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Hepatic arterioportal malformation in a dog – case report

[*Malformação arterioportal hepática em um cão – relato de caso*]

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ABSTRACT

Arterioportal communications are complex hepatic vascular abnormalities. These are rarely seen in dogs and typically manifest as neurological, gastrointestinal, and developmental changes. This report describes clinical, laboratory and imaging findings associated with hepatic arterioportal malformation in a male Shih-Tzu dog aged 12 months. The diagnosis was achieved using computed tomographic angiography. The therapeutic approach selected consisted of palliative medical management (diuretics) combined with dietary protein restriction (3.6 g/100 kcal) provided by hepatic diet and gut activity modulation using lactulose. Surgical intervention was not recommended due to the complexity of vascular changes and portal hypertension. Despite initial clinical improvement, the patient died of disease-related complications seven months after diagnosis. Computed tomographic angiography was vital for accurate diagnosis and treatment selection, that needs to be more investigated.

Keywords: liver, vascular malformation, computed tomographic angiography, hepatic encephalopathy

RESUMO

As comunicações arterioportais são anormalidades vasculares hepáticas complexas que raramente são vistas em cães. As manifestações clínicas geralmente são alterações neurológicas, gastrointestinais e no desenvolvimento dos filhotes. Este relato descreve os achados clínicos, laboratoriais e de imagem associados à malformação arterioportal hepática em um cão Shih-Tzu macho, com 12 meses de idade. O diagnóstico foi feito por angiotomografia computadorizada. A abordagem terapêutica selecionada consistiu no manejo médico (diuréticos) combinado com restrição proteica dietética (3,6g/100kcal), por meio de alimento coadjuvante indicado para hepatopatias, e modulação da atividade intestinal com uso de lactulose. A intervenção cirúrgica não foi recomendada devido à complexidade das alterações vasculares e à hipertensão portal. Apesar da melhora clínica inicial, o paciente morreu de complicações relacionadas à doença sete meses após o diagnóstico. A angiotomografia computadorizada foi vital para o diagnóstico preciso e a seleção do tratamento, que precisa ser mais estudado.

Palavras-chave: fígado, malformação vascular, angiotomografia, encefalopatia hepática

INTRODUCTION

Arterioportal communications are abnormal connections between arteries and portal veins, which result in diversion of high-pressure arterial blood flow to the low-pressure portal system, leading to portal hypertension. These communications may be intra or extrahepatic. Intrahepatic communications are more complex and involve a network of abnormal blood vessels connecting arteries and veins, whereas extrahepatic communications constitute a direct connection between implicated vessels (Specchi *et al.*, 2018).

Arteriovenous communications may be congenital, the most common being arterioportal malformations, or acquired, which may be caused by trauma or neoplastic conditions (Chanoit *et al.*, 2007; Kutara *et al.*, 2017; Weisse, 2015). The term arteriovenous fistula is

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more commonly used to describe communications involving a single artery and vein (Specchi *et al.*, 2018).

Major clinical manifestations include neurologic signs such as depression, disorientation, comatose status, behavior changes, lethargy and seizures, gastrointestinal abnormalities (vomiting, diarrhea and hyporexia) and delayed growth (Chanoit *et al.*, 2007; Weisse, 2015; Whiting *et al.*, 1986).

These malformations have seldom been described in small animals. Computed tomographic imaging findings include portal vessel enhancement during the arterial phase, enlargement of the compromised afferent artery, narrowing of the caudal segment of the aorta (Ao), calcification and dilatation of bile ducts, microhepatia, ascites, hepatofugal portal flow and multiple acquired portosystemic shunts (Specchi *et al.*, 2018; Zwingenberger *et al.*, 2005).

Arterioportal communications and portosystemic shunts share similar clinical manifestations and sonographic findings. Therefore, computed tomographic angiography (CTA) is vital for accurate diagnosis and appropriate treatment selection.

