AORTIC THROMBOEMBOLISM IN DOGS – SIGNS AND TREATMENT

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Victoria Doyle looks at how ATE can be a complication of other diseases, highlighting clinical and neurological signs, and diagnosis and treatment methods

AORTIC thromboembolism (AtE) is less commonly seen in dogs compared to cats.

However, it is an important differential diagnosis for dogs presenting with a range of clinical signs. ATE is seen more often in large-breed dogs, including border collies, Labradors and greyhounds, although there is an apparent predisposition in cavalier King Charles spaniels (CKCS). Male dogs tend to be over-represented. Middle-aged to older dogs are usually affected, with a mean age of nine years (range five to 14 years)[1].

Aetiology

ATE is seen in dogs with a range of underlying causes that may lead to a hypercoagulable state. This disease process includes cardiac disease, hyperadrenocorticism (HAC; pituitary or adrenal-dependent or iatrogenic), immune-mediated haemolytic anaemia (IMHA), disseminated intravascular coagulation (DIC), sepsis, bacterial endocarditis, parvovirus infection, hypertension, neoplasia, and protein-losing enteropathy (PLE) and nephropathy (PLN)[2-6]. No underlying cause may be identified in up to 38 per cent of cases[1]. In cats, the primary underlying cause of ATE is cardiac disease (hypertrophic, restrictive or dilated cardiomyopathy)[7]. Neoplasia, paraneoplastic thrombocytosis, foreign body and idiopathic causes have rarely been reported in the feline species[8].

Pathogenesis

Thrombosis occurs due to the disruption of blood flow, injury to the vessel wall and disruption of the balance of procoagulant and anticoagulant factors.

Cardiac disease can disrupt blood flow due to venous congestion, and the integrity of the endothelium may be affected[2]. Arrhythmias will cause abnormal intracardiac blood flow, which can precipitate thrombus formation[2].

HAC is proposed to cause thrombosis due to increased levels of clotting factors in the blood, loss of antithrombin III (ATIII) and an increase in plasminogen activator inhibitor[2].

Hypothyroidism causes atherosclerosis, which leads to an increased risk of thrombosis in both dogs and humans[6].

Up to 80 per cent of cases with IMHA have thromboembolic disease due to a number of factors, including hypoalbuminaemia, thrombocytopenia and use of corticosteroids[9].

DIC is a complex pathological process that causes spontaneous haemorrhage and thrombus formation via plasmin and thrombin activation, as well as consumption of clotting factors and platelets[3]. DIC also causes activation of cytokines leading to fibrinolysis, damage to blood-vessel walls, causing platelet aggregation, and inhibition of natural anticoagulants including ATIII[3].

Neoplasia can lead to a predisposition to clot formation due to platelet activation, a reduction in neutralisation of clotting factors and their clearance from the body, a reduction in fibrinolysis, and an increased production of factor X activator[2].

PLE and PLN cause hypercoagulability due to the loss of ATIII, which is of a similar size to albumin. Dogs with a serum albumin of less than 20g/L are highly likely to have reduced ATIII[1]. Hypoalbuminaemia may also affect platelet aggregation leading to hypercoagulability.

CKCS have a high prevalence of cardiac disease, abnormal platelet morphology, femoral artery occlusion and connective tissue disorders that may predispose them to thromboembolic disease[1],[10].

Clinical and neurological signs

Clinical presentation of a dog with an ATE is more variable than in cats. Cats tend to have a peracute presentation with ATE due to the dislodging of a cardiac thrombus, which embolises and occludes the aorta. This triggers a cascade of events, including the release of vasoactive substances, culminating in the constriction of the collateral vasculature in the pelvic limbs[11]. In dogs, presentation can be acute onset of mono or para-paresis/plegia with absent femoral pulse,

but in many cases it is chronic with exercise-induced pelvic limb weakness/ataxia[1]. Femoral pulses were reported present on clinical examination, although reduced in quality in up to 54 per cent of cases[1]. There are multiple potential causes for this, including the presence of extensive collateral circulation involving the lateral circumflex femoral, the distal caudal femoral, the caudal gluteal and the deep femoral arteries[1],[10].

The different underlying causes of ATE in dogs may allow a more gradual formation of the ATE, which allows further collateral circulation to form[1],[12]. The clinical signs in dogs may be exacerbated during defecation, as increased abdominal pressure may further compromise perfusion to the pelvic limbs. It is uncommon for dogs to have cyanotic footpads or nail beds. Pain may not be a feature, or may be difficult to localise, especially in chronic cases, but also occasionally in dogs with acute presentations[1]. A thorough clinical examination may identify a potential underlying cause for the ATE.

