Feline Arterial Thromboembolism: A Terrible FATE

Sarah Pavlina, LVT, VTS (ECC)

Feline arterial thromboembolism (FATE) is a syndrome in which an embolus forms and becomes lodged in a cat’s circulatory system, resulting in occlusion of blood flow to an area of the body. Although pathologic thrombi can lodge in blood vessels anywhere in a cat’s body (e.g., front legs, brain, kidneys, gastrointestinal [GI] tract), they are most common at the level of the aorta where it trifurcates and descends into the legs and tail. Thrombi at this location are known as saddle thrombi because of the shape they assume when they lodge. The etiology of FATE is most commonly heart disease (feline cardiomyopathy); other causes include heartworm disease, sepsis, and neoplasia. FATE may be classified as idiopathic if no underlying cause can be identified.

Pathophysiology

The pathophysiology of clot formation and dissolution is very complex, involving many different plasma proteins and cells. At any given time in the body, prothrombosis factors, which act to form clots, are in balance with antithrombosis factors, which act to prevent or limit clot formation. These factors are balanced against clot-destroying fibrinolysis factors and antifibrinolysis factors, which prevent fibrin from breaking down and resulting in clot dissolution.

The Virchow triad is often used to describe how thrombi of pathologic origin form. The triad consists of injury to the endothelium, sluggish or static blood flow, and hypercoagulability. Pathologic thrombus formation indicates that the above factors no longer work in a balanced fashion. In cats, enlargement of the left atrium caused by hypertrophic cardiomyopathy often accounts for the injury to the endothelium and likely causes blood stasis. While defining the cause of hypercoagulability is more difficult, all the components of the Virchow triad are not necessary for thrombus formation. Rather, derangement of any single component increases the risk for thrombus; however, in cats with hypertrophic cardiomyopathy, sluggish blood flow is the main contributing factor.

Patient History and Clinical Signs

The history and clinical signs of a cat with thromboembolism in any part of the body, but especially the aortic trifurcation, can be very dramatic. Cats often present with a history of peracute weakness, paresis, or paralysis in the affected limb; distress or anxiety; crying or howling (due to pain); and/or dyspnea. Cats with an embolus at the aortic trifurcation typically present in a classic fashion considered pathognomonic for this condition. There is usually paresis or paralysis of the hindlimbs accompanied by weak or absent femoral pulses. Other clinical signs include pale footpads and a purple hue to the nail beds of the affected feet, indicating a lack of oxygenation. The legs and feet may feel cool, and the gastrocnemius muscle may appear firm and painful due to a spasm caused by poor perfusion. Affected cats often present in extreme pain, resulting in tachypnea and/or loud vocalization. One reason that FATE is so painful is that cessation of blood flow to the hindlimbs causes ischemic neuromyopathy, which is caused by substances released by activated platelets in the area of the clot. Ischemic neuromyopathy is responsible for the associated paresis or paralysis of the hind legs.

It is important for technicians to recognize the clinical signs of FATE and to consider it an emergency. When a patient suspected of having FATE is admitted to a clinic, a minimum database (including a packed cell volume, a total solids value, and “paired” blood glucose analysis) is performed to rule out the source of the embolus. Monitoring for potential complications, including thrombolytic therapy, is also critical. After clot dissolution, affected cats may recover completely, or they may develop chronic arthritis or neuromyopathy due to the ischemia caused by the embolus.

