TITLE: Surgical management of a cat with hepatic arterioportal fistula

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Summary

A 9 month old domestic short haired cat presented with stunted growth and chronic gastrointestinal signs. Tachypnea, a heart murmur, and cranial abdominal bruit were present on physical examination. Echocardiography revealed volume overload in all heart chambers. Computed tomographic angiography (CTA) confirmed the presence of an abnormal communication between the hepatic arterial circulation and the portal vein, along with multiple acquired shunts (MAS). The abnormal vascular communication was surgically ligated. Echocardiography documented improvement in cardiac parameters following surgery and the cat continues to have no clinical signs 39 months post operatively. This report describes successful surgical management of feline hepatic arterioportal fistula (APF) for the first time.

Introduction

An arteriovenous fistula (AVF) is a direct communication between an artery and vein bypassing capillary beds (Hosgood 1989). Congenital fistulas can occur at any stage of embryogenesis (Hosgood 1989) and join systemic arteries with either systemic veins (AVF) or the portal vein (APF). Acquired fistulas may be secondary to trauma, aneurysm rupture, neoplasia, infection or created surgically (Hosgood 1989, Schöniger *et al*. 2008, Phillips & Aronson 2012, Adin *et al.* 2002). There are few reports of feline APF or hepatic AVF (HAVF) (McConnell *et al.* 2006), where HAVF represent an intrahepatic communication between the systemic arterial and portal venous system. There are two previous reports of AVF and HAVF in the cat, in both cats, an attempt at surgical management was made, but neither survived (Legendre *et al.* 1976, McConnell *et al.* 2006). Previously reported management techniques for canine HAVF include: hepatic lobectomy with or without caval banding, ligation of the nutrient artery alone and glue embolization (Chanoit *et al.* 2007).

Case History

A 9 month old male entire domestic short haired cat, weighing 3.58kg, was presented to the referring veterinarian with a 5 month history of reduced appetite, intermittent diarrhoea, vomiting and stunted growth. The cat remained of normal mention except during episodes of diarrhoea when depressed mentation was noted. Physical examination revealed a grade I-II/VI left, systolic heart murmur, the remainder of the clinical examination at the referring veterinary practice was reported as unremarkable. Investigations at the referring veterinary practice included haematology, biochemistry, thoracic radiography, echocardiography and abdominal ultrasound. Abnormalities identified were as follows: hypercholesterolaemia 7·74mmoL/L [reference interval (RI) 0·00 to 5·00mmoL/L], and high fasting serum bile acids (SBA) 112µmoL/L (RI 0 to 15µmoL/L), cardiac silhouette enlargement; vertebral heart score 9·1 (RI <8·1; Litster & Buchanan 2000), volume overload with dilation of all cardiac chambers. Abdominal ultrasound revealed an abnormal vessel within the hepatic parenchyma. Doses of 10 mg furosemide twice daily (Millpledge Veterinary), 10 mg spironolactone once daily (Prilactone; Ceva) and 2·5 mg benazepril once daily (Fortekor; Novartis) were prescribed. Following deterioration in respiratory rate and effort the cat was referred.

On presentation to Queen Mother Hospital for Animals at the Royal Veterinary College, the cat was quiet but alert with a respiratory rate of 64 breaths per minute and heart rate of 132 beats per minute. Cardiac auscultation identified a grade II-III/IV left sternal systolic murmur. Lung sounds were normal. Abdominal auscultation revealed a cranial ventral abdominal bruit.

Echocardiography confirmed the previous findings with left ventricular internal diameter in diastole (LVIDd) 21.5mm (RI 12.0 – 19.8), left atrium to aorta ratio (La:Ao)1.45 (RI 0.95 – 1.65) and maximum left atrial diameter on long-axis view (LAD) 16.2mm (RI 9.3 – 15.1)

(Jacobs and Knight 1985). No structural heart defects were determined; it was assumed the murmur was a flow murmur secondary to high cardiac output. Abdominal ultrasound identified multiple large blood vessels in and adjacent to the liver containing high-velocity turbulent flow, confirmed with colour Doppler. There was subjective microhepatica. Several enlarged arteries were visible caudal to the liver and multiple small blood vessels in the retro-peritoneal space adjacent to the left kidney (consistent with APF and multiple acquired shunts (MAS)). Medical management for suspected hepatic insufficiency was initiated with doses of 62·5 mg amoxicillin-clavulanic acid orally twice daily (Kesium; Alstoe) and 1.3 mL lactulose orally three times daily (Sandoz). Benazepril and spironolactone were continued unchanged and the furosemide dose was reduced (5 mg orally twice daily).

