Review

Portal hypertensive gastropathy and gastric antral vascular ectasia (GAVE) syndrome

Portal hypertensive gastropathy (PHG) and gastric antral vascular ectasia (GAVE) syndrome are recently characterised entities that can be associated with gastrointestinal blood loss in patients with and without cirrhosis. Up to 65% of patients with portal hypertension from cirrhosis will develop PHG but it can also occur in the setting of non-cirrhotic portal hypertension. In patients with portal hypertension, PHG is often associated with the presence of oesophageal and/or gastric varices. The mechanisms involved in the pathogenesis of PHG have not been fully elucidated. However, regulation of gastric nitric oxide, prostaglandins, tumour necrosis factor α (TNF-α), and epidermal growth factor (EGF) production may be involved.

The mechanisms involved in the development of GAVE syndrome are also unclear. The classic features of this syndrome include red, often haemorrhagic, lesions predominantly located in the gastric antrum which can result in significant blood loss. More than 70% of patients with GAVE syndrome do not have cirrhosis or portal hypertension. However, in the setting of cirrhosis, GAVE syndrome can be difficult to differentiate from PHG. This distinction is paramount in that PHG generally responds to a reduction in portal pressures whereas those with GAVE syndrome and coexisting portal hypertension generally do not respond to such therapy. This review will focus on the incidence, clinical importance, aetiology, pathophysiology, and treatment of PHG and GAVE syndrome, including differentiation between GAVE syndrome and PHG in the setting of portal hypertension.

Portal hypertensive gastropathy

DIAGNOSIS, INCIDENCE, AND CLINICAL IMPORTANCE

The diagnosis of PHG is made endoscopically. The New Italian Endoscopic Club has classified the severity of PHG based on the presence of four elementary lesions: mosaic-like pattern, red point lesions, cherry red spots, and black-brown spots[1] (fig 1). In mild PHG the gastric mucosa often looks reddened and oedematous with a snakeskin or mosaic pattern. The term scarletina has also been used to describe the early changes of PHG. Severe PHG is defined by cherry red spots which are typically very friable and can actively bleed during endoscopy. In PHG, changes in the gastric mucosa are typically localised to the fundus or corpus of the stomach but PHG-like conditions have been described elsewhere in the gastrointestinal tract, including the rectum, colon, and small bowel. In a study by Gupta *et al*, 61% of 230 patients with cirrhosis and oesophageal varices had PHG, and 14% were found to have portal hypertensive duodenopathy.[2] This study also showed a significant association of PHG with the presence of both oesophageal and gastric varices.

PHG occurs in up to 65% of all patients with cirrhosis and portal hypertension. Approximately 65–90% of those patients have mild PHG whereas 10–25% of patients have severe PHG.[3] The likelihood of developing PHG is thought to be dependent on the aetiology of portal hypertension and the severity of liver disease. However, PHG can occur in patients who do not have cirrhosis. Sarin *et al* reported on 107 patients with portal hypertension of whom 35 had cirrhosis, 25 had non-cirrhotic portal fibrosis, 46 had extrahepatic portal vein obstruction, and two had Budd-Chiari syndrome.[4] Of the 30% who developed PHG over a two month period following the treatment of oesophageal varices, 55% were cirrhotic and 15% had either extrahepatic portal vein obstruction or non-cirrhotic portal fibrosis.[4] In a larger study, patients were followed over a two year period and PHG was found in 56% of patients.[5] PHG was found in 61% of patients with cirrhosis, 54% of patients with non-cirrhotic portal fibrosis, and 20% of patients with extrahepatic portal vein obstruction.[5]

PHG has also been found to be common in patients awaiting liver transplantation. In the study by Zaman and colleagues,[6] 120 patients underwent upper endoscopy as screening prior to liver transplantation. All of these patients had cirrhosis, with 34% being Child A, 49% Child B, and 17% Child C.[6] In this study, 73% of patients had oesophageal varices, 62% had PHG (severe in 23%), and gastric varices were present in 16%.[6] Urata *et al* also found a high incidence of PHG in patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) therapy for portal hypertension associated bleeding.[7] In this study, 83% of patients requiring TIPS had PHG prior to the procedure.

