CONGENITAL PORTOSYSTEMIC SHUNTS IN THE CANINE

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INTRODUCTION

Portosystemic shunts are anomalous vascular connections between the portal venous system and systemic circulation that allow blood to bypass the liver. Portosystemic shunts divert venous blood draining the gastrointestinal tract, pancreas, and spleen away from the portal vein, and expel it into systemic circulation often through connections with the caudal vena cava, azygous vein, or rarely another systemic vessel.\(^1\,^2\) The portal blood carries a variety of nutrients, endogenous and exogenous toxins, metabolic byproducts, and hepatotrophic hormones, which in a normal animal are received and processed by the liver.\(^3\) In animals with portosystemic shunts, the portal blood carrying these compounds bypasses the hepatic parenchyma and sinusoids, crippling the liver’s ability to process toxins and maintain metabolic homeostasis.\(^4\,^8\) This subsequently results in pathological changes in the liver, as well as severe clinical manifestations of disease and potentially death.\(^4\) Portosystemic shunts have a significant impact on the wellbeing of affected dogs, making it imperative to be able to appropriately recognize, diagnose, and treat affected animals to preserve quality of life.

Portosystemic shunts can be either congenital or acquired, and intrahepatic or extrahepatic.\(^2\) Congenital shunts are present at birth, whereas acquired shunts develop secondary increased portal hypertension from cirrhotic liver disease.\(^7\) Portal vein hypoplasia is a congenital vascular anomaly that results in microscopic shunting of blood through the liver, or microvascular dysplasia.\(^1\,^2\) Microvascular dysplasia is a pathologic change may that may also accompany macroscopic congenital shunts in the liver.\(^1\) Surgical and medical treatments exist for macroscopic congenital portosystemic shunts, but portal vein hypoplasia and acquired shunts can only be treated medically. The purpose of this paper is to discuss the clinical presentation, pathophysiology and pathogenesis, and treatment options available for macroscopic congenital portosystemic shunts.

HISTORY & PRESENTATION
Congenital portosystemic shunts have been reported in 0.18% of all dogs, and 0.05% of mixed breed dogs, with specific breeds being overrepresented suggesting a genetic predisposition for the disorder. No sex predilection has been determined in dogs, but it is possible that male cats are at greater risk than females. In dogs and cats, single extrahepatic shunts are the most common representing 66-75% of all congenital shunts, with a solitary portocaval shunt being the most frequently encountered subtype. Small, purebred dogs are predisposed to extrahepatic shunts, with a significant prevalence in Yorkshire terriers, Cairn terriers, Maltese, Pugs, Dachshunds, and Jack Russell terriers. Intrahepatic shunts represent the remaining 25-33% of congenital shunts, and are found in the greatest frequency in large-sized, purebred dogs, including Irish Wolfhounds, Australian Cattle dogs, Old English Sheepdogs, and Labrador and Golden retrievers.

The clinical presentation of dogs diagnosed with portosystemic shunts varies depending on the volume and origin of blood that is shunted away from the liver. The clinical signs are associated with decreased hepatic metabolic activity and impairment of liver’s ability to clear endogenous and exogenous toxins. Animals may present with acute or chronic illness, and clinical signs may be inconspicuous, nonspecific, or obvious. The most common body systems affected are the central nervous system, gastrointestinal, and urinary systems. Nonspecific findings in animals that present are being “poor-doers” since birth, stunted growth and the inability to gain weight, intolerance of anesthesia, and lethargy or depression. The most common and severe clinical signs in affected animals are those associated with hepatic encephalopathy and are usually worse following a meal. Hepatic encephalopathy occurs in as much as 41-90% of cases, and causes neurologic signs such as, star-gazing, head pressing, intermittent blindness, disorientation, aggression, ataxia, circling, and occasionally seizures or coma. Many animals will have signs of lower urinary tract disease such as hematuria, stranguria, pollakiuria, from formation of ammonium urate crystals that predispose to urinary tract obstruction and secondary bacterial infections. Animals with shunts are predisposed to
ammonium urate crystaluria from decreased hepatic production of urea, resulting in increased excretion of ammonia by the kidneys. Polyuria and polydipsia (PU/PD) is not an uncommon clinical finding, and although the exact mechanism has not been proven, it has been postulated to occur from increased renal blood flow or psychogenic polydipsia from hepatic encephalopathy. Gastrointestinal signs including, vomiting, diarrhea, and anorexia, have been frequently reported. GI hemorrhage from ulceration or parasites has been known to increase signs of hepatic encephalopathy due to increased intestinal absorption of protein-rich blood. Ptyalism and a characteristic copper-colored iris are common findings in cats with portosystemic shunts. Microhepatica and large, irregular kidneys may also be found on physical exam, and ascites is uncommon unless there is significant hypoalbuminemia.

