Vet Record CaseReports

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TITLE OF CASE ***Do not include "a case report"***

Pulmonary arterial thromboses and gall bladder wall oedema in a cat with bronchioloalveolar carcinoma.

SUMMARY ***Up to 150 words summarising the case presentation and outcome (this will be freely available online)***

An 11 year old male neutered British Shorthair cat presented with acute collapse, dyspnoea and paraparesis. Left atrial enlargement and left-sided congestive heart failure were excluded by point of care ultrasonography, and gall bladder wall oedema was detected. Comparative venous blood gas analyses confirmed ischaemia of the hindlimbs, and echocardiography was consistent with pulmonary hypertension. The patient was euthanised and post mortem examination revealed pulmonary artery thromboses associated with a bronchioloalveolar carcinoma.

BACKGROUND ***Why you think this case is important – why did you write it up?***

Dyspnoea in conjunction with per-acute onset of paraparesis would most frequently be due to underlying cardiac disease with concurrent congestive heart failure in cats. The use of point of care ultrasound in this case allowed exclusion of this aetiology and successful stabilisation prior to ongoing investigations. In this case a cat developed both pulmonary arterial and femoral arterial thromboses secondary to a bronchioloalveolar carcinoma, a rare pulmonary neoplasm. Primary pulmonary neoplasms are uncommon causes of arterial thrombosis in cats. The documentation of gall bladder wall oedema (GWO) in this emergency presentation is also a novel finding.

CASE PRESENTATION ***Presenting features, clinical and environmental history***

An 11 year old male neutered British Shorthair cat was presented to the [redacted] for acute collapse. The cat had appeared normal several hours prior to presentation, but was discovered collapsed and unresponsive in the garden. The cat was breathing rapidly and had passed a large volume of diarrhoea. In the week prior to presentation the owners had noted two episodes in which the cat appeared unsteady for a few seconds before returning completely to normal. The cat had no previous medical history other than chronic otitis externa.

INVESTIGATIONS ***If relevant***

On presentation the cat was obtunded, recumbent and dyspnoeic with a respiratory rate of 200 breaths per minute and open mouth breathing. The heart rate was 164 beats per minute with no audible heart murmur or arrhythmia and weak peripheral pulses. Lungfield auscultation was unremarkable. Rectal temperature was low at 37.2°C and all extremities were cold to the touch. Mucous membranes were pink and moist with a capillary refill time of less than 2 seconds. Abdominal palpation was unremarkable and body condition score was 7/9.

Point of care ultrasonography of the thorax revealed underfilled left heart chambers, a subjectively distended right heart, no B-lines and no cavitary effusions. Point of care ultrasound of the abdomen revealed no peritoneal fluid but it did reveal GWO (Figure 1). Doppler blood pressure from a forelimb was too low to read. Patient-side blood tests revealed a packed cell volume of 40%, a metabolic acidosis (pH 7.188), a hypernatremia of 156mmol/L (reference range 140-153mmol/L), hyperchloremia of 121mmol/L (reference range 106-120mmol/L), hypokalaemia of 3.1mmol/L (reference range 3.6-4.6mmol/L), hyperlactataemia of 2.8 (reference range 0.6-2.5), and hyperglycaemia of 16.9mmol/L (reference range 3.6-13.9mmol/L).

After initial stabilisation (described below) the cat was mobile but a lateralised paraparesis became apparent, with the right weaker than the left. Forelimb function was within normal limits. Metatarsal pulses were weak despite strong femoral pulses, the hind paws were cold to the touch, and rectal temperature had reduced to 35.1°C. This raised suspicion of an arterial thromboembolism.

Full haematology and biochemistry panels were performed and were unremarkable other than a mildly elevated serum urea. Neurological examination revealed delayed hindlimb paw positioning, intact patella reflexes and reduced hindlimb withdrawal reflexes. This would have been consistent with a bilateral sciatic neuropathy or an L6-S1 myelopathy, but a primary neurological localisation did not explain the local hypoperfusion. Concurrent venous blood gas and blood glucose analyses from the right hind limb and one unaffected forelimb revealed pH, lactate, glucose and potassium differentials consistent with ischaemia (Table 1).[1]

Given the suspicion of thromboembolic disease and right-sided changes the cat underwent echocardiography. This was consistent with pulmonary hypertension, showing dilation of the right ventricle and flattening of the interventricular septum, as well as a prominent pulmonary artery (Figure 2). The left atrium was of normal size and there was mild ventricular hypertrophy, with a left ventricular free wall diastolic thickness of 5.2mm and normal thickness considered to be less than 4mm[2]. This was considered consistent with pseudohypertrophy due to underfilling or mild underlying cardiomyopathy.