On neurological examination, conscious proprioceptive deficits were reported present in 54 per cent of cases[1]. Interestingly, the patella reflex is more frequently, and more markedly, affected in dogs with ATE compared to cats where it is usually spared[1]. The pedal withdrawal in dogs is less often affected than cats. This may be due to anatomical variation between the species in the arterial supply to the pelvic limbs[1].

Diagnostic investigation

Haematology and serum biochemistry are required to assess potential underlying causes and may suggest the requirement for more specific testing, including ACTH stimulation tests or a thyroid panel. Creatinine kinase (CK) and aspartate aminotransferase (AST) are useful additions to the serum biochemistry as they are frequently elevated, especially in acute cases[1],[2]. However, they may only be mild to moderately elevated or within the normal range, especially in chronic cases.

The coagulation profiles are often within the normal range[1]. Plasma D-dimers can be measured and are usually elevated in dogs with thromboembolic disease[13]. D-dimers form from the breakdown of a stabilised clot and are only seen with active coagulation and fibrinolysis[13]. Studies have shown that D-dimers are more sensitive than fibrin degradation products (FDPs) for thromboembolic disease[13]. Urine analysis, including a urine protein: creatinine ratio (UPCR), is required to assess for protein loss via the kidneys.

Systemic blood pressure and fundic examination to exclude the possibility of hypertension as an underlying cause of the ATE are also important. Echocardiography is indicated if there is a cardiac murmur, and an electrocardiogram (ECG) is important if an arrhythmia is detected on clinical examination. Screening the thorax and abdomen with radiographs and ultrasound for primary neoplasia or metastatic disease are a vital part of the investigation. Abdominal ultrasound may also show the presence and extent of the thrombus in the distal aorta (Figures 1 and 2).

Colour flow Doppler is useful to assess whether there is any flow past the thrombus (Figure 3)[1]. Magnetic resonance imaging (MRI) of the caudal abdomen can also be used to detect the thrombus. A filling defect may be seen within the distal aorta on T2-weighted images or with time of flight angiography (Figures 4, 5 and 6)[14]. MRI can also detect ischaemic changes in affected musculature. As canine ATE is often more chronic than feline, collateral arteries can form and these may also be evident on MRI[14]. Computed tomography (CT) angiography can also be used to detect the filling defect in the distal aorta[15]. The presence of an ATE can be confirmed on postmortem and histopathology (Figures 7 and 8). However, small thrombi lyse shortly after death and can be overlooked.

Treatment

Analgesia and fluid therapy to correct dehydration or electrolyte imbalances are important in the initial stages. Medication is directed towards the underlying cause of the ATE when one is found. Thrombolysis using streptokinase (a humanlicensed plasminogen activator) has been shown to eradicate the thrombus in three dogs with ATE and reduce the size of the thrombus in another[16].

Plasminogen activators have not been successful in all dogs[2]. Side effects include reperfusion injury, cerebral thromboembolic events and clinical haemorrhage, so their use is not without risks. Heparin and aspirin have both been used to reduce the risk of further clot formation; however, neither have a veterinary licence[3]. The use of heparin also carries risks of haemorrhage, but this can be reduced with the use of low molecular weight heparin, although the optimal dose has not been determined.

Concurrent use of heparin with aspirin will increase the risk of haemorrhage. The dose of aspirin likely to be effective is debated – some authors advocate the use of ultra lowdose aspirin therapy (0.5mg/ kg/day) to prevent thromboembolic disease in patients with IMHA, while others have shown this dose is ineffective in healthy dogs.

Clopidogrel, a new humanlicensed anti-platelet drug, has been used successfully, alone and in combination with ultra low-dose aspirin, in dogs with IMHA[9]. A restricted exercise regime to prevent increased demand on perfusion to the pelvic limbs is also prudent. However, short periods of gentle exercise may encourage perfusion to the limbs and re-canalisation of the thrombus.

Prognosis

The prognosis for dogs presenting with acute or chronic signs of ATE is more favourable than for cats with ATE. Only 33 to 39 per cent of cats are reported to survive until discharge[17]. However, up to 53 per cent of dogs can survive until discharge[1,2]. After discharge, the reported mean survival time for cats is between 117 days to 345 days[7,17]. The median survival in dogs has been reported at 270 days (range 45 to still alive at 780 days), which is similar to cats[1]. Those dogs that survive to discharge tend to have a gradual improvement in their clinical signs. Those with a more chronic

history usually remain stable[1].

