

Gastrointestinal ulceration in dogs with portosystemic shunt

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Summary

Portosystemic shunt (PSS) in dogs is a common abnormality in which blood from the intestines bypasses the liver flowing directly to the systemic circulation through an aberrant vessel. The lack of hepatic detoxication can lead to a fatal outcome. Treatment of choice is a surgical occlusion of the shunt. Gastrointestinal ulceration/erosion (GUE) has been described as one of the numerous clinical consequences of PSS. As these lesions are a severe complication, and seem to be underestimated, this review presents the current knowledge about GUE in dogs with PSS. Although the pathogenesis of these lesions is not clear and experimental data are scarce, we conclude that proton pump inhibitors should be administered pre- and postoperatively to dogs with PSS to reduce the incidence of GUE and thus increase the recovery rate.

Keywords: portosystemic shunt, gastroduodenal ulcers, dogs

Portosystemic shunt (PSS) is an abnormal vascular connection between the portal vein system and the systemic circulation, typically the caudal vena cava or the azygos vein (16, 17, 25, 33). As a result, portal blood containing not only nutrients, but also toxins extracted from enteral digestion, bypasses the liver and enters systemic circulation without detoxication. The resulting disease occurs in different mammalian species, including dogs and less often cats. Though in small animals it may be acquired, this anomaly is usually congenital, mostly as a single vessel, generally not leading to portal hypertension. Congenital PSSs have been more often reported in pedigree dogs than in crossbreeds (16). PSS can be either extrahepatic, when it circumvents the liver, or intrahepatic, when it is located within the liver parenchyma. Intrahepatic shunts are usually diagnosed in large breeds (Doberman Pinscher, Labrador Retriever, Golden Retriever, Irish Setter, Irish Wolfhound, Samoyed), whereas extrahepatic connections are reported mostly in small breed dogs, e.g. Yorkshire Terrier, Cairn Terrier, Maltese, Pugs, Miniature Schnauzer, Miniature Poodle, Dachshund (17, 25). Acquired PSS can result from portal hypertension, liver cirrhosis, or trauma, or can be iatrogenic. This connection is usually extrahepatic and often consists of multiple vessels.

An important function of the liver is detoxication of harmful products that are absorbed into the portal

blood from the intestinal content. In patients with PSS, this detoxication is inefficient, and toxic substances accumulate in the systemic circulation, potentially resulting in hepatic encephalopathy (13, 24). While the role of ammonia in hepatic encephalopathy is well characterized, plenty of other factors are also involved in its pathogenesis, such as oxidative stress, endogenous benzodiazepine-like ligands, astrocyte swelling, g-aminobutyric acid-like molecules, abnormal histamine and serotonin neurotransmission, endogenous opioids, neurosteroids, inflammatory cytokines, and hyperammonemia (15). In addition, ammonium-urate urolithiasis, and systemic inflammatory response syndrome (SIRS) can also result from this anomaly (13, 17, 31). The pancreas may also be affected (10, 11). In addition, in patients with PSS, the liver is usually atrophic and inefficient in plasma protein synthesis, contribution to glucose homeostasis, production of clotting factors, and many other hepatic functions (17, 18, 29).

Though the clinical results of PSS are affected by the degree of blood shunting, they can be severe and potentially fatal. In dogs and cats, the clinical signs can include vomiting and diarrhea, polydipsia, polyuria, growth retardation, urolithiasis, anemia, and a variety of neurological disorders varying from reduced mobility or apathy to seizures and coma (9, 17, 25, 33). In some dogs the neurological signs worsen after a meal.

