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CASE REPORT

Presumptive non-cirrhotic bleeding esophageal varices in a dog

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An 8-year-old male American Staffordshire terrier was admitted for evaluation of chronic episodes of ptyalism and hematemesis after exercise. Abnormalities were not detected on routine clinicopathological tests, thoracic radiography, and abdominal ultrasonography. Endoscopic examination revealed a labyrinthine network of severely distended, hemorrhagic esophageal blood vessels. Computed tomography angiography demonstrated a network of para-esophageal vessels that communicated with the celiac artery caudally and the brachiocephalic trunk cranially, consistent with a diagnosis of non-cirrhotic esophageal varices. This is a report of exercise, ptyalism, and hematemesis secondary to presumptive, non-cirrhotic, bleeding esophageal varices in a dog.

KEYWORDS

arteriovenous fistula, endoscopy, esophagoscopy, hematemesis, pancreatitis, portal hypertension, ptyalism

1 | INTRODUCTION

In people, esophageal varices and ascites are the 2 most commonly reported complications of uncompensated liver cirrhosis.[1] An estimated 50% of human patients with portal hypertension caused by cirrhosis develop esophageal varices, and bleeding esophageal varices (BEV) are one of the leading causes of death in these patients.[2,17] In cirrhosis, increased sinusoidal resistance causes an increased hepatic pressure gradient leading to portal hypertension. Collateral overcirculation from the portal to the esophageal venous system can result in severe venous distension and intractable bleeding.

Portal hypertension is classified based on the site of vascular resistance as prehepatic, intrahepatic, or posthepatic with intrahepatic etiologies further classified as presinusoidal, sinusoidal, and postsinusoidal. Prehepatic causes include obstructive (intraluminal) or compressive (extraluminal) conditions including thrombosis, neoplasia, or primary hypoplasia of the portal vein.[4,5] Posthepatic portal hypertension is associated with increased vascular resistance in the hepatic veins or caudal vena cava, and with cardiac pathologies including right-sided heart failure, restrictive cardiomyopathy, and constrictive pericarditis.[5] Intrahepatic sinusoidal pathologies are a common cause of portal hypertension in dogs, including severe, diffuse fibrosis, and cirrhosis.[6] There are also several reports of idiopathic, non-cirrhotic, presinusoidal, and postsinusoidal portal hypertension in dogs.[4–8] In people non-cirrhotic, pre-sinusoidal portal fibrosis accounts for 10%-30% of all cases of variceal bleeding in some parts of the world.[9]

Esophageal varices are an infrequently reported complication of portal hypertension in dogs, although canine experimental models of portal hypertension did result in significant formation of esophageal varices.[3,10] To our knowledge, there are only 3 reports of naturally occurring non-cirrhotic esophageal varices in dogs. In the first report, a dog was diagnosed with esophageal varices caused by presumptive overcirculation to the esophageal venous system arising from congenital arteriovenous fistulae.[11] A larger study described circulation patterns of 13 dogs and 1 cat with portal vein or vena caval increased resistance leading to collateral overcirculation to the esophageal venous system: esophageal varices were seen in 3 of 9 dogs with increased portal resistance caused primarily by venous thrombi, and in 3 of 5 dogs with increased cranial vena cava resistance caused by thrombosis, space occupying masses, or arteriovenous communication.[12] A third report described 14 dogs with arteriovenous communication arising from the bronchoesophageal artery, 4 of which had evidence of esophageal varices.[13] Clinical signs were not associated

Abbreviations: BEV, bleeding esophageal varices; CT, computed tomography; PV/Ao, portal vein to aorta.

with the esophageal varices in these reports. This report presents a case of ptyalism and hematemesis after exercise secondary to naturally occurring BEV in a dog with relevant clinical signs.