The cat was returned for CT angiography (CTA) under general anaesthesia five days later. Pre-contrast, time-attenuation curve (TAC) and multiple-phase post-contrast images were acquired (Philips Mx8000 IDT). Time-attenuation curve was acquired during a test bolus of 150 mgI/kg of non-ionic iodinated contrast media (iohexol (Omnipaque, GE Healthcare)) at 3mL/min. The multiple post-contrast phases images were acquired after administration of 600mgI/kg of contrast media at 3mL/min, at 15s, 30s, 60s and 120s post contrast to represent arterial, portal, venous, hepatic and late phases.

Computed tomographic angiographic examination (figure 1) revealed a single abnormal vessel derived from the main hepatic artery feeding multiple small arteries that wrapped around the intrahepatic central and left divisions of the portal vein and terminated in a single dilated, tortuous portal vein (figure 1C, arrow head) all outside the hepatic parenchyma. The CTA showed almost simultaneous contrast enhancement of the portal system (>100Hu) and the aorta, prior to caudal vena cava (CVC) enhancement. There was also an extensive network of MAS between all major branches of the portal system and CVC, throughout the dorsal abdomen – extending cranially from the level of the first lumbar vertebrae to the caudal aspect of the fourth lumbar vertebrae and laterally extending to the medial aspect of

both kidneys.

Following CTA, a routine celiotomy was performed. The APF was identified adjacent to the left medial and the quadrate liver lobes (figure 2), no ascites was present. Multiple acquired shunts were seen in the mesentery adjacent to both kidneys. Mesenteric pressure (as a surrogate for portal pressure), measured via a cannula in a jejunal vein connected via a three-way tap and an extension set to a transducer, was 30mmHg. Intraoperative mesenteric portovenography demonstrated that the majority of blood flow entered the CVC through the MAS. Based on the pathoanatomy highlighted by the CTA, an abnormal arterial branch feeding the APF was identified and encircled using 2 metric polypropylene (Prolene – Ethicon). Temporary occlusion of this vessel led to an acute reduction in measured mesenteric pressure, to 8mmHg with no detrimental effect on heart rate or systemic blood pressure, this was taken as confirmation that the correct vessel had been identified. The abnormal vessel was ligated with 2 metric polypropylene. Post ligation mesenteric portovenography showed complete occlusion of the APF, there continued to be significant flow through the MAS. Recovery was uneventful; the abdominal bruit disappeared immediately, analgesia was provided by a remifentanyl (Ultiva; GlaxoSmithKline) constant rate infusion initially, titrated to methadone boluses every four hours (Comfortan; Dechra) and buprenorphine every six hours (Vetergesic; Alstoe) as indicted. The cat was discharged three days post-operatively with medications as prescribed preoperatively.

The cat was re-examined four weeks and six months postoperatively. At four weeks the cat was behaving normally, the heart murmur and gastrointestinal signs had resolved; medications other than furosemide and benazepril were stopped. By six months the cat was reported to have normal activity levels and appetite and physical examination was unremarkable. Haematology and serum biochemistry revealed: pre-prandial SBA 27µmol/l and post-prandial SBA 21.9µmol/l, all other parameters were normal. Echocardiography demonstrated subjectively mild eccentric left ventricular hypertrophy although left atrial and

ventricular size were reduced: LVIDd 18.6mm, LAD 16.0mm and La:Ao 1.32 at this point, furosemide and benazepril therapy was discontinued. During telephone interview with the owners 39 months after surgery, the cat was reported to be free of clinical signs.

Discussion

The presenting clinical signs in the cat reported here, were similar to previous reports where the age of the cats and the absence of trauma, suggest a congenital aetiology (Legendre *et al.* 1976, McConnell *et al*. 2006). The clinical features of APF are identical to those associated with congenital portosystemic shunt (CPSS) with the exception of abdominal bruit (Lipscomb *et al.* 2007, Tivers & Lipscomb 2011). Also, the clinicopathological findings wereconsistent with hepatic insufficiency, as seen in CPSS (Tivers & Lipscomb 2011). The abdominal bruit and heart murmur were the key initial findings that made us consider an APF.