CASUISTRY

An intact male Shih-Tzu dog aged 12 months and weighing 4.3kg was referred with a history of progressive weight loss, repeated vomiting, diarrhea and two convulsive episodes. Other neurologic signs, such as compulsive pacing and circling, head tremor, ptyalism and obnubilation, had been observed at the age of eight months. The dog had also developed ascites from the age of 10 months.

Physical examination revealed abdominal distension due to free peritoneal fluid, body condition score 2/9 (Cline *et al.*, 2021), moderate muscle wasting (Cline *et al.*, 2021) and depressed mental status. Free serous fluid (400 ml) was drained from the peritoneal cavity.

Laboratory workup revealed mild lymphocytosis (5,500/µL; ref. interval: 1,500-5,000/µL), increased alkaline phosphatase (440U/L; ref. interval: 20-150U/L) and alanine aminotransferase (110mg/dL; ref. interval: 10-88mg/dL) levels, low plasma protein levels (4.7g/dL; ref. interval: 6.0-8.0g/dL) and normal urea (29.2mg/dL; ref. interval: 20-40mg/dL), creatinine (0.86mg/dL; ref. interval: 0.7-1.4mg/dL) and albumin (2.6g/dL; ref. interval: 2.3-3.8g/dL) levels.

Physical examination and laboratory findings suggested hepatic compromise. Transabdominal sonography and CTA were requested for diagnostic confirmation and treatment planning purposes.

Transabdominal sonography was performed using Affiniti 70 ultrasound machine (Philips-Netherlands) with microconvex (8-5 MHz). Sonographic assessment revealed a small liver, normal hepatic echotexture and dilated, tortuous intrahepatic vessels measuring about 0.69cm in diameter, with turbulent flow in left liver lobes on color Doppler imaging (Fig. 1). Other sonographic findings were enlarged caudal vena cava and portal vein, a large network of abnormal vessels next to the liver and moderate amounts of free fluid in the peritoneal cavity. Kidney and bladder lithiasis were also detected.

Given the complexity of sonographic findings, CTA was requested. Tomographic images were acquired using a 16-detector row helical CT scanner [Mx8000 - Philips Medical Systems (Philips Medical Systems Inc., Cleveland – OH, USA)] with the patient in sternal recumbency and under general anesthesia (meperidine 3mg/kg IM, propofol 10mg/kg IV and isoflurane delivered by inhalation). Pre and postcontrast cross-sectional CT images were acquired. Contrast-enhancement was achieved with non-ionic iodinated contrast agent (iohexol, 600ml/kg) injection via the cephalic vein. The following settings were used: 120 kVp, 150 mA, 2.0 mm slice thickness, pitch factor of 0.5 and 512 matrix size. Tomographic images were analyzed using Osirix MD DICOM viewer software (Pixmeo SARL – Bernex, Switzerland).

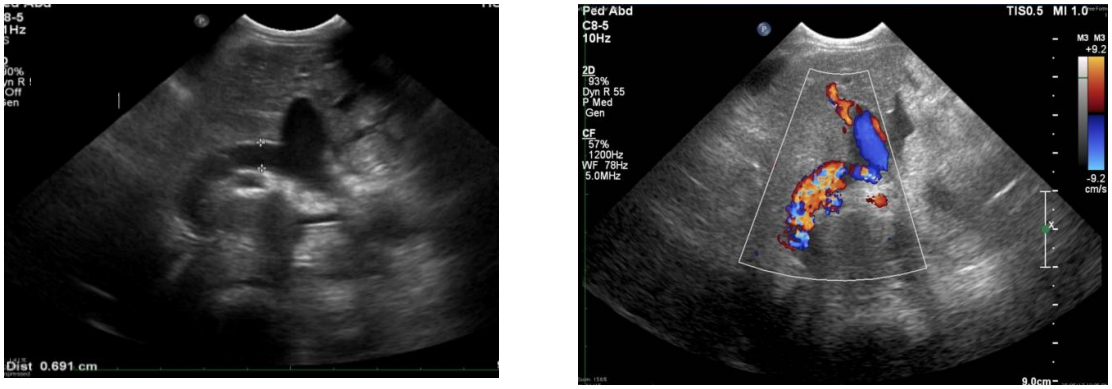

Figure 1. B mode and Color Doppler ultrasound of the liver shows a large tortuous portal vessel (measure 0.69cm in diameter) with turbulent flow.

