

Aortic thrombosis and acute kidney injury due to atherosclerosis in a dog

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OBJECTIVE

Atherosclerosis is a chronic lipid-driven inflammatory disease of the arterial wall. Due to its cardiovascular ischemic complications, it is one of the most common causes of death in people. However, atherosclerosis is seldomly reported in dogs.

ANIMAL

A 10-year-old male mixed-breed dog.

CLINICAL PRESENTATION, PROGRESSION, AND PROCEDURES

Severe acute kidney injury associated with thrombosis of the abdominal aorta.

TREATMENT AND OUTCOME

Treatment included renal replacement therapy, antithrombotic therapy, and supportive care. However, the dog developed neurological and respiratory complications and was euthanized due to worsening kidney function and lack of improvement of the thrombosis. Postmortem examination confirmed the presence of aortic thromboembolism and renal infarcts. Histology revealed severe chronic-active atherosclerosis of the distal aorta and renal arteries.

CLINICAL RELEVANCE

Aortic thrombosis is uncommon in dogs, and it is often associated with underlying conditions such as protein-losing nephropathy, endocrine disorders, cardiac disease, or hypercoagulability. In this case, no specific underlying cause was identified and atherosclerosis was considered the primary cause of the thrombosis.

Keywords: blood clot, atheroma, hypothyroidism, hypercholesterolemia, renal replacement therapy

History

A 10-year-old 43.5-kg neutered male Shepherd-type dog with a body condition score of 4/9 was referred due to 48 hours of acute anuric kidney injury with aortic thrombosis (Ath). The dog had had an episode of weakness of the hind limbs and abdominal pain 5 months prior to this episode that was successfully treated with a 10-day course of NSAIDs. Vaccinations were not up-to-date. The dog was fed a mixture of commercial wet and dry food for adult dogs. The owners ruled out access to nephrotoxins. On examination, the patient was ambulatory and lethargic and bilateral femoral pulses were absent. Cardiopulmonary auscultation revealed no murmur,

heart rate was 70 beats/min, and the dog was panting. Orthopedic and neurological examinations were unremarkable. Complete blood count revealed normocytic, normochromic, nonregenerative anemia (Hct, 34%; reference interval [RI], 37.3% to 61.7%), leukocytosis ($28.15 \times 10^3/\mu\text{L}$; RI, 5.05×10^3 to $16.76 \times 10^3/\mu\text{L}$) with neutrophilia ($24.44 \times 10^3/\mu\text{L}$; RI, 2.95×10^3 to $11.64 \times 10^3/\mu\text{L}$), and monocytosis ($1.61 \times 10^3/\mu\text{L}$; RI, 0.16×10^3 to $1.12 \times 10^3/\mu\text{L}$). Serum biochemistry revealed elevations of creatinine (11 mg/dL; RI, 0.5 to 1.8 mg/dL), urea (79 mg/dL; RI, 7 to 27 mg/dL), phosphorus (7.2 mg/dL; RI, 2.5 to 6.8 mg/dL), and total bilirubin (1.3 mg/dL; RI, 0 to 0.9 mg/dL). Cholesterol and triglycerides were in range.

Diagnostic Findings and Interpretation

The SNAP 4Dx Test (Idexx Laboratories Inc) was negative for *Dirofilaria immitis*, *Anaplasma* spp, *Ehrlichia* spp, and *Borrelia burgdorferi*. A microscopic

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agglutination test for the 8 most common serovars of *Leptospira* spp and *Leishmania infantum* serology was negative. Aerobic and anaerobic blood and urine cultures were negative. Urine density was 1.012, and there was moderate glucosuria. The urine protein creatinine ratio was > 9.05 (RI, < 0.5). Noninvasive blood pressure was within normal limits. Electrocardiogram revealed premature ventricular complexes. Total T4 was $0.6 \mu\text{g/dL}$ (RI, 1.0 to $4.0 \mu\text{g/dL}$), and thyroid stimulating hormone was 0.25 ng/mL (RI, 0.03 to 0.6 ng/mL). Prothrombin time was 18 seconds (RI, 11 to 17 seconds) and activated partial thromboplastin time 130 seconds (RI, 72 to 111 seconds). Thromboelastography showed a hypercoagulable state. Computed tomography was performed without IV contrast and revealed mineralization of the aortic lumen at the level of the bifurcation compatible with chronic aortic thromboembolism. Spondylosis deformans of T12-T13 and T13-L1 as well as multifocal disc protrusions and signs compatible with advanced degenerative coxofemoral disease were detected. Ultrasonography of the affected arteries showed hyperechoic material in both the aorta (occupying approx 95% of the aortic lumen) and in the renal artery.