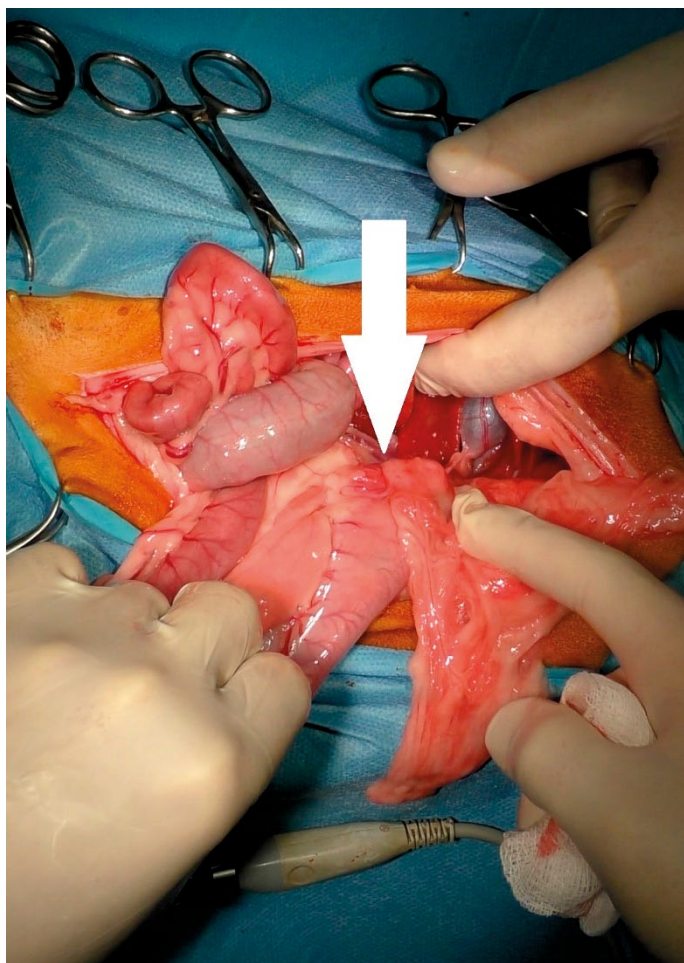


Fig 1. Intraoperative view of a perforating duodenal ulcer that underwent spontaneous omentalization in a 6-month-old Nova Scotia Duck Tolling Retriever with intrahepatic portosystemic shunt. The arrow shows adhesions between the omentum and duodenum

Among different clinical outcomes in patients with PSS, only rarely have gastrointestinal erosions/ulcerations been emphasized (22, 34). Although it has been suggested that dogs and cats with hepatic disease are at an increased risk of gastrointestinal ulceration (2, 14, 22, 30), the recent American College of Veterinary Internal Medicine (ACVIM) Consensus Statement on rational use of gastrointestinal protectants acknowledges that evidence for hepatic disease as a cause of gastroduodenal ulceration is limited and that information on the prevalence of these lesions in dogs with hepatic disease is lacking (20). Considering these discrepancies, and the possible underestimation of the role of gastroduodenal ulceration or erosion (GUE) in the pathogenesis of PSS, we present in this review the current knowledge about GUE accompanying PSS in dogs, augmented by our clinical experience.

GUE in dogs is a well-recognized complication of some pathological states and pharmacotherapies (4, 22, 23, 30). Some dogs with GUE show anorexia, vomiting, distension, abdominal pain, hematemesis, or melena (4, 8, 30). However, clinical signs may be non-specific, for example, lethargy, inappetence,

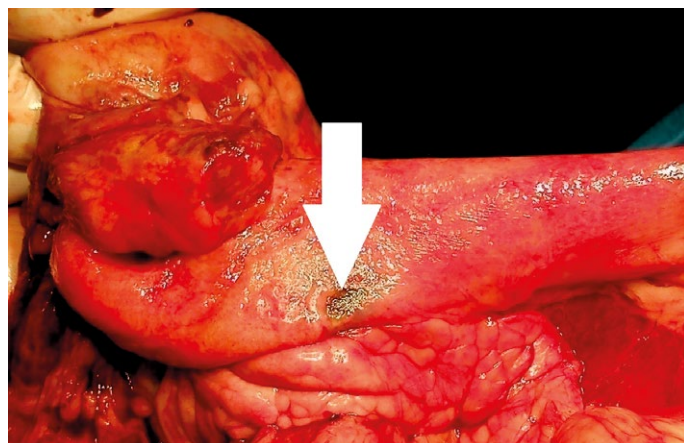


Fig. 2. Intraoperative view of a non-perforating duodenal ulcer (arrow) in a 12-month-old mix breed dog with extrahepatic portosystemic shunt