Generally, patients who develop PHG have more severe liver disease, and one could argue that PHG might be a marker of more severe liver disease in patients with cirrhosis. It has also been suggested that the presence of PHG may be a predictor of variceal haemorrhage. A study of 344 patients with cirrhosis and oesophageal varices by Zoli and colleagues[8] examined oesophageal variceal size, colour signs, and the presence or absence of gastric varices or PHG as predictors of future variceal bleeding. The presence of gastric varices and/or PHG were the only independent predictors of variceal bleeding. Not only is PHG common in patients with advanced liver disease but it can on occasion result in clinically significant blood loss.[9] In one study PHG accounted for 8% of non-variceal haemorrhages in patients with liver disease.[9] Although patients with PHG can present with melena, they more commonly present with chronic anaemia which can be transfusion dependent.[8 9]

FACTORS INFLUENCING THE DEVELOPMENT OF PORTAL HYPERTENSIVE GASTROPATHY

Following the increased use of sclerotherapy and banding in the 1980s and 1990s, studies began to report an association between the endoscopic treatment of varices and the development of PHG. One such study by Sarin *et al* found that over a 52 month follow up period, PHG increased dramatically following sclerotherapy.[4] In this study, 10.5% of cirrhotic patients were found to have PHG prior to sclerotherapy whereas 55% had PHG following sclerotherapy.

Abbreviations used in this paper: PHG, portal hypertensive gastropathy; GAVE, gastric antral vascular ectasia; TIPS, transjugular intrahepatic portosystemic shunt; TNF-α; tumour necrosis factor α; TGF-α; transforming growth factor α; EGF, epidermal growth factor; NO, nitric oxide.

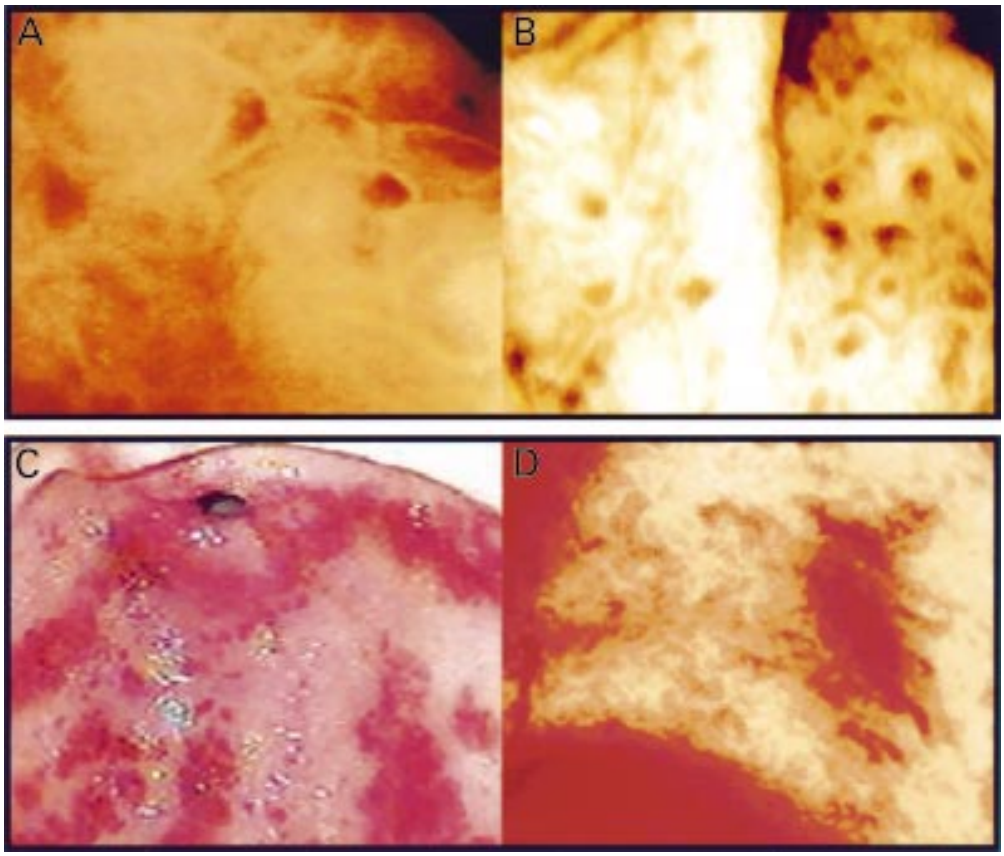

Figure 1 Endoscopic findings of portal hypertensive gastropathy (PHG) and gastric antral vascular ectasia (GAVE) syndrome. PHG: (A, B) with mosaic pattern and cherry red spots. GAVE syndrome: (C) classic or linear pattern, (D) diffuse pattern of involvement.

