PORTOSYSTEMIC SHUNTS
DIAGNOSIS, STABILISATION AND POSTOPERATIVE COMPLICATIONS

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Introduction

Portosystemic shunts are abnormal vascular communications between the portal venous system and the systemic venous circulation. They divert blood from the abdominal viscera to the heart, bypassing the hepatic sinusoids and carrying intestinal absorption products directly to the systemic circulation. The congenital form of the disease is usually that of a single shunting vessel. Single congenital portosystemic shunts (PSS) were initially managed medically and the prognosis for long-term survival was poor. With an increased understanding of shunt pathophysiology surgery has become the treatment of choice and survival rates after complete or partial attenuation have increased to 80% or greater, particularly following the introduction of techniques to cause gradual shunt occlusion.

Anatomy

The liver receives 20% of the total cardiac output and the portal vein transports 75-80% of total hepatic blood flow. The portal vein transports venous blood from the abdominal viscera to the liver. In dogs and cats the portal vein is composed of 1) the splenic vein, 2) the cranial mesenteric vein and 3) the caudal mesenteric vein. In dogs the gastroduodenal vein also empties into the portal vein.

Portosystemic Vascular Anomalies

PSS can be classified as extra-hepatic or intra-hepatic, single or multiple and congenital or acquired.

Single intrahepatic and extrahepatic PSS are congenital and are usually diagnosed in immature animals. Single intrahepatic PSS is found principally in large breed dogs such as **Old English Sheep Dogs, Doberman Pinschers, Golden and Labrador Retrievers, Irish Setters, Samoyed and Irish Wolfhounds.**

Single extrahepatic PSS occurs primarily in small breed dogs such as **Yorkshire Terriers, Schnauzers, Poodles, West Highland White Terriers Maltese Terriers, Shih Tzus and Daschunds.**

Multiple extrahepatic PSS are associated with chronic increase in hepatic portal venous resistance and portal pressure and is manifested by numerous small tortuous vessels.

CLINICAL SIGNS

Signs may develop as early as a few months of age or as late as several years.

Signs associated with PSS commonly involve the nervous system, gastrointestinal tract and urinary tract.

- Hepatic encephalopathy develops when the liver fails to remove enteric derived products such as ammonia, mercaptans, short-chained fatty acids and aminobutyric acid. Shunts also induce high levels of endogenous benzodiazepines. Abnormal neurological findings include lethargy, depression, behavioural changes, disorientation, pacing, blindness, head pressing, seizures and coma.
- Gastrointestinal signs include anorexia, vomiting, diarrhoea, polyphagia and ascites.
- Urinary disease is manifested by the presence of ammonium biurate stones and crystalluria, along with polyuria and polydipsia.

Cats may have copper-coloured irises and display ptyalism. Dogs and cats with no other clinical signs may have a poor growth rate, weight loss, hair loss or exhibit a prolonged sedation effect from anaesthetic drugs since most are hepatically metabolised.

Hepatic Encephalopathy

Ammonia is produced from the hydrolysis of urea by colonic urease-producing coliforms and anaerobic bacteria and by bacterial deamination of dietary amino acids. Normally ammonia that has been absorbed by the intestines is carried to the liver by the portal vein where it is converted to urea through the Krebs-Henseleit urea cycle. With PSS and hepatic dysfunction, ammonia is no longer adequately metabolised and is diverted to the systemic circulation.

- Ammonia is a key cerebral toxin that exerts direct effects on neurotransmission in the brain.
- The brain lacks an effective urea cycle and thus has limited ability to handle excessive ammonia concentrations.
- Blood concentrations of ammonia do not directly correlate with the severity of hepatic encephalopathy and many other toxins such as mercaptans and short chain fatty acids are thought to act synergistically with ammonia

Mercaptans are by-products of dietary methionine degradation by intestinal bacteria. Mercaptans augment the cerebral effects of ammonia and short chain-fatty acids, resulting in depressed cerebral function and coma.

GABA (gamma-aminobutyric acid) is an important inhibitory mediator in the CNS. The intestinal bacteria Escherichia coli and Bacteroides fragilis produce substances with GABA-like activity. Shunting of portal blood results in increased concentrations of these compounds and gastro-intestinal haemorrhage increases their absorption.

Precipitating factors of hepatic encephalopathy include various drugs, protein overload, hypokalemia (which potentiates renal ammonia production), alkalosis, transfusion of stored blood, hypoxia, hypovolemia, gastro-intestinal haemorrhage, infection and constipation. Increased sensitivity to sedative, analgesic, tranquilliser and anaesthetic agents may induce coma in animals with PSS, even when normal doses are given.