Glossary

- Bifurcate—divide into two branches
- Embolus—undissolved material, such as fragments of clotted blood, carried by the blood and impacted in the vascular system
- Heparin (low molecular weight)—heparin molecules that are smaller than those in unfractionated heparin
- Heparin (unfractionated)—a group of heparin molecules that vary in size (mean size: 15,000 daltons) and therefore their properties
- Hypercoagulable state—a group of conditions that alters the coagulability of blood, predisposing an animal to venous or arterial thrombosis
- Idiopathic—having an unknown cause
- Ischemic neuromyopathy—peripheral nerve injury caused by a reduction in blood supply
- “Paired” laboratory testing—in cats with FATE, performing the same laboratory tests on affected and unaffected limbs
- Thrombolysis—dissolution of a thrombus
- Trifurcate—divide into three branches
and lactate levels) should be obtained. The blood glucose level obtained from the affected limb is usually lower than the level from the central circulation, and the lactate level is often higher in the affected limb.\(^1\) Other tests to consider include a complete blood count, a serum chemistry profile, a urinalysis, an anti-thrombin level, and a thyroid profile.\(^2\) Chest radiographs should be obtained to screen for underlying heart disease.\(^3\) An echocardiogram may also be beneficial for determining the severity of cardiac dysfunction.\(^1\)

**Treatment**

The treatment of FATE involves a three-step approach, although multiple steps may be performed at the same time. Formation of the existing thrombus must be slowed or stopped, blood flow to the affected area must be restored, and the cat’s pain must be managed.\(^1\) Supportive care must also be provided.\(^1\)

**Formation Reduction**

Unfractionated or low-molecular-weight heparin (LMWH) is the drug of choice for slowing thrombus formation. Both types of heparin block several steps of the clotting cascade and help inhibit platelet aggregation.\(^1,8,9\) Heparin is administered via injection. Intravenous dosing, whether intermittent or by constant-rate infusion, is preferred in the early stages of therapy because intramuscular administration can lead to hematoma formation.\(^1,9\) After the initial stages of therapy, heparin is often switched to subcutaneous administration. There is some evidence that LMWH is absorbed better\(^1\) by this route and may be absorbed more predictably,\(^1\) especially compared with unfractionated heparin. However, LMWH is more expensive and may be cost prohibitive.\(^1,8,9\)

Because clotting times are altered by heparin administration, baseline and serial monitoring are important, as spontaneous bleeding can occur during treatment. A baseline platelet count, prothrombin time, and activated partial thromboplastin time (aPTT) should be obtained before starting heparin therapy.\(^1\) One method of measuring heparin activity is to obtain a baseline aPTT measurement and serial measurements at the clinician’s discretion. The heparin dose should be adjusted so that the aPTT is 1.5 to 2.5 times the baseline.\(^5–9\) Newer information suggests that measuring anti-Xa—a factor in the coagulation cascade—is more accurate than measuring the aPTT.\(^1,8,9\) However, the anti-Xa level test is only available through one commercial laboratory.\(^1,8,9\)

**Restoration of Blood Flow**

A major goal of treating FATE is to restore perfusion to the affected limbs or organs. This can be accomplished by surgical embolectomy or administration of thrombolytic agents.\(^1\) Surgical intervention is not well documented in the literature and is associated with a poor survival rate.\(^4\) Most authors recommend medical reduction of clots.\(^1,3\) Aspirin and clopidogrel are used for their antiplatelet activities to treat FATE.\(^1,8,9\) These drugs are discussed in more detail in the Prevention section below, but they may be used in the acute phase of treatment for their anti-thrombotic properties.\(^1\)

The drugs streptokinase and urokinase are used in humans to improve arterial blood flow through thrombolysis. Streptokinase activates plasmin, which breaks down several coagulation factors nonspecifically.\(^1,5–7\) Few studies have investigated the use of streptokinase in cats. In one study, all cats that were administered streptokinase developed respiratory distress and died during the maintenance phase of treatment.\(^1\) Another study showed spontaneous bleeding in many cats as well as reperfusion injury.\(^1\) Urokinase is similar to streptokinase but more specific for breaking down fibrin.\(^3\) In one study of urokinase, spontaneous bleeding was not observed, but a quarter of treated cats experienced reperfusion injury.\(^1\) Because of the severity of the complications associated with these drugs and the lack of evidence supporting their use, these drugs may not be the first choice for dissolving clots in cats.