Furthermore, the presence of PHG was associated with more severe liver disease (87% in Child C *v* 13% in Child A) and PHG occurred more commonly with gastro-oesophageal varices than with oesophageal varices alone. However, there was no correlation between the development of PHG and changes in intravariceal pressure.[4] Other studies have also supported the association of increased PHG following sclerotherapy. A study by Gupta *et al* showed a marked increase in PHG during a two year follow up period after sclerotherapy.[2] Of those patients that required sclerotherapy, PHG was present in 33% of patients prior to sclerotherapy compared with 79% following sclerotherapy.

The issue of whether variceal ligation is better or worse than sclerotherapy in inducing PHG has been raised. In one study that examined this question, 88 cirrhotic patients with variceal bleeds received either sclerotherapy or band ligation.[10] Band ligation resulted in a greater reduction in bleeding and fewer complications. However, there was a greater incidence of variceal recurrence and a greater increase in the severity of PHG in the banding group compared with those patients treated with sclerotherapy.[10] There was no difference in survival between these two modalities. Interestingly, another study had almost exactly the opposite results.[11] In this study, 95 patients were treated with either sclerotherapy or band ligation, with similar rates of success in arresting acute bleeding. The banding group required fewer sessions for obliteration, and rebleeding and complication rates were higher in the sclerotherapy treated group. However, the variceal recurrence rate was higher in those patients treated with ligation, and the development of PHG was almost 10-fold higher in patients treated with sclerotherapy versus banding (20.5% *v* 2.3%).[11] In another study of 90 patients treated with either sclerotherapy or banding by Hou *et al*, the probability of changing the severity of PHG was not related to the method of variceal obliteration.[12] However, those who developed PHG after variceal ligation returned to the baseline pre-eradication level of PHG faster than those who underwent sclerotherapy.[12] Furthermore, they found that the only factor associated with more severe PHG that did not return to pre-eradication level was sclerosant volume. As the increase in PHG following variceal eradication may simply be a consequence of increasing severity of liver disease over time, it seems at present one cannot definitely conclude that obliterating varices truly increases the risk of developing PHG or which mode of variceal treatment carries the greatest risk.

NATURAL HISTORY

The natural history of PHG has been addressed recently in two large studies.[13 14] In the first study, a total of 315 Italian patients with cirrhosis underwent endoscopic examinations every six months for up to three years.[13] PHG was present in 80% and correlated with duration of liver disease, presence and size of oesophageal varices, and a history of previous sclerotherapy. With a median of 18 months of follow up, the authors demonstrated considerable variation over time with deterioration noted in 23%, improvement in 23%, fluctuation over time in 25%, and in only 29% did the PHG remain stable. Bleeding from PHG was uncommon (acute bleeding in 2.5% and chronic blood loss in 10.8%) and bleeding related mortality was lower for PHG than for variceal bleeding (12.5% *v* 39.1%).[13] A study from India examined the natural history of PHG in those patients who had the condition de novo versus those who developed PHG following sclerotherapy.[14] Of 967 patients who presented with variceal bleeding, PHG

(and/or GAVE) was identified in only 88 patients (9.1%). Outcomes were compared in 22 patients who had PHG before and 64 patients who developed PHG after variceal eradication. Patients with pre-existing PHG were more likely to progress (18% *v* 9.4%) and develop bleeding (32% *v* 4.7%).[14] If PHG developed after variceal eradication it was often less severe and transient (resolving in 44% of patients).

PATHOPHYSIOLOGY

It has been clearly shown that in the setting of PHG there is an increased susceptibility to gastric damage. More specifically, an increased susceptibility to non-steroidal anti-inflammatory drug induced damage has been shown both in human and animal studies.[15–17] The role of prostaglandins in the development of PHG is controversial. Human studies have shown increased, decreased, and unchanged levels of prostaglandins in the gastric mucosa whereas animal models of PHG generally show reduced levels of prostaglandins.[18–21] Uniformly, however, a reduction in prostaglandins by inhibitors causes increased gastric damage in both animal models and patients with PHG.[15 16 18]

