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HEMATEMESIS Y PERDIDA DE SANGRE GASTROINTESTINAL
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Hematemesis necessitates a slightly different approach than we take with other vomiting cases because some rule-outs become more likely while others become much less likely. We will be including upper gastrointestinal bleeding of any cause in this discussion. For starters, we will not be discussing vomiting that produces “flecks” of blood because this can be seen in any dog (and perhaps cat) with vigorous vomiting in which the gastric mucosa is traumatized by the physical act of vomiting. It is easy to identify fresh blood in the vomited material as long as the patient is not eating something that is red or that produces a pink color to the vomited material; simple secondary to pigment leaching out of the food material. Most of the time, hematemesis is denoted by a “coffee-grounds”-like material that most clients (and some veterinarians) do not recognize as blood. A common mistake is being concerned over “dark stools”. Noting that a patient has dark stools is generally useless. Lots of dogs have dark stools and no problems or GI blood loss at all. The color of the stool is not an issue until the stool is pitch-tar-coal-asphalt black. Then it may be melena (if it is not due to Bismuth or a lot of green bile giving it a near-black appearance). If in doubt, just place some fresh feces on absorbent white paper and see if a reddish color diffuses out from the feces, confirming that there is blood present. Melena is only seen if there is acute loss of a lot of blood into the upper GI tract. Most dogs losing blood in the upper GI tract do not have any important changes in the color of the feces. Rather, you might see anemia and hypoalbuminemia. Also remember, you may or may not see hypoglobulinemia; it all depends upon what the serum globulin concentration was before you started losing blood. Sometimes the BUN is higher than expected based upon the serum creatinine, but again this is only expected if there is a lot of blood being lost in a short period of time. Fecal occult blood tests are seldom that helpful or necessary, but can occasionally be informative in confusing cases. However, you need to use a test for which the laboratory has substantial experience in dogs so that the results can be meaningfully interpreted. Some fecal blood tests will routinely give a positive reaction when used on canine feces.

When there is a substantial amount of blood being ejected from the mouth, there tend to be 3 major reasons: coagulopathy, swallowing blood from elsewhere and gastrointestinal ulceration/erosion (GUE).

Coagulopathies: Most coagulopathies cause concomitant bleeding from the nose or accumulation of blood in body cavities or petechia. However, there are many cases in which the only sign of a systemic coagulopathy is GI bleeding. Therefore, it is always appropriate to check the platelet count and some measure of clotting factor adequacy in animals with hematemesis or GI blood loss. While coagulopathies are a relatively uncommon cause of GI bleeding compared to ulceration/erosion, they can have devastating consequences if not diagnosed promptly. In particular, remember that some cats with intestinal disease will malabsorb vitamin K to the point of having vitamin K-responsive coagulopathies. Also remember that just because the patient did well during a surgical procedure a few days before the current bleeding episodes does not mean that a coagulopathy is impossible; sometimes the prior surgical procedure apparently depletes the limited amounts of coagulation factors in patients with subclinical coagulation defects, causing them to become clinical after the procedure.

Ulcers and erosions: Gastritis due to any number of causes typically has some degree of GUE present. We will not discuss this cause too much since most of these cases quickly and spontaneously resolve. Helicobacter is important in people, but to date has not been shown to have a cause-and-effect relationship with GUE in dogs and cats. There are often incredible numbers of Helicobacter found in ulcer craters; however, Helicobacter can be found in ulcers caused by almost anything. Therefore, it seems likely that the Helicobacter are there because a) they are found in most dogs and cats and b) the ulcer crater is an opportune place for them to grow. Renal disease is often named as a cause of gastric ulceration, but this is actually very rare.

The most common causes of chronic, unresolving GUE that are also the easiest to check for are mast cell tumor, drug administration and “stress”.

Drugs are still a very important cause of GUE in the dog, despite all the newer, “safe” NSAIDs. High doses of dexamethasone also have substantial potential for significant GUE. Prednisolone by itself is generally not ulcerogenic unless it is used in very high doses (e.g., > 2-3 mg/lb/day) or is administered to a patient with other “ulcerogenic” risk factors (e.g., hypoxia, poor perfusion), and even then it is not particularly bad. Combining steroids and non-steroidal drugs can be devastating. You can use ultra-low dose aspirin (0.5 mg/kg once daily) when treating IMHA dogs with steroids.

There continues to be a substantial problem with the use of nonsteroidal anti-inflammatory drugs (NSAIDs) in dogs. All NSAIDs have the potential to cause devastating GUE, and some of these non-steroidal drugs are...
renowned for their toxic effects (i.e., indomethacin, naproxen, flunixin). Ibuprofen is also particularly ulcerogenic in the dog because it undergoes an enterohepatic circulation. Flunixin is a particularly dangerous drug from the standpoint of causing GUE. It is extremely potent and can be devastating if combined with steroids like dexamethasone. While able to cause significant ulceration and bleeding all by themselves, the ulcerogenic potential of NSAIDs is particularly augmented by other factors, especially concurrent administration of another NSAID or a corticosteroid, and hypoperfusion of the alimentary tract. Even though many dogs seemingly tolerate such combination therapy, you need to realize that you are "walking on thin ice" (see comments above on use of ultra-low dose aspirin). Many to most of the dogs treated with NSAIDs have endoscopically visible erosions, hemorrhages and/or ulcers, depending upon the drug used and the dose administered. It is important to note that most dogs with GUE due to NSAIDs may be completely asymptomatic. Finally, there is tremendous between-dog variation regarding the alimentary tract response to NSAID's; some dogs may almost bleed to death because of a small dose of aspirin while most dogs would tolerate a much larger dose with relative impunity.