Tissue plasminogen activator (t-PA) is also used in human thrombolytic therapy. The drug is specific to clot dissolution but can lead to systemic bleeding at high doses.\(^1\) Another complication of t-PA is reperfusion injury, and the drug is expensive; therefore, it may not be appropriate for all FATE patients and must be considered carefully before use.\(^5–7\)

Because thrombus dissolution can be dangerous and prohibitively expensive, use of the collateral circulation to increase perfusion to the affected area is an important part of therapy.\(^1\) Some publications recommend the use of aecpromazine or hydralazine for vasodilation,\(^1,4\) but some authors say these drugs are generally not useful and may cause hypotension that requires intervention.\(^1\) This is because they act primarily on smaller arterioles, not on the large arteries where the thrombus is lodged.

**Prognosis**

Although many drugs are available for treating and preventing FATE, the survival data on FATE are somewhat grim. There is little difference in survival rates of cats that are treated conservatively or with thrombolytics.\(^1\) Cats with low rectal temperatures or slow heart rates have a lower chance of recovering from an initial embolic event. Survival of cats with FATE is between 2 months and 2 years after an initial embolic event; most cats have another thrombotic event within 9 months, making the prognosis poor.\(^2\) A potential complicating factor in treating FATE is concurrent heart failure, as underlying cardiomyopathy is responsible for the initial thrombotic event in half of cats.\(^2\) Even if a cat is successfully treated for FATE, its underlying condition predisposes it to recurrences. In my experience, because of the high cost of treatment, the high likelihood that a thrombotic event will recur within a year, and the obvious pain that affected pets endure, many clients elect humane euthanasia when their cat presents with FATE.

**Pain Management**

Analgesic therapy is one of the most important aspects of treating FATE. Opioids are generally safe and commonly used for treating pain. Butorphanol may be used\(^1,4\) but may not provide adequate analgesia. Hydromorphone, oxymorphone, or buprenorphine may be used, and fentanyl may be considered to treat extreme pain.\(^1\)
Any medications given intramuscularly or subcutaneously should be administered in a part of the body with adequate circulation to ensure proper absorption.1

**Nursing Care**

Nursing management of cats with FATE includes managing the comfort of the affected limbs. The legs should be kept warm,3 and physical therapy can include passive range-of-motion movements, massage, and warm-water bathing.2 Patients may require bladder management, including manual expression, as they may be unwilling or unable to urinate on their own. Oxygen should be provided as needed,4 ideally in an oxygen cage to minimize stress. Conservative fluid therapy may be initiated to support renal perfusion or treat hyperkalemia; 5% dextrose in water or 2.5% dextrose in 0.45% sodium chloride may be used.4

Diagnosis of the severity of any concurrent heart disease may have to be delayed until after initial stabilization of the patient, but treatment of congestive heart failure may be initiated along with thrombolytic therapy.2 Treatment of congestive heart failure may include administration of furosemide and vasodilators, such as nitroglycerine paste or nitroprusside.2

**Prevention**

Ideally, the prevention of FATE would focus on preventing an initial thrombotic event, but the lack of clinical signs associated with known risk factors prevents veterinarians from predicting which at-risk cats will develop thrombi.1 Instead, the focus tends to be on preventing a subsequent embolic event in cats that have already survived one. Treating the underlying cause of an embolic event is the most effective way to prevent subsequent events. Anti-thrombotic drugs have become an important component of long-term treatment of FATE.1 Cats with enlarged left atra caused by hypertrophic cardiomyopathy are at higher risk for FATE and may be considered for prophylactic antithrombotic therapy such as administration of baby aspirin, although evidence regarding its efficacy is lacking.1

**Antiplatelet Drugs**

Aspirin has been used as an antiplatelet agent in cats with risk factors for thromboembolism for more than 30 years and has been well studied.1,3,8 Aspirin works indirectly to prevent platelet aggregation and is therefore considered to have only moderate antiplatelet action.1 Adverse effects of aspirin have been reported in up to 25% of treated cats; GI effects such as vomiting and decreased appetite are most common.1 Historically, at-risk cats have been treated with a baby aspirin at 81 mg PO q3d.3-7 This regimen has been questioned as to whether its efficacy is appropriately balanced against the adverse effects. Some authors have recommended a low-dose regimen (5 mg PO q3d) for preventing recurrence of FATE.5,7 While more research is needed, giving this low-dose regimen may be warranted because it does not cause adverse effects in cats.3-7