There has been some debate over gastric perfusion in PHG. In both human and animal models of PHG, gastric blood flow was decreased in some studies[15 16 22–25] but increased in others.[26–31] It is most likely that total gastric blood flow to the stomach is increased in PHG; however, there may be a change in the distribution of gastric blood flow. It has been hypothesised that in PHG there is a relative decrease in blood flow to the mucosa and increased blood flow to the submucosa, muscle, and serosal layers. Furthermore, it has been suggested that in PHG there is an inability to increase blood flow to the mucosa following injury which may account for the increased susceptibility to noxious substances.[16 18]

Other defects in the gastric mucosal defence have been described, such as a decreased gastric mucus layer.[31] An increase in serum gastrin has also been found in PHG, and a relative decrease in parietal cell mass has been noted in animal models of PHG.[32] It appears that *Helicobacter pylori* is not involved in the pathogenesis of this disease state. Three recent studies have shown that the presence and severity of PHG is independent of the presence of *H pylori*.[33–35]

Increased nitric oxide (NO) production has also been implicated in the pathogenesis of PHG[36 37] as it is a potent vasodilator, and increased levels have been described in cirrhosis. Specifically, increased serum NO levels (measured as nitrate/nitrite levels) have been described in patients with PHG.[37 38] Furthermore, those with PHG have increased inducible and constitutive NO synthase levels within the gastric mucosa.[37 38] Interestingly, Lee *et al* reported that aminoguanidine (an inhibitor of inducible NO synthase) therapy in a rat model of portal hypertension corrected the hyperdynamic circulation that occurs with portal hypertension but did not affect the development of portal hypertension or PHG.[39] This suggests that the hyperdynamic circulation, and NO produced via inducible NO synthase, may not play critical roles in the development of PHG.

TNF-α has been implicated in the pathogenesis of the portal hypertension associated hyperdynamic circulation as well as in PHG.[40] TNF-α has numerous proinflammatory actions and has been associated with gastric and intestinal injury. Increased levels of TNF-α have been described in human and animal models of PHG.[40–44] The role that TNF-α plays in the hyperdynamic circulation appears to be through regulation of NO and prostacyclin.[40 41] Specifically, in a rat model of PHG, anti-TNF-α neutralising antibodies caused a reduction in gastric NO synthase activity and normalisation of gastric blood flow.[41 43] Thalidomide, an inhibitor of TNF-α, also has been noted to decrease NO synthase levels and in a rat model of portal hypertension it reduced both portal pressures and the severity of the hyperdynamic circulation: however, effects on PHG were not assessed.[42]

Alterations in growth factors have also been described in PHG. In a rat model of PHG, Wang *et al* noted increased expression of transforming growth factor α (TGF-α) and the EGF receptor in the gastric mucosa and these levels were even more highly elevated in areas of spontaneous gastric injury.[45] In a human study of gastric and duodenal biopsies from patients with PHG there was no change in TGF-α in the stomach but in the duodenum there was a marked decrease in EGF compared with non-cirrhotic control patients.[46] This reduction in EGF may account for the increased risk of duodenal ulcers in patients with PHG.

In summary, numerous changes in several inflammatory mediators have been described in PHG. The most consistent findings appear to be changes in NO production, TNF-α synthesis, and sensitivity to prostaglandin inhibition. There are definite alternations in gastric blood flow in PHG; whether this results in an increase or decrease in gastric mucosal blood flow is an area for debate and further study. The likely causes of these seemingly contradictory findings are most probably a result of both assessing differing severities of PHG and the different techniques used in the measurement of gastric flow. Additional studies in these areas are required to further define the pathophysiology of PHG with the ultimate goal of developing new therapeutic interventions.

TREATMENT OF PORTAL HYPERTENSIVE GASTROPATHY

There have been several studies assessing both medical and surgical interventions for the treatment of PHG. Clearly, H_2 blockers and sucralfate are ineffective in the treatment of PHG.[47] This may be due to the fact that some patients with PHG are hypochlorhydric.[47] The most important pharmacotherapy for PHG involves the use of β blockers. Two small studies have shown that decreasing portal pressure by β blockade with propranolol resulted in decreased gastric blood flow.[27 48] Propranolol has also been found to reduce recurrent bleeding in PHG in a small uncontrolled trial,[49] and this was later confirmed by a larger randomised controlled trial by Perez-Ayuso and colleagues.[50]

