

Approach to Gastrointestinal Bleeding

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Chronic intestinal bleeding is an under appreciated condition that can be associated with a myriad of causes and etiologies.

It is important to note that the clinical conditions associated with chronic gastrointestinal bleeding in dogs and cats is different from that of people. People commonly have helicobacter associated disease, stress related mucosal disease and drug induced disease (NSAID administration). Dogs and cat more commonly have underlying pathology. A list of the more common associations in veterinary medicine are listed below

Inflammatory enteropathies (ulcerative/erosive enteropathies)
Localized neoplasia
Intestinal parasitism (whip worms, hook worms)
Intussusceptions
Chronic foreign bodies
Vascular ectasia

Metabolic diseases (renal disease, hepatic disease, endocrinopathies)
Thrombocytopenia/pathies
Coagulopathies
Paraneoplastic disease (mastocytosis, gastrinomas)
Drug induced ulceration (NSAIDs, TK inhibitors, Corticosteroids?, chemotherapeutics)

Very similar to any other condition in veterinary medicine, clinical signs may be very mild or noticeably absent in other cases. Therefore, it is the reliance on subtle clues from the clinical history and laboratory data. That being said, some of the signs listed below can be associated with gastrointestinal bleeding depending on the etiology and location.

Vomiting
Abdominal pain
Inappetance
Hypomotility of gastrointestinal segments
Melena
Hematemesis
Licking of the lips, hard swallowing, ptyalism (nausea like signs)
Weight loss (generally associated with the underlying cause)
Generalized weakness, collapse (signs of anemia)

Factors that influence the clinical manifestations include the local or systemic pathology that is causing the ulceration. Additionally, the speed at which a patient may bleed could influence how symptomatic that patient is.

Acute life threatening bleeding should be addressed with transfusion therapy and rapid detection of the underlying cause when possible. Specific interventions that can be performed that may address the underlying cause are preferred (ie. plasma for anticoagulant rodenticides). These patients may present with clinical signs of anemia without measurable anemia in some cases with brisk bleeding. Clinical signs consistent with early hypovolemic shock (pallor, tachycardia, generalized weakness, depressed mentation and tachypnea) in a patient without marked ongoing losses should be considered as a patient that could potentially be bleeding. Serial assessment of the red cell mass (PCV, HCT) over time will ultimately detect a rapid decline in red count.

Emergency measures

General physical examination (rectal, retinal)
Quick assessment testing (PCV, TS)
Blood smear
Reestablish history (drugs, rodenticide)
Coagulation testing
F.A.S.T. evaluation (abdominal, thoracic)
Emergency stabilization (blood products, antidotes)

The acute bleeding patient presents a problem with respect to rapid identification and stabilization. However, chronic gastrointestinal bleeding poses a more common, chronic and often unnoticed dilemma.

Chronic blood loss anemia can be overlooked because of the “normal” values. It is not uncommon for clinicians to say “the BUN is normal, wouldn’t you expect that to be elevated with blood loss”. Subtle clues can be present in many patients on routine blood testing and include the following

Elevated BUN Hypoalbuminemia +/- hypoglobulinemia Thrombocytosis Microcytosis Hypochromasia Can be normochromic, normocytic (histogram) Reticulocyte count variable (iron status and timing) Other indicators of disease: renal, hepatic

It is important to note that not all patients have all of these findings and that some patients have no findings.

Diagnostic testing

Documentation of bleeding can be difficult in some patients when the bleeding is slow as this external signs may be non-existent in some cases.

Occult blood testing can be performed with o-tolidine based tests. These test have a low sensitivity with gastrointestinal bleeding when it is intermittent or low volume. Questions regarding the specificity has been raised in the past. A high degree of false positives due to detection of meat based hemoglobin has been touted. This does not appear common with o-tolidine based tests and is generally more commonly associated with guaiac based testing. It appears that specificity is not the problem with these assays and that low sensitivity is more of a concern with these tests. These tests, could potentially further support gastrointestinal bleeding in the patient that may have minimal clinical signs. Testing generally will have a greater sensitivity when used with large bowel bleeding, when volumes of blood are large and/or when recurrent colonic disease is considered.