2 | CASE HISTORY

An 8-year-old male American Staffordshire terrier weighing 41 kg was admitted for evaluation of a 4-month history of ptyalism and hematemesis after exercise. The dog lived on a horse farm and did have occasion to explore the area unsupervised. The first episode was observed after a vigorous morning walk with the owner. On returning home, the dog displayed severe ptyalism and vomited once. The vomitus was primarily white mucus with flecks of blood. The local veterinarian was consulted, but no abnormality was found on physical examination, and a CBC was within normal limits except for a high normal hematocrit and increased albumin. Abdominal radiographs and a barium study showed no evidence of gastrointestinal foreign body or obstruction. A fecal float was negative for ova and parasites, including Giardia spp. A 3-day course of maropitant and 5-day course of famotidine were prescribed, and 250 mL of subcutaneous fluids were administered. The dosages of maropitant and famotidine were not described in the transmitted medical record.

By the following day, all clinical signs had resolved. Five weeks later, clinical signs returned with several bouts of ptyalism and hematemesis after morning exercise sessions. The dog was referred to a specialty clinic where an ultrasound performed by a board certified internal medicine specialist reported an approximately 5.3 × 2.8 cm hypoechoic lobulated mass in the area of the pylorus. Abdominal computed tomography (CT) was performed 10 days later that showed no evidence of the abdominal mass, with the only abnormality noted being numerous, small hypodense foci in the pancreas. The finding was considered incidental because the surrounding pancreatic fat was normal without any areas of fluid accumulation.

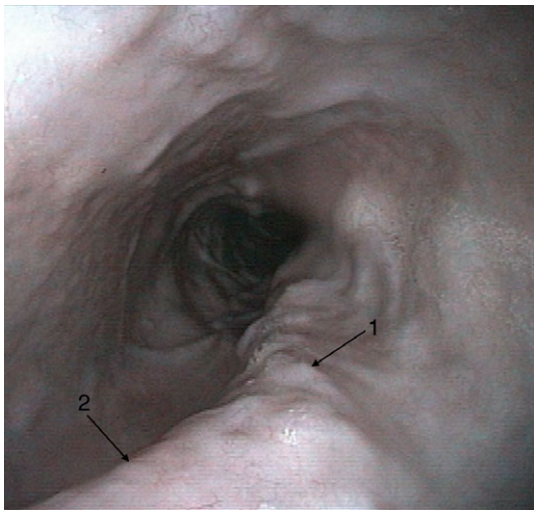

FIGURE 1 Video endoscopy of esophageal lumen, cervical section. The first signs of varices were discovered at the cranial aspect of the esophagus, where bulging vessels are seen surrounding the esophageal lumen (1). The outline of the trachea is visible at the bottom of the image (2)

Over the next 2 months, the dog maintained his normal activity level and an excellent appetite with no diarrhea, coughing, sneezing, or increases in thirst or urination reported. The dog continued to experience intermittent episodes of severe ptyalism, vomiting, and hematemesis after exercise. Approximately, 4 months after the initial signs, the dog was referred to a veterinary teaching hospital for further evaluation.

On presentation, the dog was bright, alert, and responsive. He was ideally conditioned with a body condition score of 5 out of 9 and weighed 36 kg, having lost 4 kg in the preceding 3 months. All physical examination findings were within normal limits. Blood was drawn for CBC and serum chemistry analysis, and urine was collected for urinalysis. The CBC revealed a mild lymphopenia and mild hemoconcentration: lymphocytes, 0.5 thou/uL (reference range 0.9–4.7); eosinophils, 0.0 thou/uL (reference range 0.1–2.1); segmented neutrophils, 8.4 thou/uL (reference range 2.7–9.4); hematocrit, 56%; total protein, 8.2 g/deciliter (reference range 5.9–7.8). All other CBC parameters were within normal limits. Serum chemistry profile showed a slight hyperalbuminemia, 4.3 g/dL (reference range 3.1–4.2) and minimally decreased amylase, 342 U/L (reference range 377–1220) but was otherwise within normal limits. Urinalysis revealed adequately concentrated urine with specific gravity of 1.038 and no evidence of bacteria, glucose, protein, or other abnormal constituents. Orthogonal thoracic radiographs were clinically normal, and no abnormality was detected on abdominal ultrasonography.