Somatostatin and its analogue octreotide may also be effective therapy for PHG. Three studies have shown that somatostatin significantly reduced gastric perfusion in patients with PHG.[29 51 52] Similar findings have also been noted in animal models, with administration of octreotide preventing PHG in carbon tetrachloride treated rats[53] and reducing gastric blood flow in rats with portal vein ligation induced portal hypertension.[54 53] Recently, Kouroumalis *et al* have found that somatostatin may be effective in treating patients with acute bleeding associated with PHG.[51] In this uncontrolled study, 26 patients with severe bleeding from PHG were treated with either octreotide or somatostatin and bleeding was arrested in all 26 patients. However, three patients had further bleeding in hospital and one of these three required a total gastrectomy for continued haemorrhage.[51]

Both vasopressin and glypressin have been shown to cause a reduction in gastric blood flow but at the expense of decreasing mucosal oxygenation.[28 55] However, their role in the management of PHG associated bleeding has not been assessed. Oestrogen and progesterone have been reported anecdotally to reduce bleeding from PHG. In an animal model of portal hypertension, Panes *et al* found that administration of oestrogen and progesterone caused a

Table 1 Summary of therapeutic options for portal hypertensive gastropathy (PHG) and gastric antral vascular ectasia (GAVE) syndrome

Therapy	*Clinical efficacy*	*Reference*
PHG		
Propanolol	Probable	[27 48 49]
Somatostatin and octreotide	Probable	[51 52]
Surgical portocaval shunts	Probable	[56 57]
TIPS	Probable	[7 58]
Rebamide	Possible	[61]
H_2 blockers, PPI, and sucralfate	None	[47]
Vasopressin	Unclear	[28 55]
Oestrogen and progesterone	Unclear	[30]
Liver transplantation	Definite*	[3 60]
GAVE		
Antrectomy and gastrectomy	Definite†	[71 73 74 92 93]
Laser coagulation	Probable	[72 81–84]
H_2 blockers, PPI, and sucralfate	None	[79 88]
Oestrogen and progesterone	Probable	[69 85–88]
Tranexamic acid	Possible	[80 90]
Octreotide	Possible	[94]

*PHG reverses with liver transplantation.
†Antrectomy and gastrectomy for GAVE syndrome in the setting of cirrhosis and portal hypertension has been associated with a high mortality.
TIPS, transjugular intrahepatic portosystemic shunt; PPI, proton pump inhibitors; H_2 blockers, histamine receptor type 2 inhibitors.

reduction in gastric blood flow and portal pressures, suggesting that they may be useful in preventing or reducing the development of PHG.[30]

Portocaval shunts have been used as a surgical means of controlling PHG associated bleeding. A study that followed 12 patients for up to six years after shunt surgery for PHG bleeding found that all 12 had complete resolution of PHG with no surgical deaths and only one patient developed encephalopathy.[56] Soin *et al* reported on eight patients who had no further episodes of PHG associated bleeding following splenorenal shunt.[57] TIPS is also being employed in the treatment of PHG. Sezai *et al* found that endoscopic features of PHG are dramatically reduced following TIPS placement.[58] In a similar study, improvement in PHG was seen in 90% of patients following TIPS therapy for variceal bleeding or ascites.[7] Oesophagectomy and total gastrectomy have also been performed on patients with uncontrollable PHG and variceal bleeding.[59] Liver transplantation ultimately reverses portal hypertension and therefore effectively treats PHG.[3 60] Other therapeutic interventions may be on the horizon. Recently, rebamipide, a drug that inhibits neutrophil oxidative function and adhesion, was found to reduce the incidence of PHG-like lesions that occur following arterial embolisation in patients with hepatocellular carcinoma.[61] Table 1 summarises the medical and surgical therapies for PHG.

Gastric antral vascular ectasia (GAVE) syndrome

DIAGNOSIS, NATURAL HISTORY, AND CLINICAL ASSOCIATIONS

Gastric antral vascular ectasia or GAVE syndrome was first described by Rider *et al* in 1953[62] but was accurately defined by Jabbari *et al* in 1984.[63] GAVE is characterised by red patches or spots in either a diffuse or linear array in the antrum of the stomach. This syndrome has been more commonly referred to as watermelon stomach because of its typical endoscopic appearance (see fig 1). Approximately 30% of patients with GAVE syndrome will have cirrhosis.[64] GAVE syndrome can be distinguished from PHG in that GAVE generally has more antral involvement and the classic features of GAVE syndrome including gastric ectasia, gastric dilation, thrombi, increased spindle cell proliferation, and fibrohyalinosis may be seen on biopsy.[65]

