chapter 8

Arterial Thromboembolism (ATE)

DEFINITION/OVERVIEW

- ATE results from a thrombus or blood clot that is dislodged within the aorta, causing severe ischemia to the tissues served by that segment of aorta. It is one of the most devastating complications associated with myocardial diseases in cats.

ETIOLOGY/PATHOPHYSIOLOGY

- ATE is most commonly associated with myocardial disease in cats, including hypertrophic, restrictive, and dilated cardiomyopathy.
- Although the exact etiology of ATE has not been determined, it is theorized that abnormal blood flow (stasis) and a hypercoagulable state contribute to the formation of the thrombus within the left atrium. The blood clot is then embolized distally to the aorta.
- The most common site of embolization is the caudal aortic trifurcation causing ischemic injury to both hind legs (Figure 8.1).
- Other less common sites include the front leg (Figure 8.2), kidneys, gastrointestinal tract, or cerebrum.
- Although ATE is a well-recognized complication of myocardial disease in cats, the exact prevalence of ATE is not known in the general population of cats. In one study of cats with hypertrophic cardiomyopathy, approximately 17 percent presented with signs of ATE.
- Although >95 percent of ATE in cats are associated with advanced feline heart disease, another associated condition is neoplasia, typically pulmonary carcinoma.
- ATE rarely occurs in dogs. ATE in dogs typically is associated with neoplasia, sepsis, Cushing's disease, protein-losing nephropathy, or other hypercoagulable states. Severe heart disease is not often associated with ATE in the dog.

Systems Affected

- Cardiovascular—the majority of affected cats have advanced heart disease and experience left-sided heart failure.
- Nervous/musculoskeletal—severe ischemia to the muscles and nerves served by the segment of occluded aorta causes variable pain and paresis. Gait abnormalities or paralysis results in the leg or legs involved.

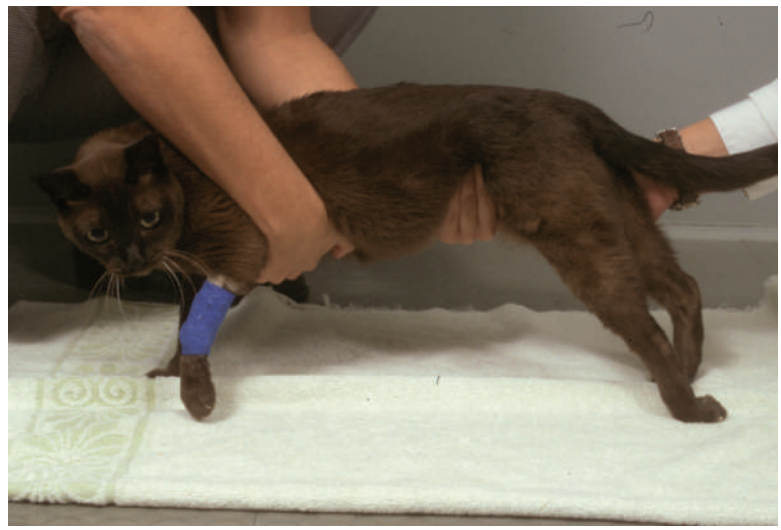

Figure 8.1 Clot in the hind limb of a cat after arterial thromboembolism. Note the extensor rigidity of the affected limb.

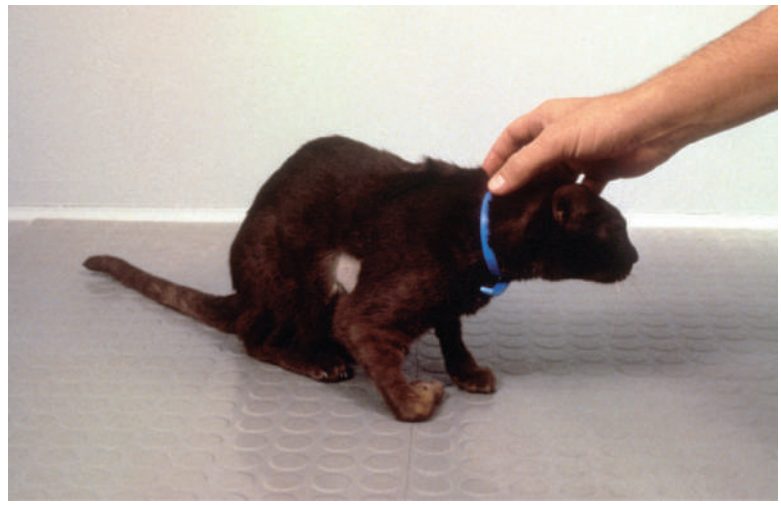

Figure 8.2 Clot in the forelimb of a cat with arterial thromboembolism. Note the conscious proprioceptive deficits.