DIAGNOSIS

History and physical examination may suggest the presence of a PSS. Clinical pathology data helps to further define the disease. Common findings include hypoproteinaemia, hypoglycemia, hypocholesterolaemia and low urea. Hypoproteinaemia is caused

principally by decreased hepatic protein production and metabolism. Plasma albumin is produced solely by the liver, accounts for 55-60% of the total plasma protein in most mammalian species and hypoalbuminaemia is one of the most common abnormalities detected in animals with PSS (although less commonly in the cat than the dog). Apart from decreased hepatic synthesis due to insufficient hepatic mass, other suggested causes of hypoalbuminaemia include anorexia , intestinal blood loss due to bowel inflammation and blood volume expansion due to sodium and water retention. Causes of hypoglycemia include decreased hepatic glycogen stores, decreased responsiveness to glucagon and abnormal insulin metabolism and response.

PSS often causes a mild anaemia with microcytosis. Causes of anaemia include 1) decrease RBC production because of poor nutritional status, low erythropoietin levels, decreased transferrin production and subsequent poor iron utilisation, 2) decreased survival of RBC's and 3) chronic RBC loss secondary to coagulopathy. Leukocytosis is reported more frequently in dogs than cats.

The liver enzymes ALP and ALT are usually normal to slightly elevated. Cholestasis is not a prominent feature of PSS and elevated ALP in a young animal may be of osseous origin.

Urinalysis often reveals low specific gravity and the presence of ammonium biurate crystals (21-74% of dogs). Decreased hepatic ammonia detoxification and uric acid metabolism result in increased renal excretion of ammonia and uric acid with eventual precipitation of ammonium biurate crystals.

The most definitive biochemical evaluations of PSS are serum bile acids and blood ammonia. (Bile acids are equivalent to blood ammonia concentrations in detecting deficiencies in hepatic mass or circulation but unlike ammonia, they are not labile in blood and are easily quantified in samples handled routinely).Serum bile acids are synthesised in the liver from cholesterol. After conjugation with Taurine, they are secreted into bile and stored in the gall bladder. Prandial neurohormonal and hormonal factors stimulate gall bladder contraction and excretion of bile acids into the small intestine, where they form micelles that enhance lipid emulsification and absorption. **At least 95% of intestinal bile acids are actively reabsorbed in the ileum and are transported back to the liver by the portal blood.** Normally post prandial bile acid concentrations are minimally increased because of rapid first- pass hepatic extraction.

Serum bile acids are elevated with cholestasis, jaundice and PSS.

Prolonged fasting may result in normal bile acid concentrations in animals with PSS thus fasting and 2 hour post prandial samples should be analysed.

Liver function tests such as evaluation of pre and post prandial bile acids are more definitive for diagnosing hepatic disease than routine biochemistry profiles but serum bile acid values cannot differentiate liver diseases, because abnormal values overlap widely. **Serum bile acid concentrations are dependent on adequate hepatoportal circulation, functional hepatic mass and normal intestinal absorption**. Abnormal serum bile acids in the absence of jaundice and abnormal liver enzyme activity indicates metabolically quiet liver disease associated with hepatoportal perfusion abnormalities or severely reduced hepatic mass.

Diagnostic Imaging

Survey radiographs normally reveal a small liver, however this is a subjective evaluation. Ammonium biurate calculi can be seen radiographically if there is magnesium or calcium present in the uroliths.

Ultrasonography can be useful in diagnosing PSS- a skilled ultrasonographer can detect the presence of a shunt and its exact location although extrahepatic shunts are more difficult to visualise; their location often being obscured by gas-filled intestines.

Various techniques for portal venography have been reported, including direct splenic injections, mesenteric vein portography or cranial mesenteric angiography. All of these are invasive procedures requiring general anaesthesia and surgical intervention.

Nuclear scintigraphy using Technetium pertechnetate (^{99m}Tc) is a safe and non-invasive method of confirming PSS but accuracy is operator dependent and this technology does not definitively locate the position of the shunt nor does it differentiate between single and multiple shunts.

PSS IN CATS

Central nervous system signs are the predominant symptom in cats occurring in greater than 75% of cases. Unique clinical signs associated with feline hepatic encephalopathy are hypersalivation and a tendency to lick constantly in an attempt to swallow secretions. The constant licking may be confused with an upper respiratory tract infection and be inadvertently treated as such. 33% of cats have a history of grand mal seizures. Since idiopathic epilepsy is so uncommon in cats, any young cat with the onset of uncontrollable seizures should be evaluated for the possibility of a PSS. On physical exam most cats are thin or stunted in growth and have a history of anorexia, occasional vomiting and intolerance to a high protein diet. Unlike dogs, haematology is usually normal. Another difference seen in cats versus dogs is that hypoalbuminaemia is rare, occurring in less than 5% of cases. Blood urea nitrogen levels are lowered in the majority of dogs but only in about 50% of cats. Ammonium urate crystalluria is seen in only 10-33% of cats and cystic calculi are rare.