Tomographic assessment revealed microhepatia, asymmetry with reduced volume of left hepatic lobes. Arterial phase imaging findings were as follows: portal vessel enhancement in the left medial and lateral hepatic lobes, with significant vessel dilation and tortuosity and aneurysmal appearance; enlarged vessels (varices) in the wall of the gallbladder, stomach and caudal esophagus; moderate amounts of free fluid in the peritoneal cavity (Fig. 2); decrease in aortic diameter caudal to the origin of the celiac artery; celiac artery ingurgitation relative to the cranial mesenteric artery (Fig. 3); large numbers of tortuous and complex vessels caudal to the liver, close to the lesser curvature of the stomach; enlarged caudal vena cava, portal vein and hepatic artery and gastro-azygos portosystemic shunt (Fig.4).

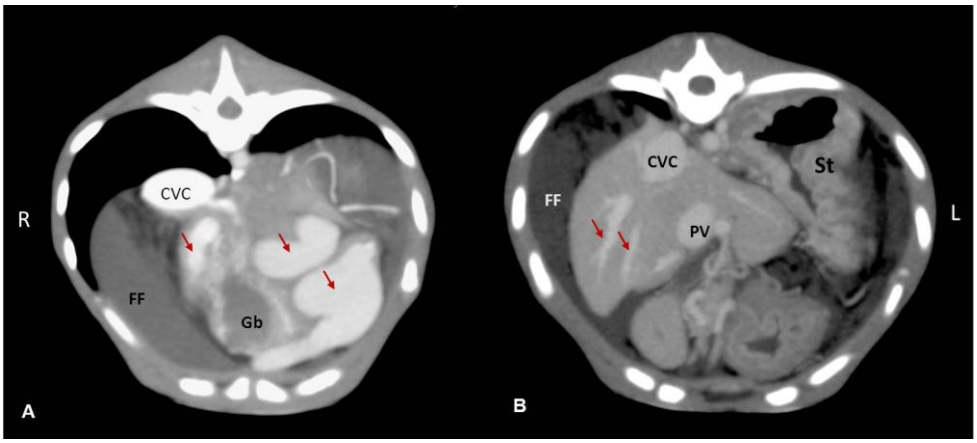

Figure 2. A: Transverse MIP image of the abdomen made during the arterial phase shows aneurysmal and dilated portal veins of the left lateral hepatic lobe (arrows). The vessels in the gallbladder wall (Gb) are distended (varicose veins). B: Transverse computed tomographic (CT) image made during the portal phase shows the normal portal veins of the right lateral hepatic lobe (arrows). The caudal vena cava (CVC) and portal vein (PV) are dilated. The vessels in the stomach (St) wall are distended (varicose veins). FF: free peritoneal fluid; R: right; L: left.