Treatment and Outcome

The dog received 5 cycles of intermittent venovenous hemodialysis with citrate anticoagulation through a double-lumen jugular catheter. Antithrombotic therapy consisted of clopidogrel 2 mg/kg every 12 hours PO and rivaroxaban 2 mg/kg/d PO. Multiple-electrode platelet aggregometry and prothrom-

bin time were performed to optimize antithrombotic therapy. Supportive care included antiemetics (maropitant, 1 mg/kg , IV, q 24 h; metoclopramide, 1 mg/kg in 24 h, IV; and ondansetron, 0.1 mg/kg , IV, q 8 h), gastroprotectants (omeprazole, 0.7 mg/kg , IV, q 12 h), antibiotics (amoxicillin-clavulanic acid, 22 mg/kg , IV, q 6 h; marbofloxacin, 4 mg/kg , IV, q 24 h; and subsequently escalated to ceftazidime, 30 mg/kg , IV, q 6 h), oxygen therapy, and parenteral nutrition. The dog was hospitalized for 8 days but developed complications including seizures and hypoxemia. Due to worsening azotemia and no improvement of the thrombosis, the dog was euthanized.

Necropsy was performed, and tissue samples from lung, spleen, liver, heart, pancreas, thyroid, parathyroid, intestine, kidney, brain, renal arteries, and abdominal aorta were collected and preserved in 10% formalin. Tissues were embedded in paraffin, sectioned at $5 \mu\text{m}$, and stained with H&E and Masson trichrome stains. Postmortem examination revealed a severe dilatation of the abdominal aorta and renal arteries and arterial thrombus up to 15 cm long, strongly adhered to the lumen surface of the abdominal aorta and extending through renal, mesenteric, and iliac arteries, with detachment and associated embolism occluding the arterial lumen. The intima showed a thickened wall with coalescing, strongly adhered, firm, large, and yellow-gray plaques and prominent subintimal streaks protruding into the vascular lumen, macroscopically compatible with atheromas. Grossly, both kidneys presented multifocal pale-white to tan and wedge-shaped areas of cortical necrosis macroscopically consistent with acute infarcts (**Figure 1**). No other relevant macro-

