borders with a moderate amount of eosinophilic fibrillar cytoplasm. The nuclei were oval to elongate, with coarsely clumped chromatin and 1 to 2 nucleoli. There were 3 to 5 mitotic figures/400X field and marked anisokaryosis and anisocytosis. Large areas of necrosis, hemorrhage, few fibrin thrombi, and scattered aggregates of mixed inflammatory cells were randomly distributed throughout the mass. The mesentery contained multiple nodules composed of neoplastic cells morphologically similar to those in the renal mass.

Morphologic Diagnosis and Case Summary

Morphologic diagnosis: arteriothromboembolism (ATE) of the left subclavian artery with extension into the left brachial artery and hemangiosarcoma of the

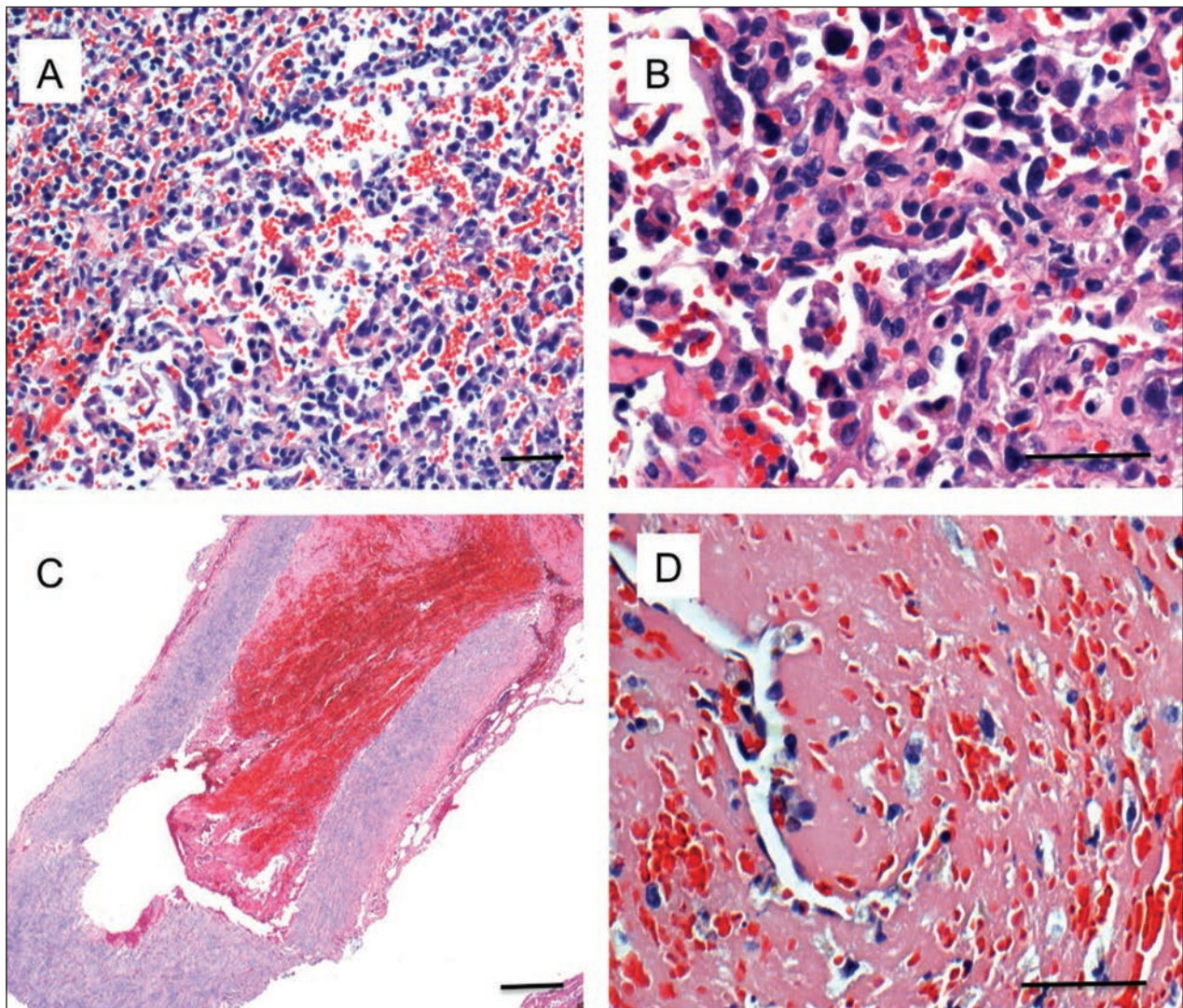


Figure 2—Photomicrographs of sections of the perirenal mass (A and B) and thrombus (C and D) in the dog in Figure 1. A—In the mass, moderately cellular neoplastic endothelial cells have formed irregularly sized and shaped blood-filled vascular channels. Variable amounts of collagen support the neoplastic cells. H&E stain; bar = 50 μ m. B—The cells have variably distinct borders, eosinophilic fibrillar cytoplasm, oval to elongate nuclei with coarsely clumped chromatin, and 1 to 2 distinct nucleoli. Notice the marked anisocytosis and anisokaryosis. H&E stain; bar = 50 μ m. C—The subclavian artery is cut at an oblique angle and close to parallel with the long axis of the vessel. An eosinophilic and hemorrhagic mass (thrombus) is adhered to and contiguous with the vascular endothelium. H&E stain; bar = 500 μ m. D—A region of recanalization of the thrombus is visible extending from the top left corner of the image to the center of the image. Notice the regularly spaced, flattened endothelial cells that line the vascular channel. H&E stain; bar = 50 μ m.

right renal capsule with multifocal metastasis to the mesentery.