In cats approximately 80% of PSS are extrahepatic, 10% are intrahepatic and 10% are acquired. The most common extrahepatic shunt is the communication between the left gastric or splenic vein and the caudal vena cava or azygous vein.

MANAGEMENT

Medical therapy of PSS should be instituted before surgery. If surgical intervention is not successful, medical management may alleviate clinical signs. Prevention of signs of hepatic encephalopathy is a primary goal of treatment. Low protein diets (initially 6% for dogs and 12% for cats) should be initiated i.e Waltham's Hepatic Support, Waltham's Low Protein diet or Hills K/d diet.

The protein load may be gradually increased depending on the individuals response. This is important since by restricting protein in an already malnourished or stunted animal, the neurological status may improve but the nutritional status will deteriorate. If insufficient protein is provided, catabolism of body proteins occurs and this in turn leads to increased blood ammonia concentrations. Those animals that are not

showing signs of hepatic encephalopathy should be fed a regular commercial pet food, with normal protein levels.
If home-made diets are used vegetable and dairy based diets should be recommended.

- Cottage cheese- provides high biologic value protein but is low in arginine
- Egg - provides a source of arginine but it should not be used as the sole protein source due to relatively high levels of methionine which is converted to mercaptans by GI bacteria
- Fish- again not as the sole protein source since it is high in purines which can increase uric acid production and lead to urate calculi formation

Whatever diet is fed, frequent small meals should be given to minimise hypoglycemia.

Gastro-intestinal haemorrhage serves as a major source of metabolisable nitrogen for the intestinal bacteria, resulting in the production of large amounts of ammonia. Liver disease often results in gastrointestinal bleeding secondary to gastritis and gastroduodenal ulceration. These occur as a result of altered gastric mucus production, decreased epithelial cell turnover, reduced mucosal blood flow secondary to portal hypertension and hypergastrinemia secondary to decreased hepatic clearance of gastrin or elevated circulating bile acid levels that stimulate gastrin release. If gastric irritation or ulceration is suspected treatment with H_2 receptor blockers such as ranitidine or cimetidine and a mucosal cytoprotective agent (sucralfate) should be instituted.

Non absorbable intestinal antibiotics that are effective against urea-splitting bacteria should be administered to decrease populations. Enemas can be used to decrease colonic bacteria and substrates. Lactulose, a synthetic dissaccharide, is hydrolyzed in the colon to organic acids that increase faecal water loss osmotically and acidify colonic contents. Acidification traps ammonia in the colon as ammonium and alters colonic bacterial flora. Alteration of intestinal transit time associated with the osmotic diarrhea decreases the time available for the production and absorption of ammonia. Traditionally neomycin has been used (orally or rectally) in combination with Lactulose- however in some patients Neomycin may actually inhibit the bacterial degradation of Lactulose, decreasing its efficacy. Metronidazole has also been used and although effective neurotoxicity is a potential side effect. Since it may be difficult to differentiate between Metronidazole induced neurotoxicity and worsening of hepatic encephalopathy its use is not recommended. Ampicillin is a safe, cheap and effective alternative to both Neomycin and Metronidazole.

Supportive care with intravenous fluids may be necessary in encephalopathic or debilitated animals. It is important to correct dehydration since pre-renal elevation of urea can cause its back diffusion across the intestinal mucosa, where it can be transformed to ammonia by the intestinal bacteria, worsening hepatic encephalopathy. The veterinary literature recommends avoiding lactated solutions since the lactate anion is converted to bicarbonate in the liver- however this is one of the last functions to be lost by the diseased liver. Careful monitoring of electrolytes, glucose and protein is necessary. Anorexic patients or those that have vomiting or diarrhoea may be hypokalemic and require potassium supplementation.

Patient stabilisation is extremely important before surgery. Although rarely required preoperative blood or plasma transfusions may be necessary in some cases. The type and duration of medical management should be based on evaluation of clinical signs and laboratory data and should be continued postoperatively until clinical and lab assessment indicate liver function has improved.

Cystitis should be treated with appropriate antibiotics based on culture and sensitivity: the response may be poor if uroliths are present. Urate uroliths may respond to a low protein diet; renal calculi have reportedly dissolved after shunt ligation.

