

Feline Arterial Thromboembolism: Prognostic Factors and Treatment

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Introduction

In feline practice, the occurrence of arterial thromboembolism or 'ATE', is one of the most distressing emergency situations for the cat, client and veterinarian. Currently, in first line practice, these patients are commonly euthanized at the moment of diagnosis. The most common underlying cause of thrombogenesis, leading to an ATE event, is cardiac disease and in the feline population, this is most commonly (in approximately 69% of cases) a cardiomyopathy, primarily hypertrophic cardiomyopathy (HCM).

Pathophysiology

Feline cardiomyopathy predisposes to formation of intracavitary thrombi due to blood stasis, endothelial injury and a hypercoagulable state, often secondary to microtrauma of a stretched atrial wall in an enlarged left atrium, fulfilling all components of Virchow's triad.

Prevalence and signalment

Several studies show divergent prevalence numbers, ranging from 0.6% in referral populations to 0.3% in general practice. In cats with HCM, ATE prevalence ranges from 12 up to 21%. Tomcats are overrepresented, though this might reflect the male predisposition for cardiomyopathy and is hence likely to be gender biased. There is no real breed predisposition. The median age is 8-9 years (range 1-20 years).

History, clinical signs, physical examination and differential diagnosis

The majority of cats with ATE have no known history of cardiomyopathy, because a significant proportion of cats with HCM have an unremarkable physical examination. At presentation, diagnosis of a saddle thrombus can be made from the physical examination alone, based on 'the 5 P's': pain, paralysis/paresis of the hind limbs, pulselessness, pallor and poikilothermy. Possible differential diagnoses of acute posterior paresis, though rare, include trauma, intervertebral disc extrusion and a spinal lymphoma. Pain or distress can cause dyspnea and tachypnea though concomitant congestive heart failure (CHF) should be excluded as this will affect treatment and prognosis.

Diagnostic tools

Administration of adequate pain medication (usually opioids), oxygen supplementation in case of tachypnea/dyspnea and reducing stress are essential parts of the emergency management and precede any further diagnostic tests.

Thoracic radiographs are currently the most reliable diagnostic test to confirm or exclude the presence of left-sided CHF and rule out possible other pulmonary pathologies which might cause tachypnea or dyspnea. However, a minority of affected cats has normal cardiac silhouettes. Echocardiography is crucial to diagnose a possible underlying heart disease. The vast majority of these patients will have a cardiomyopathy with a dilated left atrium, possibly in combination with spontaneous echogenic contrast or 'smoke' visible in the lumen. 'Smoke' is believed to be associated with increased risk of ATE in cats. The thrombus can be visualised in the terminal aorta using ultrasound imaging although the absence of a visible thrombus does not rule out ATE. Possible additional tests include biochemistry tests, blood pressure assessment and electrocardiography.

Prognosis

The general prognosis is poor with a survival rate of 33% to 39%, though prognostic factors associated with a higher survival rate are: the absence of CHF, rectal temperature at the moment of presentation $>37.2^{\circ}\text{C}$, (partial) presence of motor function, and the site of thromboembolism and associated affected limbs or other organs.

Owners should be aware that their cat might not survive to discharge or might develop a following episode of ATE in the (nearby) future, with recurrence rates ranging from 24-75%, though the major cause of death in these patients is actually CHF, and not a recurrent episode of ATE. Reports of average long-term survival vary between 51 and 350 days.

Treatment

Current treatment should always consist of initial stabilisation with adequate analgesic and antithrombotic treatment. Diuretic therapy should be administered only if concomitant CHF is diagnosed. At the moment there is no fixed medical treatment protocol and treatment approach should always be evaluated individually.

Even before discussion of further treatment possibilities with the owners, analgesia (e.g. opioid analgetics) should be administered. Furthermore, in case of respiratory distress, oxygen supplementation should be provided without distressing the cat. If cardiogenic pulmonary oedema is expected, an intravenous/intramuscular bolus of furosemide should be administered at 1-2mg/kg and repeated to effect.

Treatment of ATE can be further subdivided into thrombolytic therapies, both medically and surgically, and antithrombotic treatment (e.g. antiplatelet therapy and anticoagulants).

Thrombolytic therapy with streptokinase and tissue plasminogen activator (t-PA) have both been reported in the cat and dissolution of the thrombus has been documented, although, reperfusion injury has been reported in 40% to 70% of cats receiving thrombolytic therapy and represents the most common cause of death, with survival rates ranging from 0% to 43%.

The two major categories of antithrombotic drugs are antiplatelet agents and anticoagulants. Antiplatelet agents are currently the mainstay of treatment for feline ATE, because they may improve collateral flow by reducing the amount of vasoactive substances released by the platelets. Clopidogrel was shown to be superior to aspirin for secondary prevention, with a lower ATE recurrence rate of 49% (vs. 75%) and 1-year recurrence rate of 36% (vs. 64%) and longer median time to event (443 days) compared with aspirin (192 days). Anticoagulants, e.g. unfractionated heparin, are now less commonly used compared to anti-platelet agents, but the new classes of drugs, such as factor Xa-inhibitors (e.g. rivaroxaban) may hold promise for future use in cats. Additional supportive therapy consists of the prevention of self-mutilation of devitalized limbs and physiotherapy. An intensive care setting is essential to ensure that these patients are comfortable and early signs of possible complications are detected.

Prevention

Prospective studies regarding the primary prevention of ATE events are currently lacking in feline medicine, though some specialists recommend primary prevention in cats with an end-systolic left atrial diameter greater than 1.7 cm, a left atrium-to-aortic ratio greater than 2.0 or auricular emptying velocities of <20cm/s. Primary prevention is also indicated in cats with spontaneous contrast in the left atrium. For secondary prevention clopidogrel has been shown to be superior to aspirin (Hogan et al., 2015). Conclusively, further studies are needed to investigate possible alternative therapies and preventive measurements.