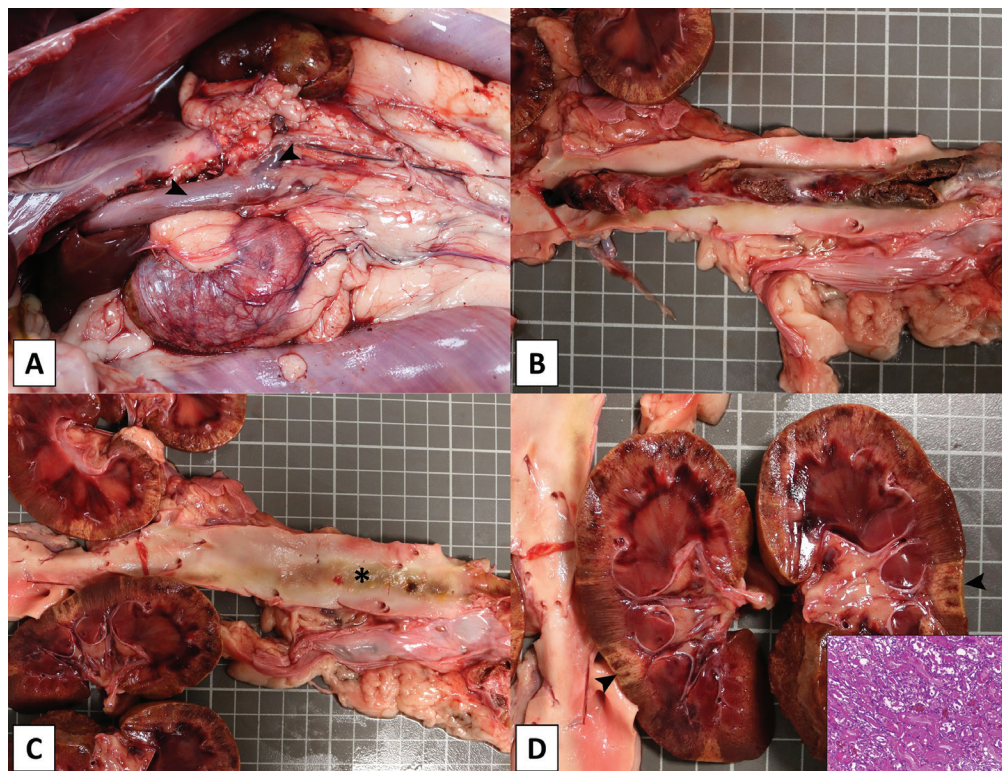


Figure 1—Abdominal aorta and kidneys. A—Note the severe dilatation of the abdominal aorta and renal arteries (arrowheads). B—Abdominal aorta containing a large (up to 15-cm) mural thrombus extending through the lumen to the iliac arteries. C—Grossly, the affected arterial wall is thickened and yellow and contains roughened yellow intimal plaques or atheromas (asterisk). D—Detail of the right kidney with acute cortical infarcts (arrowheads). Inset—Coagulation necrosis of tubular epithelial cells. H&E stain; 400X.

scopic lesions were observed during necropsy. Histopathological examination of the abdominal aorta revealed the endothelium surface covered by several layers of platelets, fibrin, and erythrocytes (arterial thrombus). The tunica intima and media showed severe fibrosis with increased thickness, disruption of elastic layers, and severe vascular luminal com-

promise (**Figures 2 and 3**). Both blood vessel layers were infiltrated by numerous linear, large, and clear acicular clefts (morphologically compatible with cholesterol) accompanied by a scant extracellular lipid matrix and surrounded by extensive areas of fibrosis, intralesional hemorrhage, dystrophic calcification, and moderate inflammation composed by