Traditionally contrast radiography has been used to evaluate for mucosal defects that may be associated bleeding. Contrast radiography will aid in complete evaluation of the internal gastrointestinal tract. However, it is important to note that many patients have very subtle lesions on these tests, leading to missed lesions. Additionally, over interpretation of psuedolesions is possible. Some potential findings on contrast radiography include mucosal regularity, mucosal thickening fingerprinting or painting of mucosal defects. It should be noted that these tests generally have a low sensitivity but in select cases may give a clear answer as to the cause of hemorrhage when other tests may not.

Gastrointestinal endoscopy offers the advantages of being able to directly visualize the gastric underlying mucosa in most patients. With this form of imaging, interventional and diagnostic procedures could before performed at the time of observation. Unfortunately, documentation gastrointestinal disease is limited by scope length and therefore prevents direct observation of more distal lesions. It is therefore critical to utilize the longest scope so that as much of the mucosal surface can be visualized. Direct observation of the ileum can be performed in some patients increasing the percentage of intestine cover. Modern endoscopic techniques in people including double balloon enteroscopy and single balloon into enteroscopy and push enteroscopy. These techniques have been used to facilitate further evaluation of the gastrointestinal tract. They involve advancement of the scope while simultaneously tethering the intestinal segment. These techniques have been used in experimental models in dogs. However, currently the feasibility of these endoscopic procedures is limited by the external diameter of the scope, experience and duration of time required to perform these procedures.

Tips when performing endoscopy

Reduce exposure to medications (sucralfate, barium) for 24-48 hours prior to the procedure Use the longest endoscope possible Cover as much small bowel as possible (ileoscopy may be helpful) Prepare the patient appropriately to facilitate mucosal visualization

When these diagnostic tests do not provide clues, further evaluation should be considered. Capsule endoscopy is a more novel approach to mucosal investigation. It offers the potential benefits of covering the entire small intestinal length but it should be noted that the sensitivity for detection is variable and dependent on the degree of bleeding. Additionally, no interventional action can be taken to address clinically significant bleeding at the time. Inability to localize the lesions within the small intestinal tract also limits its clinical utility. Currently a small number of practices are offering capsule endoscopy and the preliminary evidence suggests that this may be feasible in our patients. Practical issues regarding battery life and lack of real time data can limit its potential.

Interventional radiology has become an attractive alternative to documenting gastrointestinal bleeding and also provides a potential real time therapy through the vasculature. These procedures have changed the scope of human bleeding in that they offer a high sensitivity test, being able to detect as low as 0.5 – 1 ml/min. Active bleeding and localization can be documented through selective angiography and real time fluoroscopic imaging. Additionally, if selective angiographic procedures can be used to induce bleeding by injection of various compounds that may help to localize an intermittently bleeding process. These techniques have been attempted in our patients but are limited by patient size and need for general anesthesia. Future evaluation of these techniques may prove to be helpful in difficult patients. These techniques also provide a potential therapeutic option, with local vascular occlusion or vasoconstriction.

Additionally, nuclear scintigraphy is available at select institutions. This may become more readily available in the future. This involves the removal of autologous blood and incubation with Technetium 99m (Tc-99m) in infused with serial imaging of the gastrointestinal tract for accumulation of the tracer. Detection of the bleeding is reportedly 0.1-0.5 mg/min in people. The sensitivity is high in institutions that commonly perform this procedures. The clinical utility in our patients on a wide scale has not been critically evaluated.

Future considerations include enteroclysis with or without CT. This procedure involves distension of the small intestine with contrast via a naso-jejunal tube with CT acquired imaging. It offers a critical evaluation of the mucosal surface while simultaneously evaluate for non-mucosal disease. Diagnostic yield is variable depending on the nature of bleeding. This has not been evaluated in veterinary patients at this time.