The natural history of GAVE has not been systematically studied but important differences likely exist in patients with and without cirrhosis. The classic non-cirrhotic patient with GAVE is a middle aged female with autoimmune disease.[66] More specifically, in this study of 45 consecutive patients with GAVE, 71% were women, mean age was 73 years, most presented with occult blood loss, and 62% were transfusion dependent.[66] Autoimmune connective tissue disorders were present in 62%, with 31% having Raynaud's, 20% sclerodactyly, and 100% atrophic gastritis. Hypergastrinaemia was present in 76%.[66] GAVE syndrome has been associated with several disease states, including scleroderma,[66–68] various other autoimmune diseases,[66 67 69] bone marrow transplantation,[70] and chronic renal failure.[66 67 71] Non-cirrhotic patients are more likely to have a classic "watermelon" stomach with linear lesions within the antrum whereas in cirrhotics the disease is more often diffuse.[65 66] Contrary to PHG, those diagnosed with GAVE syndrome frequently have chronic significant blood loss often resulting in transfusion dependency.[66 67 72] Again, this may be a selection bias as the incidence of GAVE syndrome in asymptomatic non-iron deficient "control" patients has not been determined.

PATHOGENESIS

Similar to PHG, the aetiology of GAVE syndrome remains unknown. The pathology of the vascular lesions seen in GAVE syndrome suggest that they are acquired ectasia rather than congenital anomalies.[73] Some authors have suggested mechanical stress as a possible aetiology because the histological features are similar to findings of intussusception and mucosal trauma.[63] Fibromuscular hyperplasia seen on histology supports the role of mechanical stress.[74] The occurrence of GAVE in cirrhotics may therefore be in part explained by abnormal antral motility demonstrated in these patients.[75] As with PHG, increased gastrin levels have been demonstrated in patients with GAVE[66 76]; however, other studies have not confirmed this finding.[65] Other authors believe that vasoactive substances may play an important role in the aetiology of vascular ectasia. Neuroendocrine cells containing vasoactive intestinal peptide and 5-hydroxtryptamine have been found close to the vessels in the lamina propria of resected specimens from GAVE patients and it was hypothesised that the abundance of these mediators may be responsible for the vasodilatation and thus the propensity to bleed.[77] The aetiology of GAVE in cirrhotic patients may in part be explained by the shunting of blood and altered metabolism of vasoactive substances in the presence of liver disease.[74]

GAVE SYNDROME VERSUS PHG IN THE SETTING OF PORTAL HYPERTENSION

Although more than 70% of patients with GAVE do not have cirrhosis, there can be a dilemma in trying to differentiate between GAVE syndrome and severe PHG in patients with existing cirrhosis or portal hypertension. Generally, patients with GAVE syndrome have diffuse or linear red spots that are located in the antrum whereas PHG is typically more significant in the fundus or corpus. A study by Payen *et al* showed that GAVE syndrome and severe PHG are two distinct entities in the setting of cirrhosis.[65] Generally those patients with GAVE syndrome had more severe liver disease (by Child-Pugh scoring), greater blood loss, lower serum gastrin levels, and were more likely to have had previous sclerotherapy (see table 2). On biopsy, microvascular thrombi were noted in the antrum of 50% of patients with GAVE syndrome but were not seen in patients with severe PHG.[65] Antral vascular ectasia was noted in all patients with GAVE syndrome and in only 64% of those with severe PHG.[65] Using a discriminant analysis technique, the biopsy findings of spindle cell proliferation and fibrohyalinosis were found to have a diagnostic accuracy of 85% for GAVE syndrome versus PHG.[65]

Differentiating GAVE syndrome from PHG in the setting of cirrhosis is essential when considering the

Table 2 Factors allowing the differentiation of severe portal hypertensive gastropathy (PHG) from gastric antral vascular ectasia (GAVE) syndrome in the setting of cirrhosis and portal hypertension

	Severe PHG	*GAVE*	*p Value*
Clinical features			
Child-Pugh score	6.9	8.6	<0.05
Previous sclerotherapy	6/14	0/14	<0.02
Blood loss (ml/day)	8.9	21.6	<0.05
Peak acid output (mEq/h)	50.4	17.2	NS
Gastrin (pg/ml)	77.2	38.7	<0.05
Histology features			
Thrombi (antrum)	0	50%	0.006
Vascular ectasia (antrum)	64%	100%	0.04
Spindle cell proliferation (antrum)	29%	86%	<0.01
Fibrohyalinosis (antrum)	36%	92%	0.004

