Hemorrhagic Gastroenteritis

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Hemorrhagic gastroenteritis (HGE) is a syndrome associated with acute, severe gastrointestinal inflammation and resultant bloody diarrhea and vomiting. The syndrome is characterized by marked hemoconcentration of the blood.

This severe inflammatory reaction results in destruction of the intestinal epithelial barrier, exudation of plasma proteins and fluid while simultaneously resulting in potential mucosal translocation of resident bacteria.

Translocation of bacteria is also thought to be exacerbated by changes in splanchnic blood flow from hypovolemic shock. Bacterial translocation has been the topic of much debate with the potential for bacteremia/septicemia and septic shock.

The acute development of signs has lead to the potential belief that food related hypersensitivity or primary bacterial pathogenic organisms are causative. Clostridial organisms have historically been thought to be related to this condition through local production of enterotoxins. Clostridial perfringens enterotoxin (CPE) and Clostridium difficle toxins A&B have been implicated.

This is suspected to be related to marked plasma protein exudation across the gastrointestinal membrane with simultaneous fluid loss.

Diagnosis

The diagnosis of HGE is based on compatible clinical signs of hemorrhagic diarrhea, vomiting and/or inappetance. The clinical signs should be acute in nature without prior clinical signs. Clinicopathologic data complete the diagnosis with documentation of an elevated PCV (typically > 60%) with a simultaneously normoproteinemia or hypoproteinemia.

Additional laboratory data

- Hepatopathy (reactive hepatopathy)
- Hypoglycemia
- Azotemia
- Leukocytosis +/- left shift (regenerative or degenerative)
- Toxic changes

The hepatopathy is generally mild with mild to modest elevations in transaminases.

This is thought to be related to intestinal compromise and portal absorption of enterotoxins, endotoxins, bacterial products and other gut derived toxins. This is additionally complicated by decreased hepatic perfusion from systemic hypoperfusion. Occasionally, a more dramatic hepatopathy can be seen but is usually self limiting and generally not associated with overt sonagraphic hepatic changes.

The hypoglycemia that occurs in these patients may be related to the relative polycythemia in these patients and/or related to concurrent hyporexia, altered hepatic function and bacteria/septiciemia. Supplemental glucose therapy may be needed early in the stabilization but usually is transient and rarely persistent throughout hospitalization.

Azotemia can be observed in these patients and occasionally be severe in nature. This azotemia is generally pre-renal in origin. However, this azotemia may be become an intrinsic renal failure with continued hypotension and/or local hypoxemia. Documentation of concentrated urine may be difficult in these patients, as the urine output may be low.

Spectrum of clinical signs

HGE can range in severity with the most severely affected presenting in shock. Other patients may present with isolated vomiting (+/- hematemesis), isolated hematemesis or isolated inappetance. The dynamic nature of this condition may lead to rapid deterioration and development of other signs following admission.

Physical examination

Examination is generally non-specific with potential pain on abdominal palpation, hematochezia on rectal and altered perfusion parameters. It is crucial to identify the borderline patient that may be at risk of decompensation if out patient therapy is implemented. These patients may have had mild historical signs and examination is relatively unremarkable. These patients commonly have cold extremities, tachycardia and are generally “quiet”. These patients may be in a state of compensatory shock and is easily become shocky with continued losses.

Assessment of a patient in shock

- Perfusion parameters:
- Heart rate
- Mentation
- Capillary refill time (CRT)
- Peripheral temperature

- Core temperature
- Urine output
- Pulse quality
- Blood pressure
- Lactate

Immediate stabilization

Initial stabilization is focused around correction of fluid imbalances and deficits. The primary goal is to replace previous losses that have been incurred prior to presentation. It is important to note that underestimation of fluid losses are easy in these patients as many patients have 3rd spacing of fluid within the gastrointestinal tract. During fluid resuscitation, hypoproteinemia will become more obvious with exacerbation of the fluid losses through reduced oncotic pressure and restoration of intravascular hydrostatic pressure.

While colloidal support is not needed in many patients, it becomes increasingly important in some. Replacement crystalloid fluid should be provided judiciously to correct deficits and reach goal directed perfusion parameter correction. Traditional recommendations at shock rate fluids are too rigid for the individual patient and fluid resuscitation should be individualized. Initially it is recommended that shock resuscitation start with boluses of crystalloids followed by repeat assessment of perfusion parameters. Resucitation should continue until parameters are corrected. Both physical and clinicopathologic parameters are reevaluated. Restoration of perfusion should result in improved clinical paramaters and reduced PCV/HCT. Aggressive fluid support is generally continued until the packed cell volume is <50% and other parameters are improved.

Bolus approach:	Give ¼ shock bolus (10 ml per pound) and reassess
When do I consider colloids	• When >2 boluses of crystalloids needed to maintain perfusion • When < 5 g/dl TS • When progressive ongoing losses despite resuscitation • Evidence of third spacing • Patients with evidence of SIRS

It is important that a minimum database be performed with evaluation of electrolytes, blood glucose and PCV/TS. This will help to address electrolyte alterations that may need more specific intervention and/or may have therapeutic implications (ie. hypo/hypernatremia).

Antibiotics

A hot debate in HGE is whether or not antibiotic therapy is indicated. Antibiotic therapy has long been suggested due to the concern for clostridial organism potentially playing a role in the etiopathogenesis. A definitive bacterial cause of this disorder has not been proven. Additionally, a recent evaluation showed no advantage of amoxicillin with clavalanic acid in these patients. It should be noted that other potential advantages of antibiotics may exist in these patients through reducing bacteremia from translocation and/or altering enterotoxigenic absorptions through reduced production. Indiscriminant use of antibiotics is discouraged however, it should be noted that clear guidelines remain to be seen.