Pseudobleeding

It is important to note that some patients may present for “gastrointestinal bleeding” that have other localizations. It should be noted that swallowing of blood may result in the following signs that may be more typical of gastrointestinal bleeding. These include: regenerative anemia, hypoproteinemic anemia, iron deficiency anemia and melena. When this is suspected or gastrointestinal bleeding cannot be documented consideration to alternative locations such as nasopharyngeal, pulmonary and/or tracheal sources should be made. Primary respiratory signs may be subtle or absent in many cases.

Management

The principle of therapy is to address underlying disease processes when possible, provide supportive care and/or medications that could possibly facilitate healing/resolution of bleeding.

Interventional options at endoscopy include local cautery, local injection of vasoactive drugs and superficial removal of mucosal derived proliferations. These techniques can be used to address rapid bleeding in some cases, however, the relative frequencies of certain disease processes in animals vs. humans often times, limits our ability to apply these techniques in many cases.

Surgical intervention can sometimes be necessary to both document a bleeding lesion but can also allow for complete resection of a lesion when possible.

Medical options for bleeding are limited in their efficacy and influenced heavily by the disease process. They are best utilized in patients with low grade bleeding and particularly useful with gastric or duodenal bleeding, sites that are exposed to acid.

Acid suppression has long been utilized in management. The principle being that acid suppression will result in reduced gastric acidity and allow for the underlying submucosal layer to heal without acidic injury. As one can imagine, this is likely only effective in patients that have esophageal, gastric or proximal duodenal ulcerative disease; sites with potentially greater exposure to gastric acid induced injury. These medications act through the H⁺K ATPase pump and through anti-histamines. See lecture notes on these medications (Gastroesophageal reflux and *Helicobacter*-associated disease)

Additional medications

Carafate has been used extensively in veterinary medicine with little evidence to support its efficacy. It has not been recommended as a sole therapy for gastrointestinal hemorrhage in people and seems to have the most proven benefit in patients with erosive esophagitis (for prevention of strictures), duodenal bleeding and colorectal ulceration (administered as an enema). No proven benefit for distal small intestinal bleeding exists in people. The medication appears to be associated with low toxicity and given the wide variety of other potential therapeutic options in people not readily available to our patients it seems reasonable to continue administration. It should be noted that sucralfate can coat the surface of lesions on endoscopy and should not be given the day of any procedures. Additionally, it has been reported that it can interfere with absorption of various medications and scheduling of medications around administration is recommended; medications are recommended to be given a minimum of 2 hours after Carafate.

Antifibrinolytics agents have been used in humans to address post surgical bleeding (ie. cardiac surgery) and trauma. Lysine analogues (ϵ -aminocaproic acid, tranexamic acid) have been predominantly used. Some evidence in people suggest that utilization in trauma, liver disease, hereditary hemorrhagic telangiectasia and urinary bleeding. The role in veterinary medicine has not been evaluated.

Thalidomide/thalidomide analogues have anti-angiogenic effects via VEGF and non-angiogenic effects on TNF-alpha have been used for people with Crohn's induced bleeding, bleeding tumor and angiodysplasia. Evaluation of these compound on a wide scale in people or small scale in animals have not been evaluated.

Recently, estrogen-progesterone compounds have been used in veterinary medicine for the treatment of vascular ectasia with success. These compounds (ethinyl estradiol and norethindrone acetate (OvCon) or DES w/ Altrenogesta) have been used and should be considered in select cases.

Other therapies utilized in veterinary medicine with limited scientific data to support include Yunnan Baiyou, DDAVP, oral barium and somatostatin analogues.

In conclusion, gastrointestinal bleeding is more common than expected. Documentation and localization may be difficult in our patients, however, advanced diagnostic testing may improve our ability to document etiologic processes in the future. Medical options are limited at this time and the primary goal of addressing the underlying etiology is recommended whenever possible. New developments in diagnostics and therapeutics may expand our capacity in dealing with these patients.