Upper gastrointestinal tract endoscopy of the esophagus showed many varicosities along the entire path of the esophagus (Figures 1 and 2). The tortuous distended blood vessels bulged into the esophageal lumen and were pulsatile, giving the appearance of arterial flow. There was evidence of hemorrhagic red spots along several of the varices in the thoracic esophagus. The stomach and small intestine were grossly normal with no evidence of erosions or ulcerations.

The presence of pronounced esophageal varices with pulsatile flow raised suspicion for arteriovenous fistulae, and nonselective CT angiography was performed. The results revealed numerous vascular anomalies, including a network of variable-diameter, tortuous blood vessels that surrounded the cervical, thoracic, and abdominal portions of the esophagus. These blood vessels were connected to the celiac artery caudally, and the brachiocephalic trunk cranially. From the celiac artery, an artery coursed cranially, bifurcated in the cranial abdomen, and then joined the network of variable-diameter, tortuous blood vessels, especially along the abdominal and caudal thoracic esophagus (Figures 3 and 4). From the brachiocephalic trunk, an artery arose after the division of the left common carotid artery and passed caudally to anastomose with the network of vessels surrounding the cervical and cranial thoracic esophagus. The liver was normal in size with normal margins.

On review of the ultrasound and CT, a differential diagnosis of portal hypertension underlying the development of esophageal varices was considered unlikely, given that no ascites, no acquired or congenital portosystemic shunts, no portal vein distention, and no morphologic abnormalities at the liver or spleen were seen. Vessel diameters recorded at the same CT slice were portal vein 13.4 mm, aorta 14.6 mm yielding a normal PV/Ao ratio of 0.92. A recent study found that healthy dogs had a median PV/Ao ratio of 0.95 (0.80–1.15),

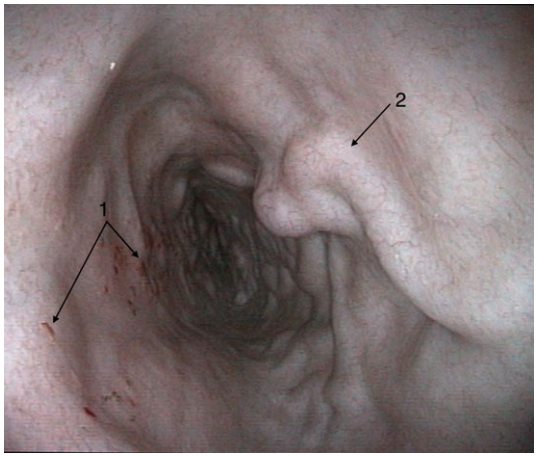

FIGURE 2 Video endoscopy of esophageal lumen, thoracic, and abdominal sections. Hemorrhagic red spots are visible along some of the bulging varices (1). Varices are most pronounced in the thoracic esophagus (2), and continue into the abdominal esophagus

whereas dogs with portal hypertension can have a normal, reduced, or increased PV/Ao ratio.[14]

Given the similarity of CT and endoscopic findings, and the lack of evidence for portal hypertension, a presumptive diagnosis of BEV secondary to arteriovenous fistulae was made. Selective celiac angiography by fluoroscopy was offered to more completely characterize the real-time blood flow characteristics in the esophagus, but declined because the results would not foreseeably alter the dog's

