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Arterial thromboembolism (ATE) is a devastating clinical entity that occurs most commonly secondary to severe cardiac disease. ATE is relatively common in cats, and was diagnosed in 1 of 145 cats presenting to a veterinary medical teaching hospital in one study. Often it is the first clinical manifestation of cardiac disease in cats, as 76-90% of cats did not have prior diagnosis of cardiac disease. In a case series of 127 cats with ATE, a majority (91%) of cats had cardiovascular disease, followed by neoplasia (6%), and no underlying cause was identified in 3% of cats. Other potential diseases that could lead to a procoagulable state and development of ATE include: sepsis, disseminated intravascular coagulation, and protein losing nephropathy or enteropathy. Hypertrophic cardiomyopathy (HCM) is the most common cardiac disease in cats suffering from ATE, probably since it is the most common feline cardiomyopathy. However, cats with restrictive cardiomyopathy have a higher risk of developing ATE (45%) than cats with HCM (15%). Left atrial dilation is necessary for development of cardiogenic ATE in cats. In one study of ATE in cats, the left atrium was severely enlarged in 57%, moderately enlarged in 14%, and mildly enlarged in 22%, with only 5% having a normal left atrial size. Thrombus formation may develop when there is an abnormality in one or more of the components of Virchow’s triangle, which include: hypercoagulability, endothelial disruption, and blood stasis. When the left atrium becomes moderate to severely dilated, the blood flow velocity is reduced, resulting in red cell aggregation, platelet activation, and subsequent thrombus formation. Blood stasis appears to be an important factor for red blood cell aggregation in cats with significant cardiac disease. Left auricular blood flow velocity was shown to be reduced in cats with echocardiographic evidence of spontaneous contrast and red blood cell aggregation. There are contradicting studies regarding whether cats with cardiac disease tend to be hypercoagulable. One recent study documented that 45% of asymptomatic cats with HCM had evidence of hypercoagulability. It is debatable whether there is platelet hyperreactivity in cats with cardiac disease, as some studies document increased platelet reactivity and others report no change in platelet function in cats with heart disease. Endothelial damage and disruption likely occurs in cats with cardiac disease, and endothelial damage and fibrin adherence to the subendothelium has been documented on pathologic examination in several cats with congestive heart failure. It is likely that a combination of mechanisms lead to development of a left atrial thrombus in cats with significant cardiac disease.

Once the thrombus becomes dislodged from the left atrium, it travels through the arterial blood system and becomes lodged in an artery depending on the size of the thrombus, with the most common location the aortic trifurcation (71%) then the right subclavian-right thoracic limb. More important than the physical obstruction of blood flow in the artery, the thrombus releases vasoactive amines including thromboxane and serotonin that cause massive vasoconstriction of the collateral arteries, leading to lack of perfusion to the limb. Clinical presentation of feline ATE is straightforward. Most cats are tachypnic (91%), hypothermic (66%), but only 57% have auscultation abnormalities such as a murmur or gallop. Tachypnea may be due to pain or congestive heart failure. Thoracic radiographs reveal cardiomegaly (90%) and congestive heart failure (70%) in a majority of cats.

Thrombolysis (either autogenous or by thrombolytic agents) causes release of large amounts of potassium, hydrogen, and lactate from the dead muscle cells, and leads to acute life threatening reperfusion syndrome. Clinical sequelae include severe metabolic acidosis, and death is from cardiac arrest due to severe hyperkalemia. Earlier electocardiographic abnormalities during hyperkalemia include in order of severity: tall tented T waves, atrial standstill, widening of the QRS complexes, and lastly ventricular fibrillation. Emergency treatment with bicarbonate, calcium gluconate, insulin, dextrose, and atropine is necessary. Reperfusion syndrome may occur hours to several days after ATE.

Prognosis is poor for cats suffering cardiogenic ATE, since there is persistent underlying severe cardiac disease. Poor prognostic indicators include hypothermia on presentation, multiple limbs, lack of motor function, bradycardia, and serum phosphorus. Body temperature of 98.9 degrees was associated with a 50% mortality in one study. Approximately 50% of cats regain partial or complete motor control without the aid of thrombolytic therapy in 1-6 weeks. Other studies estimate survival with or without thrombolytic therapy to be 30-40%. Median survival in a study of 127 cats was 117 days in cats that were discharged from the hospital, but was much lower for cats with CHF (77 days). Although non-cardiogenic ATE in cats is rare, it is the author’s opinion that they tend to have a better prognosis and it have a lower recurrence rate. Since thrombolytic therapy has not been shown to improve survival in cats with ATE, it requires a dedicated nurse in an intensive care unit setting, and is expensive, the author does not elect to treat cats with
tissue plasminogen activator or streptokinase. Anticoagulant therapy should be given to hospitalized cats, and choices include unfractionated heparin or low molecular weight heparin (LMWH). Baseline coagulation panel should be done, and the APTT should be prolonged by 1.5 times baseline with heparin treatment. CHF should be treated with furosemide, and an angiotensin converting enzyme inhibitor may be started a week later if the cat is eating, drinking, and not overtly dehydrated.

Although there are improved techniques to diagnose ATE and the underlying cause, veterinary medicine remains plagued with lack of effective preventative therapy. Any cat suffering from ATE requires anticoagulant therapy. There are several choices ranging from the least expensive option of aspirin to expensive options such as low molecular weight heparin (LMWH). Despite anticoagulant therapy, recurrence rate for cardiogenic ATE is extremely high, with reported rates ranging from 24-90%. It is the authors personal experience that aspirin is ineffective in preventing ATE, but is well tolerated. There was no difference in survival or recurrence rate in cats given mini dose aspirin (5 mg) compared to 81 mg orally every 3 days, and side effects were milder and less frequent1. Clopidogrel is a novel anti-platelet agent that irreversibly inhibits ADP receptors on platelet membranes. Clopidogrel has been shown to inhibit platelet aggregation, increase oral mucosal bleeding time, and reduce plasma serotonin concentration in normal cats at doses as low as 18.75 mg PO q 24 hours. In an unpublished, small pilot study of iatrogenic arterial thromboembolism, cats treated with clopidogrel had significant improvement in motor scores compared to cats treated with placebo, but there was no significant difference in amount of collateral circulation. A large multicenter trial (FATCAT) evaluating the effect of clopidogrel in cats with naturally occurring ATE has recently been completed, and results are pending. LMWHs such as dalteparin and enoxaparin are attractive alternatives to unfractionated heparin given their increased bioavailability and prolonged half lives. Compared to unfractionated heparin, LMWHs work more specifically upstream in the coagulation cascade against Factor X with much lower activity against thrombin (Factor II). Since there is less anti-II activity, LMWHs do not alter PT and APTT times, and therapeutic efficacy must be assessed by measurement of anti-Xa activity. There are only a few pilot studies evaluating pharmacokinetics of dalteparin and enoxaparin in healthy cats. The dose 1.5 mg/kg of enoxaparin SQ appears to adequately suppress factor Xa activity, but the optimal dosing interval is less clearly defined, and likely requires BID to TID frequency. Warfarin is another anticoagulant that has been used with success in cats, but requires careful monitoring of the PT. Candidates include indoor only cats that have an acceptable personality for repeated phlebotomies. Heparin should be given initially to prolong aPTT 1.5x baseline, and then continued for 3 days during warfarin therapy since warfarin initially causes a transient procoagulable effect by decreasing protein C. The target PT is 1.5 x the baseline. Whether combination anticoagulant therapy should be used has not been studied in cats.

Reference List


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