Adapted from Payen *et al*.[65]

therapy of these two disease states. A recent study by Spahr *et al* of cirrhotic patients with GAVE associated bleeding unresponsive to β blockers demonstrated the futility of treating such patients with shunt procedures.[74] Of these eight patients, seven underwent TIPS therapy and one had an end to side portosystemic shunt. Seven patients had rebleeding even though portocaval gradients were generally less than 12 mm Hg (a shunt blockage being noted in only one patient). Subsequently, 4/7 patients underwent antrectomy without further bleeding problems but 2/4 surgical patients in this series died within 30 days of the antrectomy from multisystem failure.[74] These results were recently confirmed in a larger series by Kamath and colleagues.[78] They performed TIPS on 40 patients with PHG and 14 patients with GAVE. Improvement in the endoscopic appearance of PHG and decreased transfusion requirements were seen in 75% of those with severe PHG, and endoscopic resolution was seen in 89% of those with mild PHG. Patients with GAVE had neither endoscopic resolution nor decreased transfusion requirements following TIPS.[78]

Identification of GAVE in the setting of cirrhosis is important as a reduction in portal pressures by β blockers, TIPS, or surgery does not appear effective in the treatment of GAVE associated bleeding.[74 79 80] In the setting of cirrhosis, red spots within the antrum of a cirrhotic patient probably represent GAVE. If the endoscopist is unsure of the diagnosis, a biopsy of the lesions can be safely performed. GAVE has classical histological findings which can distinguish it from PHG[65] but the false negative rate is quite high as the lesions are focal and therefore a negative biopsy does not exclude GAVE.

THERAPY FOR GAVE SYNDROME

Several therapeutic modalities have been used for the treatment of GAVE syndrome. Laser coagulation has been found to improve lesions and decrease blood requirements but generally is not as effective in those patients with diffuse GAVE syndrome.[72 81–84] In several case reports, oestrogen and progesterone have decreased bleeding in GAVE syndrome but have not been effective at eradicating the lesions associated with GAVE syndrome.[69 85–88] Interestingly, the antifibinolytic agent tranexamic acid has been found in two separate case reports to be effective in the treatment of GAVE syndrome. Tranexamic acid has been used previously in the treatment of upper gastrointestinal bleeding, and in a meta-analysis was found to cause a 20–30% reduction in bleeding, 30–40% reduction in the need for surgery, and a 40% reduction in overall mortality in patients with a variety of causes of upper gastrointestinal bleeding.[89] Park *et al* reported on the use of tranexamic acid in a patient with GAVE syndrome and alcoholic liver disease and found it reduced blood loss.[90] More recently, McCormick *et al* reported a patient with GAVE syndrome and cirrhosis that was unresponsive to propranolol therapy and TIPS, who had previously required 130 units of packed red cells.[80] After initiation of tranexamic acid, the patient required no further blood transfusions over a 30 month period despite the ongoing endoscopic presence of GAVE lesions. Of note, the use of tranexamic acid is not without risk as there have been reports of ischaemic episodes and pulmonary embolus with the use of this agent.[91] Surgical treatment, including antrectomy, can cure GAVE syndrome, but in the setting of portal hypertension and cirrhosis it can be associated with a significant mortality risk.[71 73 74 92 93] Chronic octreotide injections appeared to have some efficacy in controlling GAVE associated blood loss in a study of three patients with GAVE syndrome that were not surgical candidates[94] but this approach was unsuccessful in another case report.[95] Table 1 summarises the therapeutic options for GAVE syndrome.

Summary

PHG commonly occurs in the setting of cirrhosis and portal hypertension but can also complicate portal hypertension in the non-cirrhotic patient. Generally the incidence of PHG increases with increasing severity of liver disease and has been found to be associated with the presence of both oesophageal and gastric varices. Furthermore, the presence of PHG in the setting of oesophageal varices has been found to be a strong predictor of future oesophageal variceal bleeding. The exact aetiology of PHG is presently unclear but obliteration of oesophageal varices may increase its incidence. Therapy of PHG is directed at lowering portal pressure via β blockers or shunt procedures. GAVE syndrome typically occurs in non-cirrhotic patients and is managed with endoscopic coagulation or surgery. When GAVE syndrome complicates cirrhosis, it is essential to differentiate it from PHG because therapies directed at reducing portal pressures are not effective treatment for GAVE syndrome.

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