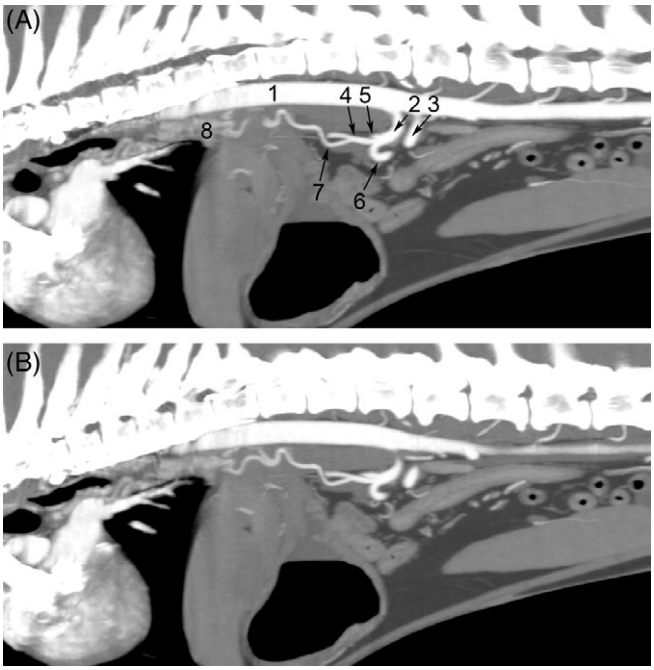

FIGURE 3 Sagittal (A) and parasagittal (B) computed tomography angiography scans of the trunk: aorta (1), celiac artery (2), and cranial mesenteric artery (3). The left gastric artery (4) arises from the celiac artery as do the hepatic artery (5) and splenic artery (6). The esophageal artery (7) arises normally from the left gastric artery but then terminates in an abnormal nest of small-diameter tortuous esophageal blood vessels (8). Image B provides increased visibility of the abnormal communication between the esophageal artery and the terminal esophageal blood vessels

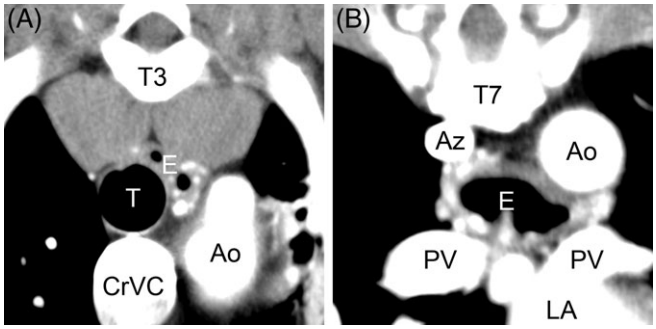

FIGURE 4 Transverse computed tomography angiography scans of the thorax at the level of third (A) and seventh (B) thoracic vertebrae (T3 and T7, respectively): trachea (T). Numerous small-diameter blood vessels (ie, esophageal varices) are observed in or around the wall of the esophagus (E): aorta (Ao), cranial vena cava (CrVC), portal vein (PV), azygous vein (Az), and left atrium (LA)

management. In people BEV's are often surgically addressed via endoscopic techniques to ligate the varicosities.[15] This and other surgical options are also documented in dogs, which have long served as a translational model for esophageal varices.[10,16] However, surgery for naturally occurring esophageal varices in dogs is not documented to the authors' knowledge.

The dog was discharged with a guarded prognosis and instructions for an immediate reduction in the exercise routine, transition to a soft-food diet, and replacement of the choke collar with a chest halter. If these measures were ineffective, use of beta-blockers to reduce blood pressure would be considered. One week, 2 week, and 3 week follow-up calls with the owner indicated that the dog was no longer suffering from its clinical signs, so no medications were started. Long-term follow up with this case revealed that the dog went on to live 4 more years in good health in the absence of clinical signs related to end stage hepatic dysfunction, and ultimately succumbed to pelvic osteosarcoma, an apparently unrelated condition.

3 | DISCUSSION

Naturally occurring esophageal varices have been infrequently reported in the veterinary literature: in Bertolini's proposed radiographic classification system for collateral circulation disorders based on anatomic location at least 3 dogs had evidence of esophageal varices because of portal hypertension.[12] Esophageal varices have also been documented in dogs with increased cranial vena cava resistance and in dogs with congenital or acquired arteriovenous communications.[11,13] However, none of these reports document clinical pathology associated with esophageal varices.