Both of the previous cats and 15/20 dogs with AVF presented with ascites secondary to portal hypertension (Chanoit *et al.* 2007). Ascites was not present in the cat reported here, despite evidence of portal hypertension, instead, this cat was presented because of stunted growth and gastrointestinal signs. Gastrointestinal signs were the second most frequent presenting sign in dogs (Chanoit *et al.* 2007) and are the second most common presenting sign in cats with CPSS (Lipscomb *et al.* 2007, Tivers & Lipscomb 2011). The shunting fraction and portal hypertension are possible explanations for gastrointestinal signs. Feasibly, further clinical signs could have become evident in this cat over time. Portal hypertension induced ascites results from a combination of hypoproteinaemia and increased portal hydrostatic pressure. The absence of ascites is partially due to absence of biochemical evidence of hepatic insufficiency (e.g. normal albumin) and possibly a lower shunting fraction - the presence of hepatopetal flow may support this. Furthermore it is possible the portal hypertension was gradual in onset allowing for the development of collateral vessels. However, as ascites secondary to portal hypertension is rare in cats (Van

den Ingh *et al.* 1995), it is possible, in the previous two cases, the ascites was caused by right sided cardiac failure.

The heart murmur was also a key physical examination finding in this cat, also in contrast to dogs; only five of 20 dogs in a previous study had a heart murmur, one of which was due to pulmonary stenosis. In dogs the absence of a heart murmur in spite of a volume-overloaded right heart is due to the presence of hepatic sinusoids between the AVF and heart which increase resistance (Chanoit et al. 2007). The heart murmur detected in this cat may be due to the size of shunting fraction through the MAS however; this is not supported by the improvement seen in cardiac parameters following surgery. Neither of the previous cats with AVF or HAVF are reported to have a heart murmur, it is possible this is a feature specific to this case (Legendre *et al.* 1976, McConnell *et al.* 2006).

Both the cats previously reported in the veterinary literature died; one post operatively following an attempt at surgical treatment (Legendre *et al.* 1976) and the other was euthanised intraoperatively following abdominal exploration (McConnell *et al*. 2006), whereas surgical treatment in the cat reported here was relatively straightforward with an uneventful recovery. The reasons for this success are unclear although it is possible that the young age of the cat reported here, compared to the age of the previously reported cat (Legendre *et al.* 1976), may have played a role; specifically, the secondary cardiac and hepatic changes might have been less severe. In addition, the absence of reflex bradycardia (Nicoladoni or Branham‘s sign) following ligation of the APF in this cat, might also suggest that the shunting fraction was less relative to the circulating blood volume, than in previous reports. This reduced flow volume could be because of a small initial diameter of the congenital APF, or because there was less time for the APF diameter to increase. An alternative explanation, given that the portovenogram showed the majority of blood flow through the MAS, could be that significant shunting through the MAS prevented the increase in afterload required to cause the reflex bradycardia. The effect of preoperative medical

management is also hard to quantify; anecdotally, the authors have found animals with CPSS appear to have an improved postoperative recovery if managed medically for a period of time before surgery, particularly if clinical signs related to hepatic insufficiency or MAS are present and this may also be applicable to animals with APF. Finally, the anatomy of the abnormal vasculature in the cat reported here made it readily amenable to identification and ligation without the need for extensive dissection. Clearly, there will be a great deal of variation in anatomy between animals with APF and the pathoanatomy in this cat was straightforward compared to previous patients on which one of us (DJB) had attempted surgery.

Once the abnormal vessel was ligated, the long-term clinical outcome was dependent on the absence of pre-existing or new collateral APF channels. Abolition of the APF (without further APFs developing) would allow reverse remodelling of the heart and improved cardiac function and this outcome was supported by objective improvement in cardiac size on follow up echocardiography. Reduced blood flow through the MAS should result in increased portal flow to the liver and improved hepatic function. As portal pressure is normally higher than pressure in the CVC, there remains a strong haemodynamic reason for blood to continue to flow through MAS, once they are formed, despite reversal of the inciting pathology. Residual flow through MAS may explain the marginal elevation in SBA after apparently successful abolition of the APF. Importantly, the cat was clinically normal six months after surgery which suggested that both cardiac and hepatic systems were recovering well and according to the owners, the clinical improvement has been durable.