Clopidogrel is a direct antiplatelet drug that is thought to prevent recurrence of arterial thromboembolism. One study found that clopidogrel combined with t-PA is more effective than aspirin or heparin at preventing clot formation.8,9 There is some evidence that clopidogrel may cause vomiting. To help prevent this, the drug should be given with food or in a gel capsule.1

**Anticoagulant Drugs**

Warfarin belongs to a group of drugs that interferes with vitamin K–dependent coagulation factors and thus disrupts the clotting cascade. Multiple authors1,3,8,9 recommend initiation of warfarin therapy only in conjunction with heparin therapy, as warfarin may initially increase the tendency for blood coagulation because of the drug’s inhibitory effects on clotting proteins. Warfarin interacts with many other medications and should be compounded for cats by a pharmacist rather than given in a standard human dose.1 In addition, warfarin is associated with a high risk of spontaneous bleeding. Clients should be warned about the risks associated with warfarin. When patients are receiving the drug, even a minor injury could result in hemorrhage.1 Frequent rechecks, including serial monitoring of clotting function, should be recommended to clients, who should also be made aware that long-term warfarin therapy in cats is very challenging.5,7

LMWH can be used in clot prevention and can be administered subcutaneously. The most common adverse effect of this drug is minor bleeding.1

There are human drugs that have efficacy against factor Xa without affecting other clotting factors. Due to the selectivity of these drugs, their efficacy can be measured only by checking the anti-Xa level. These drugs have not yet been studied in veterinary medicine.1

**Conclusion**

Technicians may be responsible for caring for cats with FATE, so we must know how these patients present, how to properly triage them, how to perform a workup, and how to prepare a nursing care plan. Because FATE presents so dramatically, clients may be overwhelmed by their cat’s condition and may look to us for guidance. Therefore, we should be well informed to help our clients make the best choice for their cat and to provide high-quality nursing care.

**Suggested Reading**


References

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1. Which of the following should be included in treating FATE?
   a. pain management
   b. diuresis
   c. restoration of blood flow to the affected area
   d. a and c

2. Which of the following is not an aspect of the Virchow triad?
   a. hypercoagulability
   b. lack of perfusion
   c. endothelial injury
   d. static blood flow

3. Which of the following is an aspect of nursing care for FATE?
   a. cold-water bathing and passive range-of-motion therapy
   b. manual bladder expression and NSAID administration
   c. opioid administration and warming of affected limbs
   d. oxygen administration and aggressive fluid therapy

4. What is the most common cause of FATE?
   a. heart disease
   b. neoplasia
   c. renal failure
   d. heartworm disease

5. Which drug can be used to treat and prevent FATE?
   a. warfarin
   b. t-PA
   c. LMWH
   d. streptokinase

6. Which is a negative indicator for survival in cats with FATE?
   a. bradycardia
   b. which limb is affected
   c. normal rectal temperature
   d. hyperthyroidism

7. Which parameter is commonly used to measure response to heparin therapy?
   a. prothrombin time
   b. anti-Xa level
   c. platelet count
   d. aPTT

8. Minimum baseline blood work for FATE should include
   a. a complete blood count and a urinalysis.
   b. a packed cell volume, a total solids value, and a lactate level.
   c. a serum chemistry profile and a lactate level.
   d. a urinalysis and a blood glucose level.

9. Which blood component is responsible for ischemic neuromyopathy?
   a. fibrin
   b. degenerate neutrophils
   c. plasmin
   d. platelets

10. A major complication of clot-dissolving drugs is
     a. reperfusion injury.
     b. hypothermia.
     c. bradycardia.
     d. renal failure.