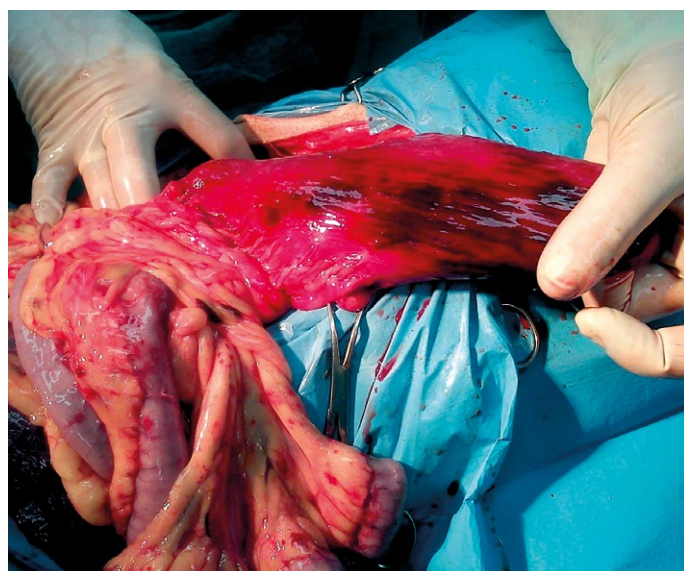


Fig. 3. Intraoperative view of the stomach wall hyperemia due to diffuse hemorrhagic gastritis in a 12-month-old mix breed dog with multiple extrahepatic portosystemic shunts

weakness, weight loss, and elevated or subnormal rectal temperature. Thus, the variety of clinical signs and diagnostic test results often makes the diagnosis very difficult or even impossible (4). The incidence of GUE in dogs is not known. However, undetected and untreated, these lesions can cause substantial morbidity and mortality (30, 34).

By far the most commonly suggested risk factor predisposing to GUE is prolonged administration of nonsteroidal anti-inflammatory drugs (NSAIDs), especially if given concurrently with another NSAID or a corticosteroid (4, 7, 19, 23, 32). These drugs inhibit prostaglandin synthesis in the gastrointestinal mucosa, thus directly affecting the protective barrier of the stomach and small intestine (23). Other factors potentially predisposing to GUE include gastrointestinal neoplasia, hepatobiliary disease, injury of the intestinal wall caused by a foreign body or inflammation, and even strenuous exercise (6, 23, 26, 28, 30).

In humans, abnormal mucosal blood flow due to portal hypertension is the most common cause of gastrointestinal bleeding (12). Impairment of the mucosal defense results from thrombosis of mesenteric vessels because of circulatory stasis, from bacterial overgrowth due to lack of intestinal bile acids, from alterations in gastrointestinal motility, as well as from mucosal edema because of increased vascular permeability (3). Hyperproduction of vasoconstrictors, such as endothelin-1, and increased generation of free oxygen radicals have also been implicated in the pathophysiology. Portal hypertension has also been postulated as an explanation of GUE in dogs (3), but in congenital canine PSS, portal hypertension hardly occurs. In general, gastric acid hyperproduction is crucial in GUE development. The release of gastric acid is stimulated by gastrin. The liver is important for degradation of some forms of gastrin. Therefore, in dogs with hepatic disease, impaired hepatic inactivation of gastrin and/or increased gastrin production stimulated by elevated serum bile acid concentrations, abnormal blood flow, hypoprostaglandinemia, poor mucosal integrity, and abnormal mucus production have been proposed as possible mechanisms for GUE (27, 33). However, not all study results confirm this hypothesis, as in some investigations, low serum gastrin concentrations were found in dogs with liver disease (1, 21). Nevertheless, clinical observations showed that, in dogs with PSS, reduction of gastric acid production in both pre- and postoperative periods by the application of proton pump inhibitors dramatically reduced the incidence of GUE (34). It has also been suggested that coagulation abnormalities could contribute to excessive bleeding in PSS patients. Dogs with PSS have a lower activity of clotting factors compared to control animals, which

results in a prolonged activated partial thromboplastin time (APTT) (18). Occlusion of the shunt increased abnormalities in coagulation immediately after surgery, but hemostasis normalized after complete recovery, in contrast to dogs with persistent shunting (18). Finally, it should be considered that the unclear pathogenesis of GUE in dogs with PSS can be further complicated by the use of NSAIDs or corticosteroids before the diagnosis is made, at least in some of these patients. One could speculate that if the definitive diagnosis is delayed due to nonspecific clinical signs, NSAIDs could be given to such dogs either on the prescription of the veterinarian or by the owner.