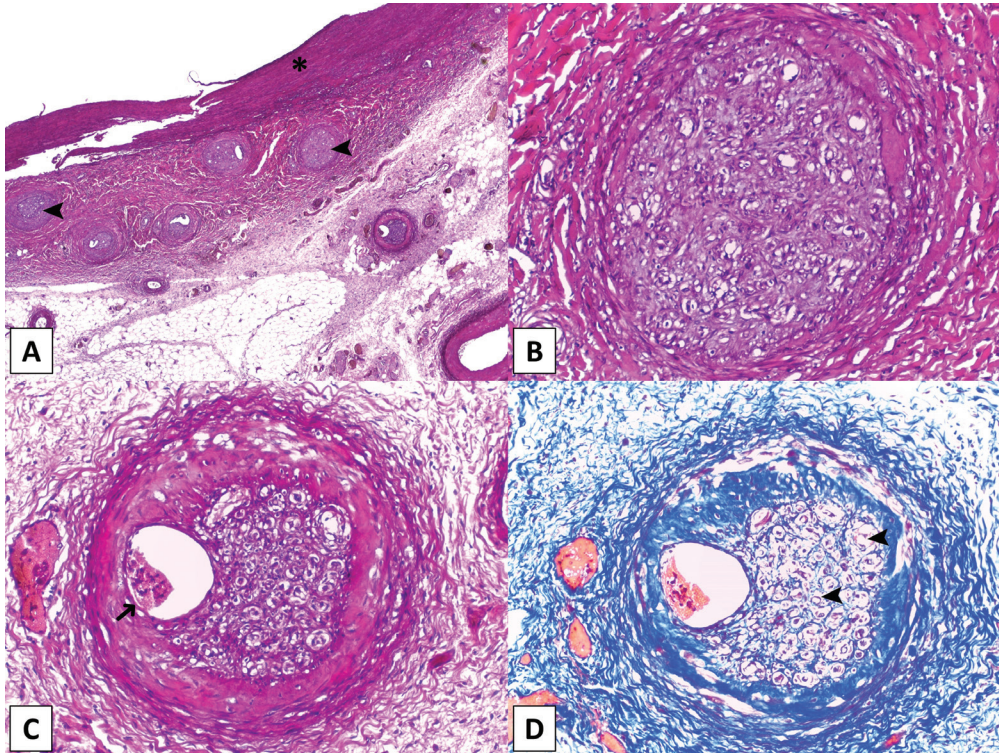


Figure 2—Arterial thrombosis, complete transversal section of the abdominal aorta. A—Severe intimal and medial thickening (asterisk) and occlusive thrombosis of the vasa vasorum (arrowheads). H&E stain; 40X. B—Higher magnification of panel A. Occlusive mural thrombus and recanalization of the arterial vasa vasorum. H&E stain; 200X. C—Note the vascular channel laterally to the thrombus (arrow). H&E stain; 200X. D—Numerous endothelial-lined vascular channels through the fibrotic area or thrombus recanalization (arrowheads). Masson trichrome stain; 200X.

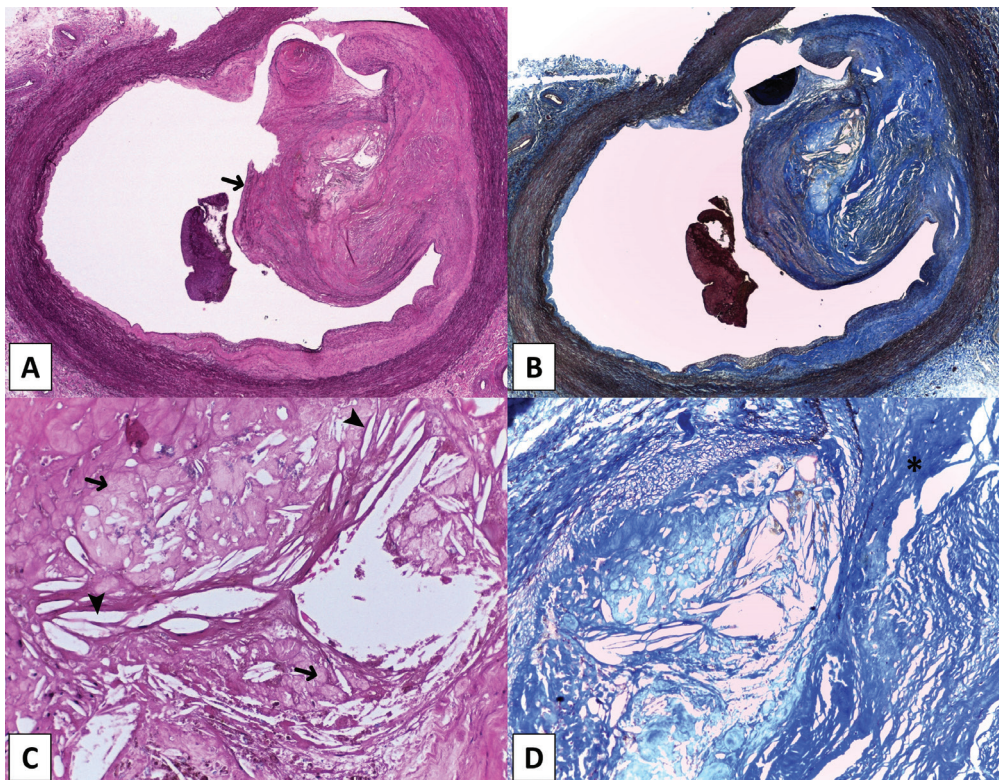


Figure 3—Abdominal aorta, atherosclerosis. A—Severe arterial thickening due to atherosclerosis associated with luminal narrowing (arrow). H&E stain; 40X. B—Marked disruption of the elastic layers and severe fibrosis and necrosis (arrow). Masson trichrome stain; 40X. C—Higher magnification of panel B. Note the accumulation of lipid-filled macrophages or foam cells (arrows) throughout the thickened intima and media accompanied by an increase in extracellular lipid matrix and cholesterol clefts (arrowheads). H&E stain; 200X. D—Numerous lipid-laden macrophages, cholesterol clefts, and fibrous tissue (asterisk) infiltrating the vessel wall. Masson trichrome stain; 200X.