The difference in prognosis between cats and dogs may be due to the potential for development of collateral circulation in dogs and the variety of underlying causes possible. Unfortunately, further thrombus formation is possible even if the underlying cause is treated and the dog is receiving antiplatelet therapy, so relapses are a possibility[2].

Conclusions

While ATE is less commonly seen in dogs compared to cats, it is an important complication of a range of different diseases. The clinical signs seen in dogs are significantly different from those in cats. The clinician must remain aware of the possible clinical signs that can be seen in dogs and institute further diagnostic procedures if the clinical suspicion of ATE arises.

The most successful treatment for ATE in dogs is not known, although different options are available that can be trialled with owner consent. The short-term prognosis is more favorable than in cats, but the long-term prognosis may be comparable.

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References

- 1. Goncalves R et al (2008). Clinical and neurological characteristics of aortic thromboembolism in dogs, *J Small Anim Pract* **49**(4): 178-184.
- 2. Boswood A, Lamb C R and White R N (2000). Aortic and iliac thrombosis in six dogs, *J Small Anim Pract* **41**(3): 109-114.
- 3. Fox P R, Petrie J and Hohenhaus A E (2005). Peripheral vascular disease. In *Textbook of Veterinary Internal Medicine*, Ettinger S J and Feldman E C (eds), Elsevier Saunders, St Louis, 1,145-1,165.
- 4. Boswood A (1996). Resolution of dysrhythmias and conduction abnormalities following treatment for bacterial endocarditis in a dog, *J Small Anim Pract* **37**(7): 327-332.
- 5. Sykes J E et al (2006). Clinicopathologic findings and outcome in dogs with infective endocarditis: 71 cases (1992-2005), *J Am Vet Med Assoc* **228**(11): 1,735-1,747.
- 6. MacGregor J M et al (2004). Cholesterol-based pericardial effusion and aortic thromboembolism in a 9-year-old mixed-breed dog with hypothyroidism, *J Vet Intern Med* **18**(3): 354-358.
- 7. Laste N J and Harpster N K (1995). A retrospective study of 100 cases of feline distal

aortic thromboembolism: 1977-1993, *J Am Anim Hosp Assoc* **31**(6): 492-500.
- 8. Reimer S B, Kittleson M D, and Kyles A E (2006). Use of rheolytic thrombectomy in the treatment of feline distal aortic thromboembolism, *J Vet Intern Med* **20**(2): 290-296.
- 9. Mellett A M, Nakamura R K and Bianco D (2011). A prospective study of clopidogrel therapy in dogs with primary immune-mediated hemolytic anemia, *Journal of Veterinary Internal Medicine* **25**(1): 71-75.
- 10. Buchanan J W, Beardow A W and Sammarco C D (1997). Femoral artery occlusion in cavalier King Charles spaniels, *J Am Vet Med Assoc* **211**(7): 872-874.
- 11. Smith S A and Tobias A H (2004). Feline arterial thromboembolism: an update, *Vet Clin North Am Small Anim Pract* **34**(5): 1,245-1,271.
- 12. Guglielmini C et al (2008). Internal thoracic artery-caudal epigastric artery as a collateral pathway in a dog with aortic occlusion: a case report, *Vet J* **178**(1): 141-145.
- 13. Nelson O L and Andreasen C (2003). The utility of plasma D-dimer to identify thromboembolic disease in dogs, *J Vet Intern Med* **17**(6): 830-834.
- 14. Brofman P J and Thrall D E (2006). Magnetic resonance imaging findings in a dog with caudal aortic thromboembolism and ischemic myopathy, *Vet Radiol Ultrasound* **47**(4): 334-338.
- 15. Kirberger R M and Zambelli A (2007). Imaging diagnosis – aortic thromboembolism associated with spirocercosis in a dog, *Vet Radiol Ultrasound* **48**(5): 418-420.
- 16. Ramsey C C et al (1996). Use of streptokinase in four dogs with thrombosis, *J Am Vet Med Assoc* **209**(4): 780-785.
- 17. Smith S A et al (2003). Arterial thromboembolism in cats: acute crisis in 127 cases (1992-2001) and long-term management with lowdose aspirin in 24 cases, *J Vet Intern Med* **17**(1): 73-83.