SIGNALMENT/HISTORY

- Typically middle-aged to older male mixed breed cat.
- Median age is typically 7 to 10 years (Range 1–20 years).
- Males are more commonly affected than females (2:1).
- The most common breed affected is the mixed breed cat. However, certain breeds have been overrepresented, such as Ragdolls, typically mirroring breeds that are prone to cardiomyopathies.

Risk Factors/Causes

- Although clear risk factors have not been defined, it is theorized that an enlarged left atrium or spontaneous echo contrast of the red blood cells or "smoke" observed on an echocardiographic examination may be risk factors.

Historical Findings

- Acute onset paralysis/paresis and pain are the most common owner complaints.
- Lameness or other gait abnormality may be seen.
- Tachypnea or respiratory distress is common.
- Vocalization and anxiety are common.

CLINICAL FEATURES

- Usually paraparesis or paralysis of the rear legs. Typically both rear legs are affected equally but occasionally one leg is worse than the other. Less commonly, monoparesis of a front leg.
- Pain upon palpation of the affected legs. Gastrocnemius muscle often becomes firm several hours after embolization.
- Absent or diminished femoral pulses
- Cyanotic or pale nail beds and footpads (Figure 8.3)
- Affected limbs will be cooler than unaffected limbs upon palpation.

Figure 8.3 Differential cyanosis. Note the cyanotic discoloration of the footpads in the limb affected by the clot.

- Cardiac murmur or gallop sound may or may not be present. Despite the typical presence of severe heart disease in cats, often times a murmur or gallop may not be heard.
- Tachypnea or respiratory distress, sometimes with open mouth breathing, is often present either due to pain associated with the ischemic leg injury or due to concurrent congestive heart failure.
- Cardiac dysrhythmias may also be present. Dysrhythmias are more common during treatment and are often associated with reperfusion injury and hyperkalemia.
- Hypothermia is common in cats with ATE and is often associated with poor systemic perfusion and worse prognosis.

DIFFERENTIAL DIAGNOSIS

- Hind limb paresis secondary to other causes such as spinal neoplasia, trauma, myelitis, fibrocartilaginous infarction, or intervertebral disk protrusion.

DIAGNOSTICS

- Typically, the diagnosis of ATE is made by physical exam alone. Many cats are in distress and empiric treatment is often initiated *prior to* diagnostic testing. In the cat, further diagnostic evaluation is helpful to better evaluate the severity and nature of the associated cardiac disease as well as systemic effects of the ATE. This information may be helpful for prognosis and treatment.
- In the dog, diagnostic evaluation is helpful to better understand the associated disease causing the hypercoagulable state.

Complete Blood Count/Biochemistry Panel/Urinalysis

Common abnormalities include:

- Elevated CPK, AST, ALT
- Stress hyperglycemia
- Azotemia with elevated BUN and creatinine as a result of possible low effective circulating volume or renal emboli
- Electrolyte abnormalities are common (i.e., hyponatremia, hyperkalemia, hypocalcemia and hyperphosphatemia) and are likely associated with poor renal perfusion and reperfusion injury.
- CBC and urinalysis changes are nonspecific.
- In the dog, a protein-to-creatinine ratio is advised if proteinuria is identified.

Other Laboratory Tests

- Routine coagulation profile typically does not reveal significant abnormalities.
- In the dog, D-dimers are typically markedly elevated.

- Baseline coagulation profile may be helpful to titrate heparin and possibly warfarin dosages.
- Thyroid hormone should be measured in cats over 7 years of age.

Thoracic Radiography

- Cardiomegaly is common and radiographic signs of congestive heart failure (i.e., pulmonary edema and/or pleural effusion) is seen in approximately 50–66 percent of cats.
- The presence of a pulmonary mass in the absence of heart disease in a cat with ATE is concerning for pulmonary carcinoma associated embolus.

Echocardiography

- The majority of cats will have hypertrophic cardiomyopathy characterized by left ventricular hypertrophy, nondilated left ventricular lumen, and enlarged left atrium.
- Other types of heart disease are also possible such as unclassified, restrictive, or dilated cardiomyopathy and thyrotoxic heart disease.
- Regardless of the type of myocardial disease present, the majority (>50%) have severe left atrial enlargement, (i.e., a left atrial to aortic ratio of ≥2.0).
- Occasionally, a left atrial thrombus or spontaneous echo contrast of the red blood cells (smoke) may be seen (Figure 8.4).