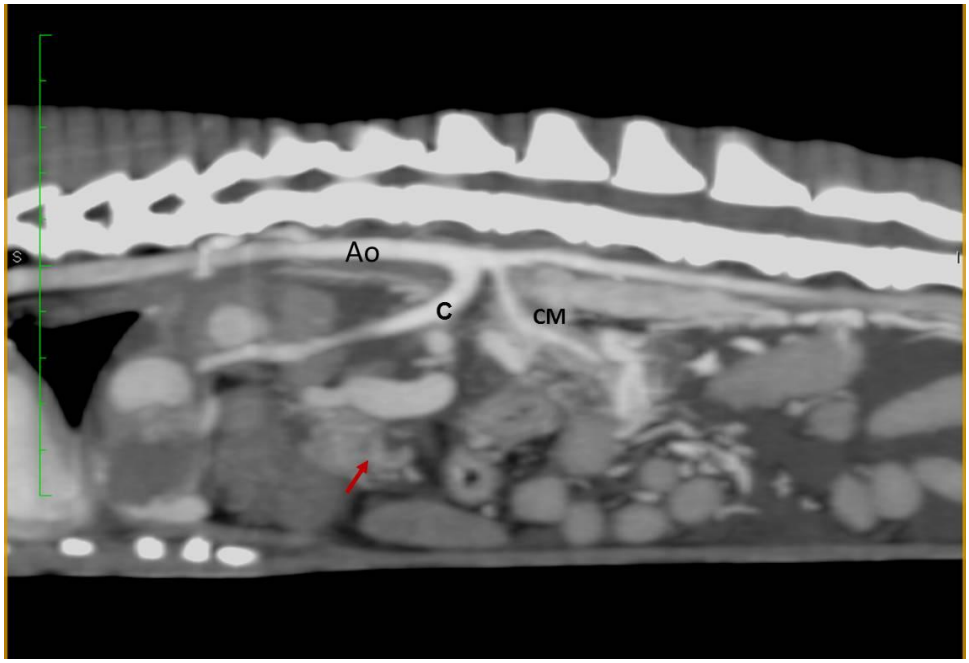

Figure 3. Sagittal reformatted image of the abdomen made during the arterial phase. There is a decrease in size of the aorta (Ao) caudal to the origin of the celiac artery. The celiac artery (C) was enlarged, and the cranial mesenteric artery (CM) was small. Arrow: formation of collateral veins.

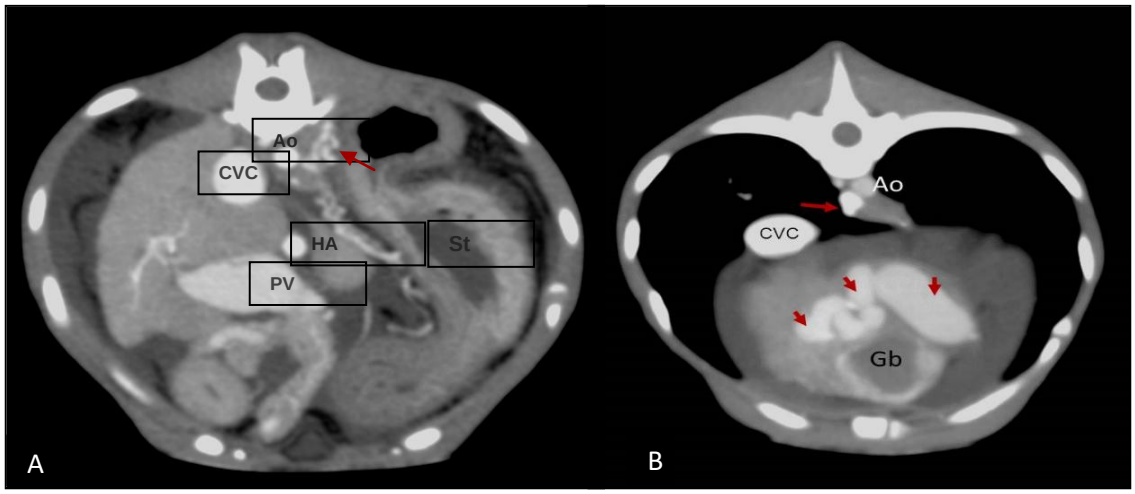

Fig. 4. Transverse computed tomographic (CT) images of the abdomen made during the arterial phase of a dual-phase CT. A: Collateral veins are observed at lesser curvature of the stomach (arrow). The caudal vena cava (CVC), portal vein (PV) and hepatic artery (HA) are dilated. B: The entrance of the extrahepatic shunt into the dilated azygos vena (arrow). Arrowheads: dilated and tortuous portal veins in the left medial hepatic lobe. Ao: aorta; St: stomach; FF: free peritoneal fluid; Gb: gallbladder.