Dogs with congenital portosystemic shunts can be diagnosed as early as early as 6 weeks of age, but the typical age of diagnosis varies depending on when clinical signs present. The majority of congenital shunts are diagnosed before 1 to 2 years of age, but some dogs have been documented to present at ages greater than 10 years. One study compared 124 dogs with congenital portosystemic shunts and showed the age at time of diagnosis ranged from 2 to 73 months, with a mean age of diagnosis being 14 months. Those dogs with extrahepatic shunts were diagnosed between 2 to 73 months with a mean age of diagnosis being 15 months, and the dogs with intrahepatic shunts were diagnosed between 2 and 12 months with a mean age of diagnosis at 5 months. This study supports that dogs with intrahepatic shunts may present with more severe clinical signs at an earlier age than those with extrahepatic due to the larger volume of blood being shunted through the intrahepatic shunt.

PATHOPHYSIOLOGY

Congenital portosystemic shunts are hereditary disorders that occur secondary to failure of closure of the ductus venosus (intrahepatic), or abnormal connections arising between the fetal portal and non-portal abdominal veins (extrahepatic) during embryological development. The portal blood contains a variety of trophic factors, bacterial and intestinal toxins, and nutrients
that the immature fetal liver is incapable of processing.\textsuperscript{3, 4} The ductus venosus is the embryologic vessel that allows the majority of the oxygenated blood flowing from the placenta via the umbilical vein, to bypass the immature fetal liver and return it directly to the heart through the caudal vena cava.\textsuperscript{19} Normally, functional closure of the ductus venosus occurs within approximately 2-6 days after birth, and complete structural closure of the vessel occurs within 3 weeks.\textsuperscript{25} Incomplete or failure of closure of the ductus venosus results in inability to establish normal hepatic circulation and becomes an intrahepatic portosystemic shunt.\textsuperscript{7} Congenital extrahepatic portosystemic shunts arise through persistence of inappropriate vascular connections between the fetal vitelline veins, which develop into the entire extrahepatic portal system and portal vein, and the cardinal veins, which form the non-portal abdominal veins, including the caudal vena cava and azygous vein.\textsuperscript{17, 18} Thus, extrahepatic portosystemic shunts may develop between the portal vein or its tributaries (cranial and caudal mesenteric veins, left gastric vein, splenic, and gastroduodenal vein), and the caudal vena cava or azygous vein.\textsuperscript{8, 18}

The portal blood carries a variety of essential nutrients, trophic factors, bacterial and intestinal derived toxins from the gastrointestinal tract and abdominal organs, as well as 50\% of the liver’s oxygen supply.\textsuperscript{8} When shunting is present, the liver is deprived of nutrients and hepatotrophic factors (glucagon, insulin, insulin-like growth factor, and hepatocyte growth factor), resulting in hepatic atrophy and reduced hepatic metabolic function (gluconeogenesis, urea cycle, uric acid cycle).\textsuperscript{7, 8} In addition, the liver is unable to appropriately clear toxins and metabolites (ammonia, gut-associated encephalopathic toxins, benzodiazepine-like substances, aromatic acids etc.), allowing these substances to persist in systemic circulation.\textsuperscript{4, 7, 8} These substances, most notably ammonia, have neurotoxic affects and contribute to the development of hepatic encephalopathy.\textsuperscript{4} Ammonia is produced in the intestines as byproduct of intestinal protein metabolism, and by conversion of urea to ammonia by urease-producing colonic bacteria. Plasma ammonia concentration is an important diagnostic tool in dogs with portosystemic shunts,
and medical treatment aimed toward decreasing ammonia production and absorption is one of the mainstays of reducing signs of hepatic encephalopathy.4

**DIAGNOSTIC APPROACH & CONSIDERATIONS**

**CLINICOPATHOLOGIC ABNORMALITIES**

In cases of suspected congenital portosystemic shunts a CBC, serum biochemistry, urinalysis, and liver function testing should be among the first diagnostics considered.