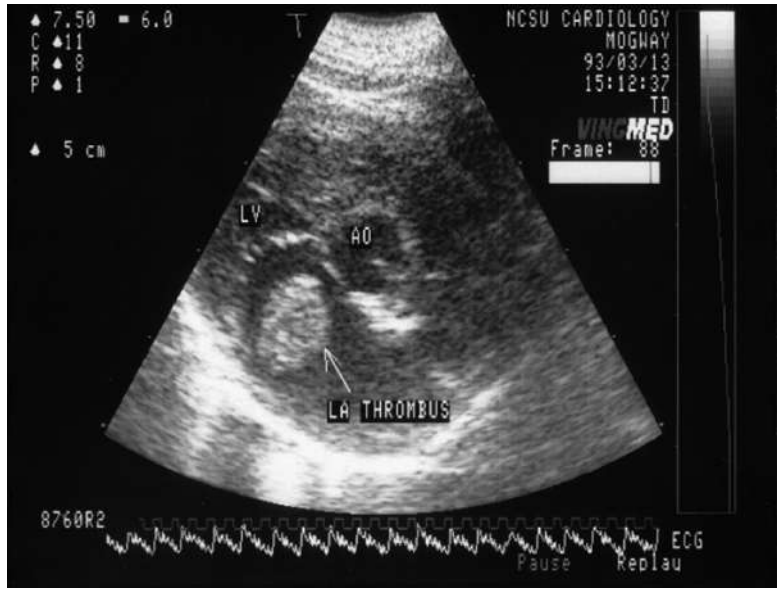

Figure 8.4 Echocardiographic image of an enlarged left atrium that contains a thrombus.

Abdominal Ultrasonography

- An experienced sonographer may be able to identify the thrombus in the caudal aorta. However, this imaging modality typically is not necessary to reach a diagnosis, especially in a cat.
- Abdominal ultrasound may be more useful in the dog to both identify the thrombus and look for associated diseases.

Computed Tomography Scan

- As with abdominal sonography, a multidetector CT scan is not necessary for diagnosis in a cat but could be helpful in a dog to reach a diagnosis, evaluate the extend of the thrombus and look for associated diseases.

Pathologic Findings

- Thrombus typically is identified at the caudal aortic trifurcation.
- Occasionally, a left atrial thrombus is seen.
- Emboli of the kidneys, gastrointestinal tract, cerebrum, and other organs also may be observed.

THERAPEUTICS

The main objectives of treatment are threefold:

- First, immediate treatment of the pain associated with ischemic injury of the legs, typically with injectable opioids.
- Treatment directed at resolving the actual thrombus with anticoagulants or possibly thrombolytic agents.
- Treatment of the cat's heart disease and possible congestive heart failure.

Drug(s) of Choice

Pain Management

Once the diagnosis is reached, addressing the pain and distress associated with ATE is an immediate concern. If possible, intravenous opioid administration is preferred because of its rapid onset of action, bioavailability, and safety profile.

- In the cat, buprenorphine at 0.005 to 0.01 mg/kg IV every 6 to 8 hours as needed is an initial good choice. Buprenorphine can also be given in the cheek pouch or SQ if intravenous access is not obtained.
- Fentanyl (2–3 µg/kg intravenous bolus, then 1–5 µg /kg per hour IV CRI).
- Hydromorphone (0.025–0.1 mg/kg IV or SQ every 4–6 hours)
- Butorphanol (0.05–0.3 mg/kg IV or SQ every 2–6 hours as needed) has fewer analgesic effects than buprenorphine but is a good sedative. If no other opioids are available or if the cat's pain is assessed as mild, then butorphanol is a reasonable choice.

- Cautious use of low dose acepromazine (0.01 mg/kg IV or SQ every 8–12 hours as need) may be helpful for additional sedation and vasodilation. Avoid acepromazine in patients with hypotension or hypothermia because of concerns of worsening systemic perfusion.