Due to the complexity of the case and the inability to identify an afferent vessel, medical management consisting of oral furosemide (2mg/kg every 24 hours), spironolactone (1mg/kg every 24 hours) and lactulose (333mg/kg every 12 hours) was recommended. Nutritional support consisting of low-protein extruded feed (3.6g of crude protein/100 kcal) was also prescribed. These foods are made with plant protein sources (hydrolyzed soy protein) and are specifically indicated for hepatic disease treatment. Maintenance caloric needs were estimated using the following formula: 95 x $BW^{0.75}$.

The patient was followed for 2 months. During this period, treatment recommendations were duly followed, and clinical improvement achieved, with mild (700g) body weight gain, mental alertness, and absence of neurologic signs. The owner did not return for scheduled follow-up appointments but could be reached by telephone call and informed the dog had progressed to death within 5 months of the last follow-up assessment, after repeated convulsive episodes, anorexia and progressive weight loss. Survival time under medical management exclusively was 7 months.

DISCUSSION

Arteriovenous malformations are thought to account for 2% of portosystemic vascular anomalies in dogs (Cocca *et al.*, 2017) and have been described in some case reports and case series (Chanoit *et al.*, 2007; Cocca *et al.*, 2017). Clinical manifestations in this case (hepatic encephalopathy, vomiting, diarrhea, lethargy, weight loss and ascites) are often seen in patients with hepatic arterioportal malformations (Chanoit *et al.*, 2007; Schaeffer *et al.*, 2001; Zwingenberger *et al.*, 2005) and with exception of ascites, also can be observed in dogs with portosystemic shunts. Ascites as well as collateral vein formation and acquired extrahepatic shunts result from portal hypertension (Weisse, 2015).

Likewise, increased serum activity of hepatic enzymes such as alkaline phosphatase and alanine aminotransferase are common laboratory findings in patients with hepatic arterioportal malformations and portosystemic shunt, due to reduced blood flow to the hepatic parenchyma (Chanoit *et al.*, 2007; Yoshizawa *et al.*, 1997).

Imaging findings in this case were consistent with arteriovenous malformation (Chanoit *et al.*, 2007; Schaeffer *et al.*, 2001; Specchi *et al.*, 2018; Yoshizawa *et al.*, 1997; Zwingenberger *et al.*, 2005). Computed tomographic angiography is the gold standard for appropriate diagnosis of arterioportal malformations and is vital to distinguish this type of malformation from portosystemic shunts, since clinical signs, laboratory changes and findings derived from other imaging modalities may be common to both conditions. Most arterioportal malformations affect the right and central hepatic lobes and more than one lobe is involved in approximately 25% of cases (Weisse, 2015). Nevertheless, in the case reported, malformations affected the left hepatic lobes. Portal vessel enhancement in the arterial phase of CTA suggests arterioportal malformation or fistula (Zwingenberger *et al.*, 2005).

Communication sites and in particular the origin of implicated afferent arteries are often difficult to determine (Specchi *et al.*, 2018; Weisse, 2015). Indeed, the origin of compromised afferent arteries could not be accurately detected in this case. Malformations may involve branches of several arteries, such as the right and left hepatic, left gastric, phrenic, gastroduodenal, and other neighboring arteries (Weisse, 2015). Narrowing of the aorta caudal to the celiac and cranial mesenteric arteries in the case described may suggest arterial blood diversion to the portal system (Zwingenberger *et al.*, 2005), a potential cause of caudal hypoperfusion. Caudal hypoperfusion combined with portal hypertension results in congestion, which may explain ascites development and intestinal malabsorption in the case reported. Similar findings have been described in animal and human patients with arterioportal communications (Zwingenberger *et al.*, 2005).

Varices in the wall of the gallbladder, stomach and caudal esophagus were present. These are abnormal dilatation of submucosal vessels in response to increased vascular resistance driven by portal hypertension and are thought to develop from pre-existing vascular canaliculi. However, recent studies suggest neoangiogenesis plays a potential role in varice formation (Fernandez *et al.*, 2004; Kovacs and Jensen, 2019; Miñano and Garcia-Tsao, 2010).