Diagnostic imaging was essential and CTA proved an extremely helpful form of abdominal imaging in the cat reported here. Abdominal ultrasound examination identified abnormal vessels adjacent to the liver and documented hepatofugal blood flow in the portal vein; known to be associated with APF (Zwingenberger *et al.* 2005). The complex three-dimensional nature of the abnormality is extremely difficult to appreciate in a two-dimensional imaging modality, explaining the apparent discrepancies on initial inspection of

the imaging descriptions between ultrasound and CTA. Computed tomographic angiography provided sufficient detail to allow identification of the single “feeder” vessel as a target for ligation and to appreciate a single dilated termination of the abnormal vessel, allowing classification of the abnormality. This is consistent with the value of CTA for abdominal vascular anomalies in man (Santoro *et al.* 2009). The significant detail provided by the CTA preoperatively limited the additional value of the intraoperative portovenography as the CTA made identification of the APF straightforward. The portovenography did however confirm preferential flow of contrast through MAS rather than a single CPSS and the cannulated jejunal vessel allowed estimation of portal pressure. Echocardiographic evaluation was essential for evaluating cardiac remodelling secondary to volume overload and their resolution following treatment. We conclude, because of the superior anatomical information gained, CTA is highly recommended in animals suspected of having such vascular malformations.

Hepatic artery to portal venous communications are infrequently reported in the cat but they are the most common AVF reported in dogs (Chanoit *et al.* 2007). Congenital HAVF are an embryological abnormality, caused by a local failure of differentiation of arteries and veins from a common capillary bed (Schaeffer *et al.* 2001). Dogs have been reported to have different HAVF configurations (Chanoit *et al.* 2007). These include: APF - a single connection between a systemic artery and the portal vein (Guzman *et al.* 2006), HAVF and HAVM - direct multiple arterial and portal venous communications within the liver parenchyma (Berent & Tobias 2009). It is unclear from the literature whether a true hepatic artery direct to systemic vein fistula has ever been described, as most descriptions of these conditions describe portal hypertension with MAS in these dogs, implying the presence of a hepatic artery to portal vein anastomosis. Historically, this condition has been described as HAVF or HAVM and whilst these are not inaccurate terms, it might be more accurate to describe two forms of hepatic artery to portal venous fistula: namely hepatic artery to portal vein fistula (HAPVF) describing a solitary vessel between the hepatic artery and the portal

vein and, hepatic artery to portal vein malformation (HAPVM) to describe multiple anastomoses between the hepatic artery and portal vein system. In dogs, it has been suggested surgical ligation is ideally suited to APF, liver lobectomy is more appropriate for localized HAVM and interventional radiography (IR) guided cyanoacrylate embolism suitable for those with diffuse HAVM (Chanoit *et al.* 2007).

The cat reported here had a direct communication between the hepatic artery and a branch of the abnormally appearing portal vein, although there were a number of smaller vessels between the two single vessels, importantly for both classification and treatment, the abnormality originated and terminated in a single feeder vessel that was outside of the hepatic parenchyma, therefore we argue, could be classified as a true APF. Regardless of classification, we believe an important factor in the successful outcome of the cat described here rested on the appreciation of a specific feeder vessel. This communication between hepatic arterial and portal systems was only fully appreciated on CTA and we would argue in such instances, occlusion of feeder vessels would represent the most appropriate initial treatment option. The best treatment will depend on the pathoanatomy in each individual, emphasising the importance of advanced imaging such as CTA or selective angiography.

In conclusion, APF are rare in cats but, a successful outcome is possible as illustrated by the cat described.

No conflicts of interest have been declared.

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Figure legends

Figure 1

3D reconstructions of the early-phase CT angiogram. The aorta (Ao), left kidney (LK) and right kidney (RK) are identified. The tortuous anomalous tributary of the portal vein (PV) is also identified. Figure 1A is a view from the left dorsolateral aspect. The arrowheads delineate the coeliac artery and the hepatic artery. This vessel terminates in a network of small vessels in the region of the porta hepatis. Figure 1B is a view from the right lateral aspect. The arrowheads delineate a vessel which has formed from the small vessels in the region of the porta hepatis. It can be seen that this vessel terminates in a dilated portion of an aberrant portal vein tributary. Figure 1C is a ventral view. The arrowhead delineates the termination of the vessel identified in 1B. The asterisk marks the region of multiple acquired shunts, too small to be visible individually.

Figure 2

Intraoperative photograph showing the hepatic arteriovenous fistula (star), immediately caudal to the liver (Li) having been fully attenuated with an in situ Prolene ligature.