Our investigation of the present case demonstrates probable arteriovenous fistulae originating from both the brachiocephalic trunk and from the celiac artery. The course of the fistulae originating from the celiac artery in this dog is easily interpreted via the CT angiograms. Simultaneous enhancement of the celiac artery, left gastric artery, esophageal arteries, and the torturous esophageal venous system provides morphologic evidence of arteriovenous communication in the abdominal esophagus. Following the exact course of the fistulae in this dog from the brachiocephalic trunk however, was difficult, but

visualization of the final communicating branches between arterial flow and the esophageal venous system near the third thoracic vertebrae strongly supports the diagnosis of arteriovenous fistulae.

In people, several studies have reported that patients with red spots on esophageal varices are considered to be at high risk for variceal hemorrhage, and despite advances in diagnostic and treatment options, mortality for first variceal hemorrhage remains high (20%-35%).[17] The combination of variceal red spots observed on endoscopic exam and multiple episodes of hematemesis concurrent with exercise, in the absence of esophageal or gastric ulcers or erosions, supports a diagnosis of BEV's in this dog. We hypothesize that the esophageal varices became hemorrhagic and partially obstructive when he exercised attributable to increased blood flow into the esophageal venous system via arteriovenous fistulae, leading to ptyalism and hematemesis. The question of why BEV's in this dog did not cause more severe clinical signs remains unanswered, although it is reasonable to propose that BEV's in dogs might not have similar morbidity and mortality characteristics as are reported in people.

Whether arteriovenous fistulae arose from persistent embryonic vessels and only became problematic in this dog's senior years, or whether they were acquired secondary to trauma or another disease process is unknown. A suspected congenital arteriovenous fistula with esophageal varices has been described in a dog however the persistent embryonic vessels were not identified.[11] An intriguing explanation consistent with this dog's history and husbandry is that the fistulae were acquired secondary to trauma, such as a strike from a horse hoof. This could explain why this dog had a mass-like lesion near the pylorus on abdominal ultrasound, that later resolved. The lesion might have been a hematoma. Trauma is a frequently documented etiology for arteriovenous fistulae in people, particularly in combat casualty care when both artery and vein are injured, and can be caused by either blunt or penetrating trauma.[18] The lack of evidence of cutaneous bruising in this dog however, does argue against the notion of trauma-induced fistula formation. Another, perhaps more reasonable explanation for the mass-like lesion that quickly resolved is consolidation of a blood clot in the gastric lumen from swallowed blood.

Given the waxing and waning nature of this dog's clinical signs, chronic pancreatitis-induced portal hypertension could also explain the development of BEV. The splenic vein courses directly over the surface of the pancreas, and extension of inflammation from the pancreas to the perivascular tissues could potentiate splenic vein thrombosis.[19] Pancreatitis-induced splenic vein thrombosis is the primary cause of sinistral portal hypertension in people, which can lead to acquired gastric and esophageal varices.[20,21] Pancreatitis has been documented as a comorbidity in dogs with splenic vein thrombosis, but the development of associated sinistral portal hypertension is not reported.[19]

Prehepatic, intrahepatic, and posthepatic portal hypertension were also not wholly ruled out as potential causes for the development of esophageal varices in this case. Doppler examination to confirm velocity and direction of portal flow was not performed and no direct or indirect measurements of portal pressure were performed. Hepatic histopathology to investigate possible etiologies for intrahepatic portal hypertension was likewise not pursued. Normal portal pressure was presumed, but not confirmed, based on the lack of clinical evidence of ascites, acquired portosystemic shunts or hepatic disease, and the finding of a normal PV/Ao ratio, although dogs with portal hypertension can still have a normal PV/Ao ratio.[14]

In the authors' experience, this dog's disease process represents a rare syndrome. As in people, cases of severe esophageal varices such as the one reported here do appear to potentially lead to BEV in dogs. Based on the findings presented, including esophageal varices as a differential diagnosis for ptyalism and hematemesis could be warranted in some dogs.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

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