**Complete Blood Count**

The most common hematologic abnormality encountered in dogs with portosystemic shunts is a mild to moderate microcytic, normochromic nonregenerative anemia, which is contributed to faulty iron metabolism.5,9 Leukocytosis may also be present due to decreased hepatic removal of bacterial antigens and toxins.5

**Serum Chemistry**

On serum chemistry decreased BUN, albumin, blood glucose, and cholesterol are common findings due to impaired hepatic production.4,5 Increase in liver enzyme activity (ALP and ALT) is also typical.4,5

**Urinalysis**

Decreased urine specific gravity and ammonia biurate crystalluria are expected findings on UA.10

**Liver Function Testing**

Fasting plasma ammonia testing in animals with portosystemic shunts is considered nearly 100% sensitive, whereas ammonia tolerance testing is rarely indicated and potentially dangerous for dogs with high basal ammonia concentrations.4,5,21 Pre and postprandial bile acids will likely be increased, but are less specific than fasting ammonia for diagnosing portosystemic shunts.27

**Coagulation Times**
Prolonged PTT with a prolonged or normal PT have been reported in dogs with portosystemic shunts due to decreased synthesis of clotting factors, but coagulation profiles are usually normal.\textsuperscript{2, 4, 22}

**Protein C Testing**

Protein C is an important vitamin-K dependent enzyme that is produced in the liver that has anticoagulant affects.\textsuperscript{5} Protein C activity in dogs with congenital portosystemic shunts is lower than dogs with portal vein hypoplasia, but higher than dogs in liver failure. It has also been shown to increase following surgical correction of the shunt.\textsuperscript{23} Protein C activity may be applicable in supporting a diagnosis of portosystemic shunts, ruling out other causes of hepatic disease, as well as aiding in monitoring response to surgical attenuation.\textsuperscript{23}

**DIAGNOSTIC IMAGING**

There are various imaging modalities that have been employed to aid in the diagnosis of congenital portosystemic shunts, and these vary in their availability, invasiveness, and diagnostic value.

**Survey Abdominal Radiographs**

Abdominal radiographs are among the fastest, easiest, and cheapest imaging methods that can be utilized to suggest a diagnosis of a portosystemic shunt. Microhaptica and bilateral renomegaly are common findings, but are only suggestive of a diagnosis of a portosystemic shunt.\textsuperscript{10} The use of more advanced imaging is necessary to obtain a definitive diagnosis.

**Abdominal Ultrasound**

Abdominal ultrasound is noninvasive and convenient method for imaging portosystemic shunts. Intrahepatic shunts and extrahepatic shunts can be visualized with this method, but the sensitivity and specificity are highly dependent on operator experience and equipment.\textsuperscript{24} The use of Doppler has been shown to considerably improve sensitivity and specificity to 95% and 98%, respectively.\textsuperscript{25}

**Computed Tomographic Angiography**
CT angiography is quickly becoming the preferred method for diagnosing and visualizing portosystemic shunts in veterinary medicine.\textsuperscript{5} CT is fast, noninvasive, and provides accurate localization of intrahepatic and extrahepatic shunts with a sensitivity and specificity of 96\% and 89\%, respectively.\textsuperscript{26} It provides a 3-dimensional image and vivid anatomic detail of the shunt that is helpful in surgical planning.\textsuperscript{5}

Other Imaging Modalities

Magnetic resonance angiography, trans-splenic/trans-colic portal scintigraphy, and portovenography are other available methods for imaging portosystemic shunts.\textsuperscript{4} These methods are rarely used due to availability of equipment (MRI, gamma camera, fluoroscopy), invasiveness (portovenography), use of radioactive materials (scintigraphy), expense, and the reliability of imaging modalities previously described (CT, ultrasound).\textsuperscript{4, 5}