Neurologic signs associated with arterioportal communications reflect the buildup of toxic compounds in the bloodstream due to compromised hepatic function, which manifests as hepatic encephalopathy (Maddison, 2013) and must be distinguished from other hepatic vascular anomalies.

Hepatic lobectomy or ligation of the implicated afferent artery (depending on location) is the surgical treatment of choice for arteriovenous communications. Alternatively, combined lobectomy and glue embolization or glue

embolization alone can be used, particularly in cases involving more than one hepatic lobe. However, surgical treatment options are not fully satisfactory and are often associated with postoperative complications such as portal or mesenteric thrombosis, anemia, ascites, hepatic encephalopathy, icterus, dyspnea, diarrhea, lethargy, hemorrhage, and non-intentional glue spillage. Survival time ranging from 16 to 24 months has been reported following glue embolization and longer survival (141 months) has been achieved in one case submitted to afferent artery ligation, with no clinical signs or need of medical management (Chanoit *et al.*, 2007). Moreover, these surgical procedures are limited to simple arterioportal fistulae and do not provide good outcomes in cases with multiple malformations or fistulae.

Surgical intervention may provide transient resolution of blood flow diversion. Inappropriate surgical procedures may also result in patient deterioration, with potentially negative impacts on future management strategies. Given the vascular complexity of the condition, treatment is often palliative or non-curative in nature (Bertolini, 2019; Chanoit *et al.*, 2007; Specchi *et al.*, 2018; Weisse, 2015).

Successful medical management has been reported in a case of canine hepatic arteriovenous fistula that did not involve acquired portosystemic shunt (Isidoro *et al.*, 2017). In that case, surgical correction was recommended but declined by the owner. Patient survival following diagnosis was 19 months, much longer than the 5 months of this reported dog.

Surgical intervention was not recommended in the case reported due to the anatomical complexity of the vascular malformation, difficulties associated with identification of compromised afferent vessels and presence of acquired portosystemic shunts secondary to portal hypertension. The conservative management consisting of protein-restricted diet and gut microbiota modulation (Laflamme *et al.*, 1993; Maddison, 2013) was prescribed. Low levels of dietary protein limit intestinal production of neurotoxic nitrogen compounds and are thought to mitigate the inflammatory reaction induced by vascular compromise (Shawcross and Jalan, 2005; Tivers *et al.*, 2015). Gut microbiota modulation can be achieved via conservative measures such as antimicrobial therapy, or via more aggressive approaches such as supplementation of fermentable compounds to drive intestinal pH down and decrease ammonia absorption. Intestinal growth of deamination-promoting microorganisms is therefore limited, whereas fecal excretion of azotemic compounds is enhanced (Bongaerts *et al.*, 2005; Wambacq *et al.*, 2016). As in previous arteriovenous fistula case reports in animals (Chanoit *et al.*, 2007; Cocca *et al.*, 2017), treatment with lactulose was too prescribed. In addition to cathartic effects, lactulose reduces intestinal nitrogen compound absorption (Beynen *et al.*, 2001; Serrano *et al.*, 2022). Diuretic agents were also used to alleviate the accumulation of abdominal fluid (Chanoit *et al.*, 2007). Antibiotic was not used in this case because low evidence of clinical improvement (Serrano *et al.*, 2022).

Some limitations must be acknowledged in this case report. The patient died at home and post-mortem examination was not performed. Therefore, portal vessel hypoplasia, described in some cases of arterioportal fistula (Schaeffer *et al.*, 2001), could not be investigated.

CONCLUSION

Arterioportal malformations have significant systemic consequences and are not always responsive to surgical treatment. Conservative treatment is aimed at symptomatic management. However, survival time will depend on the severity of disease-related changes. This therapeutic modality is indicated in cases in which surgery is not an option and resulted in survival time of 7 months in the case described. Computed tomographic angiography was vital for accurate diagnosis and appropriate treatment selection.

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