Case summary: left subclavian arterial thrombosis and perirenal hemangiosarcoma in a dog.

Comments

In the dog of the present report, the primary disease process was hemangiosarcoma. The left subclavian ATE was a suspected complication of a hypercoagulable state secondary to systemic neoplasia.

Hemangiosarcoma is a common, malignant neoplasm of the vascular endothelium. Hemangiosarcoma most commonly affects the spleen in dogs (28% to 50% of cases); less common sites include the right atrium (3% to 50%) and the skin and subcutis (13%). The primary tumor in the dog of this report had a retroperitoneal and renal capsular origin with metastasis to the mesentery. This type of noncutaneous hemangiosarcoma is associated with high morbidity rate and a grave prognosis.¹

Arteriothromboembolism is a relatively common clinical disease process in cats and people but is uncommonly reported for dogs. In veterinary medicine, ATE occurs most commonly in cats with hypertrophic cardiomyopathy, usually in the aorta at the level of the external iliac arteries (saddle thrombus). Less commonly, ATE in cats may affect a single thoracic limb or all 4 limbs.² Approximately 20% of cases of ATE among humans are a result of occlusion of the subclavian artery or its descendant vessels.³

In dogs, a diagnosis of ATE is not common, and the etiopathogenesis of the condition remains poorly understood. In general, thrombosis occurs as a result of diseases associated with a hypercoagulable state, compromised vascular endothelial integrity, or blood stasis. In a necropsy-based study⁴ of 36 dogs with aortic, iliac, or femoral ATE, 18 dogs had primary thrombi, which were associated with severe renal disease (n = 9), thyroid disease (4), aortic intimal fibrosis (4), and iatrogenic hyperadrenocorticism (1). In addition, 11 dogs had embolic thrombi (neoplastic emboli and emboli from a patent ductus arteriosus correction site), and 7 dogs had thrombi of cardiac origin (valvular endocarditis or valvular endocardiosis with or without ruptured chordae tendineae).⁴ One of the dogs with neoplastic emboli had perirenal hemangiosarcoma,⁴ similar to the dog of this report. In addition to neoplastic and endocrine disease, infectious disease, especially blastomycosis and *Spirocerca lupi* infections, can predispose dogs to ATE.^{5,6} In the veterinary medical literature, there is 1 report⁷ of a dog with dilated cardiomyopathy and a subclavian artery thrombus and aneurysm.

In the case described in the present report, the ATE was not a tumor embolus, but rather was suspected to be secondary to the hypercoagulable state that often accompanies disseminated neoplasia. Interestingly, at the time of diagnosis, the dog was in a hypocoagulable state, likely a result of consumptive coagulopathy following hypercoagulability.

The lack of rigor mortis in the affected limb of the dog of this report deserves mention. In living cells, ATP binds the heads of the myosin heavy chains in the

skeletal myocytes, reducing myosin's affinity for actin, breaking the cross bridges between the 2 proteins and relaxing the muscle. During rigor mortis, there is a lack of ATP, which leaves the cross bridges intact and the muscle set in its rigid state.⁸ The delay in onset of rigor mortis is variable and determined by factors such as environmental temperature, glycogen stores, and pH of muscle tissues at death.⁹ The cessation of rigor mortis occurs with the advance of tissue autolysis that degrades actin and myosin. In the dog of the present report, the affected limb was not in rigor mortis at 19 hours after death; either rigor mortis had occurred but had been terminated by premature autolysis caused by the lack of blood flow to the tissues or rigor mortis had never occurred because of antemortem autolysis secondary to the ATE.

Treatment of noncutaneous hemangiosarcoma ideally involves surgical resection of the primary tumor (which was not possible in the dog of this report) and follow-up chemotherapy.¹ Animals with ATE are usually managed supportively to allow time for potential recanalization or development of collateral circulation. Thrombolysis or thrombectomy can be considered; however, reperfusion injury can be deleterious. Additionally, the risk of further emboli is thought to be minimized by treatment with a combination of anticoagulants (unfractionated or low-molecular-weight heparin) and antiplatelet drugs (clopidogrel or acetylsalicylic acid).¹⁰

Arteriothromboembolism should be considered as a differential diagnosis in a dog with sudden onset lameness of 1 limb, especially with signs of pain, paresis, and lack of pulses in that limb and if the limb is cold to the touch. Identification of ATE in dogs should then prompt a search for the underlying disease that contributed to hypercoagulability.

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