CLINICAL SIGNS ASSOCIATED WITH HEPATIC ENCEPHALOPATHY

- Hyperactivity/excitement
- Depression
- Head-pressing (common in dogs, uncommon in cats)
- Circling/pacing
- Central blindness-bumping into objects
- Physcogenic polydipsia/polyuria (common in dogs, uncommon in cats)
- Aggression (common in cats, uncommon in dogs)
- Fits (common in cats, uncommon in dogs)
- Hypersalivation (common in cats, uncommon in dogs)
- Coma

Typical Findings

ABNORMALITY	MECHANISM
Biochemistry	
• Increased bile acids (pre and post prandial)	shunting of portal blood
• Increased fasting ammonia	shunting of portal blood reduced urea cycle capacity
• Low blood urea	ammonia bypassing liver reduced urea cycle capacity reduced protein diet renal washout
• Mildly raised liver enzymes	altered hepatocellular organelle activity
• Reduced total protein (albumin, globulin or both)	reduced hepatic formation insufficient intake
• Hypoglycaemia	reduced hepatic glycogen stores abnormal metabolism or responsiveness to insulin, corticosteroids and glucagon

Haematology	
Mild anaemia	Altered iron metabolism? Altered red cell survival/production
Red cell microcytosis	Altered iron metabolism
Urinalysis	
Low specific gravity	Reduction in renal medullary concentrating ability due to low blood urea and washout (PU/PD) Altered metabolism of cortisol and antidiuretic hormones. Alterations in portal vein osmoreceptors
Uric acid or ammonium urate crystalluria /calculi	Reduced hepatic conversion of uric acid to allantoin. Increased blood ammonia

ACUTE ENCEPHALOPATHIC CRISIS

- Remove precipitating cause (i.e stop dietary protein intake, treat constipation, treat gastrointestinal ulceration, stop blood transfusion)
- Nil by mouth for 48 hours
- Administer intravenous fluids (saline or dextrose saline) for maintenance and to reverse any dehydration and ongoing losses
- Ensure the animal is not hypokalemic. If potassium is low add 5mmol per 250ml fluids. Do not administer potassium faster than 0.5mmol/kg/hour
- Dextrose should be administered initially to treat a seizuring PSS patient. This helps drive an energy dependent reaction within the brain in which ammonia is metabolised to glutamine, helping to lower CNS ammonia levels. Give 50% dextrose at 1ml/kg IV as an initial emergency measure in a seizuring animal, then 5 to 10% dextrose in IV fluids
- Avoid fluid overload which will worsen cerebral oedema
- Decrease colonic toxin production and absorption by administering enemas: warm water, warm 10% povidone-iodine or 50% lactulose. Repeat every 6-8 hours
- Administer antibiotics i.e Ampicillin as a prophylaxis against bacteraemias of gut origin
- To control seizures if dextrose administration is unsuccessful administer propofol or diazepam.

  Use a bolus of Propofol at 1mg/kg to abolish seizure activity (repeated if necessary), then maintain the animal on 0.1mg/kg/minute infusion. This dose is low enough that the animal is often conscious and able to eat whilst on the infusion. The infusion is continued for 12- 24 hours.

  Diazepam is best given in increasing increments at 0.25-0.5mg/kg IV

- AVOID barbiturates and acepromazine- these interact with GABA receptors and require hepatic inactivation.

POSTOPERATIVE COMPLICATIONS

Immediate

- prolonged recovery from anaesthesia
- hypoglycemia
- hypothermia
- portal hypertension- clinical signs of which vary and can be divided into 3 groups

1. Mild ascites- usually resolves in 7-14 days
2. Ascites and signs of hypovolemia. Some of these animals can be managed with colloid/crystalloid volume expansion
3. Acute abdominal distension, pain, haemorrhagic diarrhoea and cardiovascular collapse. Patients in this category require aggressive circulatory support and exploratory laparotomy to remove the ligature or thrombus from the shunt vessel. With the introduction of gradual occlusion techniques such as the Ameroid constrictor, acute portal hypertension is unlikely, however it may be seen due to the weight of the device causing kinking and hence premature occlusion of the shunt

- seizures- can be seen upto 3-6 days postoperatively and are a poorly understood complication. It has been suggested that they are caused by altered CNS metabolism following shunt ligation. Treatment is as mentioned above.
- pulmonary edema

Medium to Longer term

- Wound dehiscence
- Vomiting- continued use of H_2 blockers and sucralfate may be necessary in some patients
- Failure to abate clinical signs/recurrence of clinical signs.

Possible explanations include

1. Failure to accurately identify the shunt vessel
2. Inadequate occlusion of the shunt
3. Development of multiple shunt vessels secondary to portal hypertension
4. The presence of a second congenital shunt vessel that was not detected at the original surgery

Other

- chyloabdomen
- failure of dissolution of uroliths and obstructive uropathy