TREATMENT & MANAGEMENT OPTIONS

Both medical and surgical options are available for the treatment of congenital portosystemic shunts, and are most often used in combination to provide desirable clinical outcomes. Multiple surgical techniques have been described with the goal being occlusion of the shunt to restore normal hepatic blood flow.\textsuperscript{4, 5} The goal of medical therapy is to decrease clinical signs and contributing factors associated with hepatic encephalopathy.\textsuperscript{4, 5} Medical therapy should be implemented preoperatively until clinical signs are managed to decrease anesthetic risk and improve post-operative outcomes.\textsuperscript{5}

MEDICAL MANAGEMENT

In patients with acute signs of hepatic encephalopathy, aggressive stabilization measures should be implemented to decrease circulating levels of ammonia and other neurotoxic substances. Patients should be placed on IV fluids with dextrose if hypoglycemia is present, and potassium supplementation if hypokalemia (from GI losses) is noted.\textsuperscript{1, 28} Lactulose can be given as an enema or orally (if stable). Lactulose acts as a cathartic and acidifies the colon to trap ammonia molecules in the intestines.\textsuperscript{1} Seizures should be controlled initially with a
benzodiazepine and then managed with a long acting anticonvulsant, such as levetiracetam or phenobarbital.\textsuperscript{1,7} The patient should be placed on antibiotics such as, metronidazole, ampicillin, or neomycin, to decrease intestinal bacterial numbers and production of ammonia.\textsuperscript{1,7} Patients with hepatic encephalopathy should be placed on a highly digestible low-protein liver diet such as, Hill’s L/D, to decrease ammonia production.\textsuperscript{1} Animals with gastrointestinal bleeding or parasites should be treated accordingly to reduce protein in the intestines.\textsuperscript{1} Nutraceuticals such as, SAMe, ursodiol, milk thistle, and vitamin E, are rarely indicated for animals with portosystemic shunts that are amenable to surgical treatment.\textsuperscript{4} Medical management should be continued during the preoperative period until the patient is clinically stable.

**SURGICAL MANAGEMENT**

Multiple surgical options are available for congenital portosystemic shunts, and treatment options differ depending on the type of shunt present. Common surgical techniques for extrahepatic shunts include gradual occlusion over 2-5 weeks with placement of an ameroid constrictor or cellophane band, or acute ligation using nonabsorbable silk suture.\textsuperscript{5} Intrahepatic shunts are occasionally amenable to ameroid constrictor placement or cellophane banding, but more often require ligation or intravascular occlusion using interventional radiography.\textsuperscript{1,5} Although not necessary, intravascular occlusion of extrahepatic shunts has been described with success.\textsuperscript{29} The main goal of surgical therapy is to provide occlusion of the shunting vessel without development of portal hypertension to prevent formation of multiple acquired shunts.\textsuperscript{5} Gradual occlusion methods are preferred when possible because they are less likely to result in portal hypertension and other postoperative complications.\textsuperscript{4}

**Anatomical & Surgical Considerations**

The majority of extrahepatic portocaval shunts can be found entering the caudal vena cava cranial to the renal veins and caudal to the hepatic veins at the level of the epiploic foramen.\textsuperscript{4} The only vessels that should be found in this region of the vena cava are the phrenicoabdominal veins, and any other vessel within this area are anomalous.\textsuperscript{1} Portoazygous
shunts pass through the diaphragm and are usually found near the esophageal or aortic hiatus.⁵ Many other variants of extrahepatic shunts and their anatomic locations have been described in the literature.³⁰ Extrahepatic shunts should be occluded as close to their termination on the caudal vena cava or azygous vein as possible to ensure all shunt tributaries are included.⁴ A thorough exploratory is necessary during surgery to rule out the rare possibility of a second shunt.¹¹

Intrahepatic shunts are often difficult to identify during surgery and may require the use of intraoperative imaging such as ultrasound or interventional radiology.⁹ Intrahepatic shunts are managed differently depending on their location, but are treated by occluding/ligating the hepatic vein draining the shunt or the branch of the portal vein supplying the shunt.³¹