numerous macrophages with severe cytoplasmic vacuolization (“foam cells”) extending throughout the thickened tunica intima and media. Multifocally, the vasa vasorum of the adventitial tunica also presented occlusive thrombosis, narrowing of the vessel lumen, epithelialization with invasion of fibroblasts and new endothelial-lined blood channels consistent with severe recanalization and vascular repair. No histologic evidence of recanalization or vascular repair was observed in renal arteries, and this could be suggestive of an acute renal thromboembolism related with clinical and macroscopic findings. The microscopic lesions observed in the abdominal aorta were morphologically consistent with chronic atherosclerosis, and this was considered the most probable cause of primary endothelial injury related to the thromboembolic process extending through the renal, mesenteric, and iliac arteries. No similar lesions were observed in other tissues during microscopic examination. Renal microscopic lesions were mainly coagulation necrosis of the tubular epithelial cells surrounded by mild interstitial fibrosis, scant lymphocytes and plasma cells, and mild dystrophic mineralization of the interstitium, basement membranes, and tubules, consistent with an acute necrotic process (infarct) involving both kidneys. Scant clusters of fine black deposits of carbon pigment phagocytosed by macrophages and located in the peribronchial tissue were found (incidental anthracosis), and no histologic lesions compatible with aspiration pneumonia were microscopically observed.

Comments

Unlike cats, in which > 90% of cases are attributable to cardiac disease, dogs tend to develop Ath in relation to endocrine disorders, protein-losing nephropathy, steroid administration, neoplasia, and other concurrent conditions associated with hypercoagulability. However, the number of cases in which no associated causes were identified varies between 23% and 50%.¹

This dog exhibited prior hind limb paresis, which could potentially be linked to chronic Ath, as it commonly manifests with neurological impairments, pain, absent femoral pulses bilaterally, and bilateral abdominal locomotor abnormalities.¹ However, this lameness could have been caused by advanced degenerative coxofemoral disease, given the positive response to NSAIDs.

One of the main disorders associated with hypercoagulability is protein-losing nephropathy.² In this specific case, the dog exhibited severe proteinuria. Further examination of renal histopathology ruled out glomerulopathy, amyloidosis, or neoplasia as the primary cause. The most likely explanation for the proteinuria in this case was prerenal causes and direct renal damage due to thromboembolic and ischemic processes.³

Atherosclerosis is a vascular disease characterized by intimal lesions called atheromas or fibrofatty plaque. Atheromas are well formed with an acellular necrotic core containing free cholesterol and covered by a thick fibrous cap consisting of smooth muscle cells

in a proteoglycan-collagen matrix.⁴ The progression of this vascular disease involves endothelial dysfunction, substantial lipid buildup in the vessel walls (media) that eventually results in luminal narrowing, heightened innate and adaptive immune responses, proliferation of smooth muscle cells in the blood vessels, and restructuring of the extracellular matrix. These processes culminate in the development of an atherosclerotic plaque. The interaction between the exposed components of the plaque, receptors on platelets, and coagulation factors can lead to platelet activation, aggregation, and the formation of a thrombus.⁵

Hyperlipidemia has been associated with atherosclerotic plaques in dogs, as well as hypothyroidism, diabetes mellitus, and idiopathic hypereosinophilic syndrome. Atherosclerosis has been induced in dogs with normal serum thyroid hormone concentration by feeding a high-fat diet resulting in hypercholesterolemia.⁵

In this case report, it is improbable that the dog had hypothyroidism, as there were neither clinical signs typically associated with this condition nor evidence of hypercholesterolemia, which is commonly observed in 75% of hypothyroid dogs. If the clinical signs do not align with hypothyroidism, it is also possible that this presentation could be attributed to the natural process of aging, normal breed variations, or nonthyroidal illness. Furthermore, no evidence of elevated levels of triglycerides or cholesterol were observed.

In conclusion, this case report highlights the rare occurrence of Ath in a dog and emphasizes the importance of considering atherosclerosis as a potential underlying cause.

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Disclosures

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