The most current literature suggests that mortality, duration of hospitalization and bacteremia (determined by blood cultures) were not effected by the addition of antibiotics. However, it should be noted that the authors used a biased population that could tolerate oral antibiotic therapy vs. those that present in shock and/or have refractory vomiting. This population, may likely have had less severe disease, limiting the ability to show a statistically significant effect. Additionally, it is uncertain that oral antibiotic absorption and normal gastrointestinal transit time exist in this patient population. That being said further research into appropriate use of antibiotics needs to be made in the future. The authors of this paper noted a positive blood culture rate of ~20% suggesting that potential for end organ bacterial deposition is possible. Additionally, the authors of this paper site a quicker resolution of soft stool in the antibiotic group, which suggests that some positive benefit is seen. Finally, while clostridial disease far been documented in HGE, concurrent quantification of the cpe gene and CPE may further characterize if true infection is present. Additionally, the prevalence of CPE in this case series is higher than control groups reported in other studies suggesting minimally a secondary role of C. perfringens in these patients.

Currently, the author uses antibiotics in the following scenarios

- Animals with concurrent predispositions for translocation (hypovolemia, decreased oxygen carrying support, gastrointestinal stasis)
- Hypoglycemia
- Documented bacteremia
- Left shit (regenerative, degenerative)
- Toxic change

- Neutropenia
- Concurrent immunosuppressive medications or disease process
- Positive CPE and cpe (combined)
- Positive CPE or cpe (solitary)

The author generally uses broad spectrum antibiotic therapy with unasyn or metronidazole

Supportive care

Anti-emetics

It is recommended that these patients be started on anti-emetic therapy to mitigate vomiting when vomiting is part of the history. Other considerations for the addition of anti-emetics include patients that are recumbent, as they are at increased risk of aspiration pneumonia.

Analgesics

It is not uncommon for patients with HGE to have moderate to marked abdominal pain and likely could benefit from analgesia. A fine balance between appropriate analgesia and minimization of hypotension or aspiration risk exists in these patients. In my experience buprenorphine or short acting titratable opoids may allow for good analgesia without excessive sedation or cardiovascular depression.

Buprenorphine	0.005 -0.02 mg/kg q 8 IV
Fentanyl	2–5 micrograms/kg IV loading 2-5 ug/kg/hr IV CRI

Plasma therapy

Generally, not indicated in these patients unless coagulation testing should suggest hypocoagulable DIC or overt DIC. This could be further documented on TEG testing in hospitals with this readily available. It should be noted that some patients developed a coagulopathy from resuscitation efforts and concurrent colloidal therapy which can contribute to a dilution coagulopathy. These effects are reduced with some colloids with voluven having a minimal effect on coagulation and more consistent molecular weight. Patients generally do not benefit from plasma transfusions for hypoalbuminemia, however, in small patients large volumes of plasma may provide some colloidal benefit/albumin replacement.

Patients at risk of coagulopathy

- Hypovolemic patients
- Hypoglycemic patients
- Patients requiring large volumes of crystalloids for rescuscitation
- Patients receiving large volumes of colloids per day (especially dextrans > HES)

Gastrointestinal protectants

These patients commonly have hematemesis associated with their disease process suggesting local gastroduodenal erosions/ulcerations. Treatment with an effective acid suppressant may help to minimize discomfort and local tissue injury from denuded mucosa. The gastrointestinal tract is compromised and simultaneous hypotension, gastrointestinal stasis and secondary bacterial overgrowth may put patients at risk of translocation. Rarely, significant gastrointestinal bleeding may occur in these patients with development of anemia and exacerbation of hypoproteinemia. Currently I am recommending the addition of a PPI when possible due to their superior efficacy on gastric pH in multiple animal models. Given the inability to tolerate oral medications in many cases, injectable pantoprazole can be considered. The concurrent use of H2 blockers prior to the initiation of PPIs has been suggested by some; acid suppression has been documented with PPIs in animals in as soon as 48 hours after initiation (maybe sooner but not critically evaluate) making this practice likely unnecessary.

Pantoprazole	1mg/kg q 24 IV 1mg/kg/day CRI
Omeprazole	1-2 mg/kg q 12-24
Famotidine	0.5-1 mg/kg q 12

Animals with severe persistent gastrointestinal hemorrhage should have their coagulation status evaluated and should be considered for other gastrointestinal supportive medications like sucralfate. It should be noted that sucralfate can affect intestinal absorption of some medications and appropriate alteration of drug schedule should be made. A rare consideration would include the addition barium to coat the surface of the intestines. The author has used this sporadically and has visualized endoscopically the adherent nature of barium to the mucosa.

Monitoring

These patients can be critical within the first 24-48 hours of therapy with need for minute to minute intervention. Generally, the patient population tends to be smaller breeds and massive fluid shifts can occur from thirds spacing into the intestinal lumen, decreased COP with interstitial leakage and simultaneous ongoing vomiting/diarrhea. Careful evaluation of perfusion parameters can help to identify which patients may benefit from earlier intervention. Monitor the body temperature and providing heat support can be heat support is important. Serial evaluation of body weight, PCV/TS and clinical hydration status will provide clues to hydration status/dehydration deficit. Routine electrolyte testing is important to ensure that we are addressing arising alterations/rapid shifts.

Recurrent disease?

If recurrent bouts of HGE are reported then attempts to document an underlying etiology is recommended. HGE is an acute, disease that generally is not associated with recurrence, however, occasionally animals with repeatable bouts have been observed. If recurrence is observed, then considerations regarding management of chronic large bowel diarrhea must be made (see lecture notes).