DIFFERENTIAL DIAGNOSIS ***If relevant***

Aetiologies for this cat's presenting signs could have included cardiogenic, obstructive, hypovolaemic or vasodilatory shock. A classical aortic thromboembolism due to underlying hypertrophic cardiomyopathy with concurrent congestive failure was excluded during initial investigations. Large volume gastrointestinal losses could not be completely excluded as a cause of a purely hypovolaemic presentation, and anaphylaxis as a cause of vasodilatory shock was initially considered a differential diagnosis due to the concurrent diarrhoea, dyspnoea and the finding of GWO[3,4].

After stabilisation, clinical signs indicated femoral arterial thromboemboli, and further diagnostics confirmed ischaemia of the hindlimbs. The limbs were less affected proximally so the more common site of embolism at the origin of the external iliac arteries was

unlikely, but femoral pulses can still be palpable with obstruction of the internal iliac arteries[5]. The evidence of pulmonary hypertension alongside per-acute onset respiratory distress and cardiovascular collapse were highly supportive of a pulmonary thromboembolism (PTE)

TREATMENT ***If relevant***

The patient received flow-by oxygen therapy, a total of 15ml/kg of compound sodium lactate in intravenous bolus format and a single intravenous dose of methadone (0.2mg/kg), which were associated with rapid normalisation of mentation, respiratory effort and systemic perfusion indices/blood pressure/pulses?.

OUTCOME AND FOLLOW-UP

Considering the most likely differentials (neoplastic) the owners elected to have the patient euthanised. A post-mortem examination was performed revealing a 3x2x1.5cm mass in left caudal lung lobe, the histology of which revealed a bronchioloalveolar carcinoma. In pulmonary arteries closely associated with the mass, there was arteriosclerosis and several organising fibrin thrombi with evidence of recanalization (Figure 3). A thrombus was not identified in the distal aorta or the iliac arteries, although it is possible that they had lodged more distally in the limbs.

DISCUSSION ***Include a very brief review of similar published cases***

The cat's acute signs appear to have been caused by thrombotic events in the pulmonary and hindlimb vasculature, causing acute respiratory distress, cardiovascular instability and paraparesis. The previous episodes of unsteadiness reported by the owner were likely caused by previous smaller pulmonary arterial thromboses; this is supported by the recanalization of pulmonary artery thrombi documented on post mortem examination. Chronic renal infarcts were present that may also indicate a more prolonged period of hypercoagulability, although these are often incidental findings in older animals[6]. The patient's initial hypotension was likely due to obstruction in the pulmonary circulation caused by a thrombus; the sudden increase in right ventricular afterload impairs right heart function, left sided return and left ventricular filling (owing to interventricular interdependence and evidenced by interventricular septal flattening), resulting in systemic hypoperfusion[7,8]. Whilst ischaemia of the hindlimbs was demonstrated, iliac artery thrombosis was not identified on post mortem examination, and may have been present more distally in the femoral arteries. Whilst the hindlimb ischaemia was embolic in nature it cannot be confirmed whether the presumptive thrombosis was purely haematogenous or represented tumour embolisation as has been reported previously[9]. Tumour embolisation was considered less likely given the lack of other detectable metastases, however[10].

The most common cause of arterial thrombosis in cats is primary cardiac disease followed by neoplasia, particularly pulmonary neoplasms, and less commonly hyperthyroidism and immune mediated diseases have been reported[6,10–12]. Similarly, for PTE the most common underlying diseases in cats have been reported either as neoplasia or cardiac disease, with other reported comorbidities including anaemia, protein-losing nephropathy, sepsis, disseminated intravascular coagulation, steroid use and pancreatitis[13,14].

In this case the cause of pulmonary thrombosis and femoral artery thromboemboli appears to be a bronchioloalveolar carcinoma. The proximity of the mass to the thrombosed pulmonary arteries and the associated arteriosclerosis suggests that local haemodynamics played a significant role in formation of a thrombus in situ, for example

via induction of local hypertension and blood stasis or endothelial dysfunction, but distant thromboembolisation to the hindlimbs also suggests systemic hypercoagulability.