Antithrombotic Management

- Thrombolytic therapy with drugs such as streptokinase and tissue plasminogen activator is used extensively in human and infrequently in cats. These drugs are expensive, carry a significant risk for bleeding complications, need to be administered within a few hours of ATE, and have not demonstrated significant therapeutic benefit over conservative management in veterinary medicine. Thus, they are rarely used in general practice settings.
- Unfractionated heparin is the preferred drug in most clinical practices. Heparin actually has no effect on the established clot; however, it prevents further activation of the coagulation cascade and allows the body's endogenous fibrinolytic system to break down the clot. The initial dose typically is given IV then followed with subcutaneous administrations every 6 to 8 hours. The initial intravenous dose is 100 to 200 units/kg and the subsequent subcutaneous dose is 200 to 300 units/kg. Alternatively, an intravenous CRI of heparin at 600 units/kg per day could be used after the initial bolus. The dose is then ideally titrated to prolong the aPTT approximately twofold.
- In addition to heparin, the concurrent use of an antiplatelet agent is also advised. The two antiplatelet options are aspirin (5–81 mg PO every 3 days) or clopidogrel (18.75 mg (1/4 of a 75-mg tablet) PO ever 24 hours).
  - The higher dose of aspirin may be associated with more gastrointestinal adverse effects.
  - The theoretical benefit of clopidogrel is less gastrointestinal adverse effects and possible enhanced efficacy.
- Once signs of clinical improvement are seen, heparin therapy is gradually weaned over 1 to 2 days and long-term therapy is continued.

Dog

- Acute antithrombotic management considerations are similar in the dog.
- The dose of heparin in the dog is generally the same as in the cat. The doses of the antiplatelet agents are different.
  - Canine aspirin dose is 0.5 to 1 mg/kg PO every 24 hours.
  - The dose of clopidogrel dose in the dog is approximately 2 mg/kg PO every 24 hours.
    - A higher loading dose of 10 to 11 mg/kg could be used on the first day if active clot is associated with significant ischemia.

Long-Term Therapy

- Recommendations for long-term anticoagulation are variable because no one treatment modality has shown clear benefit over another.

- Factors involved in deciding which long-term therapy to use include expense, ease of oral as opposed to subcutaenous administration, need for reevaluation, and monitoring.
- Commonly used long-term anticoagulant therapies include aspirin, clopidogrel, or a low molecular weight heparin. None of these treatment options require monitoring for therapeutic efficacy.
- Aspirin (5 to 81 mg every 3 days) is the least expensive option and is dosed every 3 days but carries a higher risk of gastrointestinal and renal adverse effects.
- Clopidogrel (18.75 mg every 24 hours) is moderately expensive and is dosed daily but may have enhanced long-term efficacy.
- Low molecular weight heparins have also been used in the long-term management of cats surviving an ATE.
  - Dalteparin (100–200 unit/kg SQ every 12–24 hours) or enoxaparin (1.5 mg/kg SQ every 12–24 hours) are two commonly used low molecular weight heparins.
  - The disadvantages of these medications are expense, subcutaneous administration, and controversy over the therapeutically efficacious dose in the cat.

Congestive Heart Failure Management

- Oxygen-rich environment
- Furosemide (1–4 mg/kg as needed, not to exceed 12 mg/kg per day) IV or SQ should provide immediate relief of respiratory distress due to concurrent congestive heart failure.
- Other cardiac therapies such as enalapril, diltiazem, or pimobendan may also be indicated.

Precautions/Interactions

- Anticoagulant therapy with heparin, clopidogrel, or the thrombolytic drugs may cause severe bleeding complications.
- Reperfusion of severely ischemic legs may be associated with severe hyperkalemia. Death due to hyperkalemia and ischemia-reperfusion injury is a common cause of in-hospital mortality.
- Avoid a nonselective β-blocker such as propranolol as it may enhance peripheral vasoconstriction.

Alternative Drugs

- Warfarin, a vitamin K antagonist, is the anticoagulant most widely used in humans and could be considered if recurrent ATE.
  - The initial dose is 0.05 to 1 mg/kg PO every 24 hours. It should be overlapped with heparin therapy for 3 days. The dose is then adjusted to prolong the PT approximately two times its baseline value or to attain an INR of 2.0–4.0.
  - Warfarin has an unpredictable dose-to-response effect and is highly protein bound. Thus, frequent monitoring and titration of the dose are required. Warfarin also carries a more significant risk of bleeding.

Diet

- Initially, most cats are anorexic. Tempt these cats with any type of diet. It is important to keep these cats eating to avoid hepatic lipodosis. Appetite stimulants are often used. Naso-esophageal tube feedings may be indicated if more than 3 days of anorexia. Chronic dietary management usually involves sodium restriction.