As already mentioned, GUE has rarely been described in dogs with PSS. In one study, it was found that signs indicating GUE (melena, hematochezia, consistent blood work changes) or confirmed ulcer/perforation were common among 90 dogs with PSS both before percutaneous transvenous embolization of the shunt (in 15% of the patients) and thereafter (in 21%) (34). There were no significant differences in survival time post-embolization with respect to preoperative gastrointestinal bleeding. However, dogs with postoperative gastrointestinal bleeding had a significantly shorter survival time (929 days) compared with patients without postoperative bleeding (2435 days) (34). More recently, in another study, 4 patients with GUE were found among 13 dogs with congenital PSS (21).

Over the last 7 years, we have operated on more than 200 dogs with PSS, and GUE confirmed during laparotomic occlusion of the shunt, was not an uncommon finding, especially in patients that died in the postoperative period (unpublished data). The most recent 6 patients are presented in Table 1.

Tab. 1. Clinical data of dogs with portosystemic shunt and concurrent gastroduodenal ulceration/erosion (GUE) that we have operated on recently

Patient	Vascular abnormality	The time of GUE diagnosis	Clinical signs, Description of GUE	Surgical treatment	Clinical outcome
6-month-old male Nova Scotia Duck Tolling Retriever	Single intrahepatic right divisional shunt	During laparotomic shunt occlusion	Gag reflex, salivation Perforating duodenal ulcer coated by omentum (Fig. 1)	Additional omentalization	Recovery
12-month-old male mix breed	Single extrahepatic splenocaval shunt	During interventional relaparotomy 30 days after shunt occlusion	Gag reflex, vomiting Non-perforating duodenal ulcer (Fig. 2)	Surgical resection of the ulcer, suturing, and omentalization	Recovery
12-month-old male mix breed	Multiple extrahepatic shunts	During laparotomic shunt occlusion	Vomiting, salivation Stomach wall hyperemia/bleeding due to diffuse hemorrhagic gastritis (Fig. 3)	Treatment ceased due to negative prognosis because of too many shunting vessels	Euthanasia
9-month-old female Yorkshire terrier	Single extrahepatic splenocaval shunt	During interventional relaparotomy 7 days after shunt occlusion	Vomiting, fever, ascites Perforating duodenal ulcer, diffuse peritonitis	Omentalization and peritoneal lavage	Death 2 days after relaparotomy
10-month-old female Polish Hunting Dog	Single extrahepatic splenocaval shunt	During interventional relaparotomy 10 days after shunt occlusion	Vomiting, fever, ascites Perforating duodenal ulcer, diffuse peritonitis	Omentalization and peritoneal lavage	Death a few hours after relaparotomy
11-month-old male Maltese dog	Single extrahepatic gastrocaval	During interventional relaparotomy 6 days after shunt occlusion	Perforating duodenal ulcer, diffuse peritonitis	Omentalization and peritoneal lavage	Death on the day after relaparotomy

Given this experience, we started to administer proton pump inhibitors to all dogs with PSS in both the pre- and postoperative periods, whereas we discourage the application of NSAIDs in such patients. Our first observations after changing the treatment protocol seem to confirm a report by another clinical team claiming that proton pump inhibitors dramatically reduced the incidence of GUE in dogs suffering from PSS (34). Proton pump inhibitors are crucial in the treatment of non-perforating GUE, as reduction of gastric acid production facilitates regeneration of the mucosa. In the case of perforating GUE, resection of the lesion and closing of the gastric/intestinal wall, usually followed by omentalization, is the treatment of choice in small animals (35).

In conclusion, gastrointestinal ulcerations/erosions seem to be an underestimated complication in dogs with portosystemic shunt. This complication negatively influences the postoperative prognosis. Although the pathogenesis of these lesions is not clear and experimental data are scarce, clinical observations suggest that proton pump inhibitors administered pre- and postoperatively to dogs with PSS reduce the incidence of gastrointestinal ulcers, thus increasing the recovery rate.

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