**Cellophane Banding & Ameroid Constrictors**

Cellophane bands and ameroid constrictors are the most commonly used methods for gradual occlusion of congenital portosystemic shunts. Both methods yield good outcomes, and technique preference is usually up to the surgeon.⁵ Ameroid constrictors are made up of ring of casein that is surrounded by a stainless steel ring. The internal diameter of the ameroid constrictor should be approximately equal to or slightly larger than that of the shunting vessel.⁵ Initial occlusion of the shunt is facilitated by swelling of the casein protein with water, reducing the internal diameter by 32%.³² Further closure of the shunt is facilitated by fibrosis that occurs over 2-5 weeks.²

Cellophane bands are constructed from nonmedical grade cellophane.⁴ The cellophane is folded on itself into long strips that are placed around the shunting vessel and secured with hemoclips in an alternating fashion.³³ Securing the band with or without partial occlusion of the vessel has been shown to be effective, but portal pressures need to be monitored if partial occlusion is desired.³⁴ Gradual occlusion with cellophane banding occurs over 4-6 weeks facilitated by an initial inflammatory reaction followed by a foreign body reaction.²

**Silk Suture Ligation**
When using suture ligation, the amount of occlusion applied to the vessel should be based on evaluation of portal pressures. Portal hypertension can be assessed by monitoring changes in the patient’s abdominal viscera with each degree of occlusion, or by measuring portal pressures via a catheter placed in the jejunal vein. Signs of portal hypertension, and therefore too much attenuation, include pallor or cyanosis of intestines, intestinal hypermotility, and cyanosis or edema of the pancreas. Most patients will not be able to tolerate complete occlusion.

Interventional Radiology

The use of interventional radiology, such as fluoroscopy, to facilitate intravascular occlusion of shunts is more commonly employed for intrahepatic shunts because of the availability of surgical procedures for extrahepatic shunts. However, acute intravascular occlusion using the Amplatzer vascular plug has been described successfully in 6 out of 7 dogs with extrahepatic shunts. The percutaneous transjugular coil embolization technique is available at only a few institutions, and has been shown to significantly reduce intraoperative complications and mortality in patients with intrahepatic shunts compared to other treatment options. This is a minimally invasive technique that uses jugular access to deploy a thrombogenic coil in the shunt while using fluoroscopy for visualization.

Complications & Post-op Management

Dogs undergoing surgical correction of portosystemic shunts must be vigorously monitored for signs of portal hypertension, hypoglycemia, hypotension, and seizures postoperatively. Abdominal pain and distention, increased capillary refill time, pale mucus membranes, and GI hemorrhage are characteristic clinical signs of portal hypertension. Medical management with lactulose and a low-protein diet should be continued for a minimum of 2-4 weeks following surgery, and liver function testing and serum biochemistry should be rechecked 2-3 months following surgery. Medical management should continue until liver function testing is normal and any clinical signs are resolved.

EXPECTED OUTCOME & PROGNOSIS
One study showed long term survival for dogs undergoing surgical treatment (MST – 2,156 days) for congenital shunts was significantly greater than dogs that received medical management alone (MST – 836 days). In addition, frequency and severity of clinical signs were considerably lower in dogs receiving surgical treatment, and age at time of diagnosis did not influence survival times. Another study showed that the severity of histologic changes in liver biopsies at the time of surgery did not correlate with prognosis.

Ameroid constrictor placement or cellophane banding yields a great prognosis for dogs with extrahepatic shunts, with 85% of dogs being clinically normal at 4 months. Due to the difficulty of surgery, dogs with intrahepatic shunts experience higher intraoperative mortality rates between 5 and 25%. The use of interventional radiology techniques in dogs with intrahepatic shunts significantly decreases surgical mortality rates, and long term survival is improved when dogs are placed on omeprazole for life. This is due to the fact that dogs with intrahepatic shunts are more predisposed to gastrointestinal ulceration.

CONCLUSION

Congenital portosystemic shunts are heritable vascular anomalies that can result in significant debilitating illness in affected dogs. Surgical and medical treatment options exist, with the best prognosis being achievable though surgical intervention. Being able to diagnosis and effectively treat dogs with portosystemic shunts as a veterinarian is critical in ensuring quality of life and survival.

REFERENCES


33. McAlinden AB, Buckley CT, Kirby BM. Biomechanical evaluation of different numbers, sizes and placement configurations of ligaclops required to secure cellophane bands. Vet Surg 2010;39:59–64.