Activity

- Activity should be restricted. The cat should be kept quiet, stress free and indoors only.

Surgical Considerations

- Surgical embolectomy typically is not recommended because these patients are high risks for surgery and anesthesia as a result of their heart disease.
- Rheolytic thrombectomy has recently been evaluated in the treatment of feline ATE with favorable treatment results but is not commonly available even at tertiary referral centers.

COMMENTS

- It should be emphasized that the finding of tachypnea, even open mouth breathing, upon initial examination should not presume congestive heart failure. Some cats may be tachypneic solely as a result of pain. If the tachypnea persists after appropriate analgesic therapy, or if physical examination (crackles) or radiographic findings are compatible with pulmonary edema, then furosemide therapy is indicated.
- Fluid therapy may be necessary in the initial stages if the cat is not in congestive heart failure.
- Initially, the affected legs should be minimally handled because reperfusion results; long-term, physical therapy (passive extension and flexion of the legs) may speed full recovery.
- No venipuncture should be performed on the affected legs.
- Initially, these cats may have difficulty posturing to urinate and may need to have their bladders expressed periodically to prevent overdistention of the bladder or urine scald.

Client Education

- Owners should be aware of the poor short- and long-term prognosis. Many cats will have advanced heart disease and are at risk for re-embolization. They will require lifelong medications, re-evaluations, and an indoor lifestyle if the cat survives to discharge.
- Typically, most cats that survive an initial episode will recover complete function to the legs; however, some neurologic or musculoskeletal deficits may persist.

Patient Monitoring

- Hourly to daily examination of the legs, femoral pulses, and respiratory rate should be performed to assess clinical response to therapy.
- Continuous ECG monitoring is helpful to identify hyperkalemia cardiac arrhythmias/conduction disturbances associated with severe reperfusion injury.
- aPTT can also be monitored once daily to titrate the heparin dose.
- Periodic evaluation of thoracic radiographs, electrolyte, and renal parameters are also helpful in evaluating response to therapy.

Prevention/Avoidance

- Because of the high rate of re-embolization (25 to 75 %) after surviving an initial episode, prevention with either chronic aspirin, clopidogrel or low molecular weight heparin is strongly recommended. See above for doses.

Possible Complications

- Death is unfortunately a common outcome either due to progression of disease or complication of therapy.
- Bleeding complications may arise with the anticoagulant therapy.
- Life-threatening hyperkalemia and arrhythmias due to reperfusion injury is a complication of therapy.
- Permanent neurological deficits or muscular abnormalities in the hind limbs may arise in some cats (~15 percent) with severe and prolonged ischemia.
- If a cat survives initial episode of ATE, recurrence of ATE and congestive heart failure is common.

Expected Course and Prognosis

- Both short-term and long-term prognosis are generally poor. Most cats (>50 percent) are euthanized or die during their initial ATE event regardless of therapy utilized.
- Admitting rectal temperature of >99°F, fast heart rate, only one limb affected and presence of motor function are all associated with better short-term prognosis.
- Concurrent congestive heart failure is associated with a worse long-term prognosis. In one study, cats with concurrent congestive heart failure had a median survival time of 77 days verus those without congestive heart failure of 233 days.
- Refractory congestive heart failure or recurrence of ATE is typical terminal issues if a cat survives an initial ATE event.
- Expected course of recovery is generally days but can be weeks for return of function to the legs.
- Most cats that survive an initial episode will recover completely but approximately 15 percent of cats may suffer permanent neuromuscular deficits or ischemic injuries such as loss of digits or tip of tail.

Synonyms

- Saddle thrombus

Abbreviations

- ALT: alanine transaminase
- aPTT: activated partial thromboplastin time
- AST: aspartate aminotransferase
- ATE: arterial thromboembolism
- BUN: blood urea nitrogen
- CBC: complete blood count
- CPK: creatine phosphokinase
- CRI: constant rate infusion
- CT: computed tomography
- ECG: electrocardiogram
- INR: international normalized ratio
- IV: intravenously
- PO: by mouth
- PT: prothrombin time
- SQ: subcutaneously

Suggested Reading

Hogan, DF, Andrews, DA, Green, HW, Talbott, KK, Ward, MP, and Calloway, BM. Antiplatelet effects and pharmacodynamics of clopidogrel in cats. *J Am Vet Med Assoc* 2004;225:1406–1411.

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Schoeman, JP. Feline distal aortic thromboembolism: a review of 44 cases (1990–1998). *J Feline Med Surg* 1999;1:221–231.

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