Bronchioloalveolar carcinoma is an uncommon tumour in cats that accounts for approximately 10% of primary lung neoplasms, with primary pulmonary neoplasms in general reported to have an prevalence of only 0.5% in all cats presenting for post mortem examination[15,16]. This type of tumour commonly metastasizes the tracheobronchial lymph nodes, and pleural metastasis has also been reported[17,18]. Metastasis to the digits is also reported, but was excluded in this case[10]. No specific survival times for bronchioloalveolar carcinoma have been reported in cats, but primary lung tumours in general in cats have a poor prognosis with a median survival time of 115 days reported in one study[15].

In a case series of nine cats with bronchioloalveolar carcinoma, one patient was reported to have a PTE on post mortem exam[17], and in a case series of 29 cats with PTE two cats were diagnosed with bronchioloalveolar carcinoma[14]. Actual incidence of thrombosis may be higher as they are easily overlooked on post-mortem if not clinically suspected. There is one reported case of aortic thromboembolism associated with a diagnosis of bronchioloalveolar carcinoma[19]. In that case there was a paraneoplastic thrombocytosis and a membranous glomerulopathy which were thought to have contributed to hypercoagulability and thrombosis. In the case described here, the platelet count was within normal limits and there was no clinical or histological evidence of glomerular disease.

During initial diagnostics GWO was detected. This has been found to be a sensitive marker of anaphylaxis in the dog, but is also reported in sepsis, cardiac and biliary diseases[3,20–22]. There is less literature on this finding in cats, although it has been described in cholecystitis[23]. One case series described a cat with GWO secondary to a ventricular septal defect with right ventricular enlargement and pericardial effusion[22]. The GWO in that case was likely due to right-sided venous congestion. A similar aetiology is suspected in the case described here, however, a study investigating the prevalence of GWO in dogs with pulmonary hypertension failed to identify any cases[24]. To our knowledge GWO in a cat secondary to pulmonary hypertension has not been described previously.

In conclusion, this case demonstrated both pulmonary arterial and presumptive femoral arterial thromboses in association with a bronchioloalveolar carcinoma. Both have previously been reported but not concurrently. The finding of GWO initially raised suspicion of anaphylaxis but appears to have been caused by pulmonary hypertension, which is a novel finding in this cat.

LEARNING POINTS/TAKE HOME MESSAGES ***3 to 5 bullet points – this is a required field***

- Gall bladder wall oedema may indicate the presence of pulmonary hypertension in cats, and this should be considered if there are compatible clinical signs.
- Thoracic imaging to screen for pulmonary neoplasia should be considered in cats with arterial thromboembolism where underlying cardiac disease has been ruled out.
- Comparative venous blood gas, electrolyte, lactate and glucose analyses can be used to confirm limb ischaemia.
- In situ pulmonary arterial thrombosis may be associated with per-acute onset of clinical signs, without necessarily an embolic component.

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FIGURE/VIDEO CAPTIONS ***figures should NOT be embedded in this document***

Figure 1: Image from a point of care ultrasound scan at the diaphragmaticohepatic site. The gall bladder wall (red line) was striated and measured up to 2.6mm in thickness, with the normal gall bladder wall thickness in a cat being up to 1mm[23]. ~~A slight hypoechoic rim consistent with a gall bladder wall oedema can be seen[22].~~

Figure 2: Right parasternal, long axis, four-chamber echocardiographic cine loop showing dilation of the right ventricle and flattening of the interventricular septum, as well as possible mild hypertrophy of the left ventricle.

Figure 3: Histologic section through the pulmonary parenchyma adjacent to the mass. There are marked, chronic, degenerative changes of the walls of the large pulmonary arteries, with marked thickening of the tunica intima (A) and media (B) (arteriosclerosis). Haematoxylin and eosin stain, x 100 magnification. Scale bar 0.1 mm.

Table 1: Comparison of selected venous blood gas and blood glucose results between an affected hindlimb and an unaffected forelimb confirming ischaemia.

OWNER'S PERSPECTIVE ***Optional***

PLEASE SAVE YOUR TEMPLATE WITH THE FOLLOWING FORMAT:

Corresponding author's last name and date of submission, e.g.,

Smith_June_2017.doc