While the newer Cox-2 NSAIDs (e.g., carprofen, etogesic, deracoixib, meloxicam, etc) have much less potential for causing GUE than the older NSAIDs, you can still see GUE (and even perforation) due to these drugs. Part of the problem is that these “safe” drugs are being used so extensively and casually. The problem often revolves around using inappropriately high doses (after all, the drug is so safe that ...), using the drug at the wrong time (e.g., when the patient is experiencing shock or has poor perfusion to the alimentary tract), and possible using the drug too soon after stopping some other NSAID. The concept of a “washout” period when changing from one NSAID to another is extremely controversial. There is published literature to the contrary, but the fact is that nobody really knows at this time.

**Stress**, when mentioned as a cause of ulcers, specifically refers to substantial decrease in visceral perfusion (e.g., hypovolemic shock, neurogenic shock, Systemic Inflammatory Response Syndrome) that is typically obvious from history and/or physical examination; or, it can refer to extreme exertion (e.g., sled dogs running in subzero weather for 100 miles).

**Mast cell tumors** may look like any skin lesion. In particular, they can perfectly mimic the appearance and feel of lipomas, such that the only way to distinguish them from lipomas is by aspirate cytology. When these tumors degranulate, they release histamine which if of sufficient magnitude can cause gastric acid hypersecretion. This can result in severe ulceration, especially just inside or just beyond the pylorus.

**Hepatic failure** seems to be another important cause of GUE in the dog. Anytime a dog with hepatic disease suddenly becomes clinically worse (especially if it becomes obviously encephalopathic), you should consider the possibility of GUE. Bleeding into the intestine counts as a high protein meal and predisposes to hepatic encephalopathy in these patients. In ill patients that cannot be scoped, aggressive therapy with famotidine and/or carafate is reasonable. Hepatic disease may cause disseminated intravascular coagulopathy which can cloud the picture when trying to determine the cause of hematemesis.

**Gastric tumors** may cause bleeding. The leiomyoma and leiomyosarcoma in particular may cause especially dramatic bleeding due to their propensity to ulcerate. This is especially important because this tumor is often curable with surgery, as opposed to lymphomas and carcinomas that are more common, have less dramatic signs, seldom cause GI blood loss and yet have a much worse prognosis. Unfortunately, it can be hard to adequately image the stomach with ultrasound, and these masses can be missed if there is blood, ingesta and/or air in the stomach.

**Surgery** can be responsible for GI bleeding. If the closure is done improperly and the mucosa does not cover the defect, then bleeding can easily result.

**Hypoadrenocorticismo** may be responsible for severe hematemesis that can produce life-threatening shock. Such severe hematemesis appears to be a rare complication of hypoadrenocorticismo, but should be considered in cases with appropriate history, CBC and/or serum biochemistry changes, as well as patients that do are not readily diagnosed with other causes.

**Inflammatory bowel disease** has been reported to be associated with GUE, especially in the dog. Right now, the definition of IBD is under scrutiny, but at any rate it appears IBD is not commonly associated with GUE. However, when idiopathic GUE is found during endoscopy, the stomach and duodenum should be biopsied.

**Heavy metal intoxication** causes hematemesis, but this is fortunately uncommon at this time.

**Gastrinomas** are typically small pancreatic tumors which produce large quantities of gastrin, a hormone which causes gastric acid secretion. Multifocal duodenal ulceration/erosion is very suggestive of this tumor, as is a large ulcer just past the pylorus (as for mast cell tumors). Gastric erosions are sometimes seen, but gastric ulcers...
appear to be rare in this disorder. GI bleeding is not particularly common in these patients although it is possible. Since the gastric mucosa is stimulated to grow, ulceration typically occurs in the duodenum instead of the stomach. Esophageal ulceration may also occur if there is gastroesophageal reflux of the highly acidic gastric contents. Measurement of serum gastrin concentrations may be diagnostic. However, anything which causes gastric distention or renal failure can produce increased fasting serum gastrin concentrations. Treatment with H-2 receptor antagonists has been rewarding, although unexpectedly large doses or the more potent proton-pump inhibitors (e.g., omeprazole or lanosprazole) may be necessary. Consider gastrinoma in any older dog that has vomiting, weight loss, and diarrhea of unknown origin, you usually need to measure serum gastrin concentrations to diagnose gastrinoma, the ulcers are usually found in the duodenum (not the stomach), and esophagitis is common.

Foreign objects get a lot of press as causes of GUE, but in fact they are relatively uncommon causes. However, they are particularly important in patients that have GUE because even the most innocuous of GI foreign objects (e.g., paper, small piece of soft cloth) can sometimes prevent a pre-existing ulcer from healing. They typically need to be removed in patients with GUE.

Ingesting blood: This is a possibility that is typically forgotten. However, it is surprisingly easy to have bleeding pulmonary lesions in which the blood is coughed up, swallowed, and later vomited. In most of these cases, the client does not report coughing (perhaps because the hematemesis “wipes” all else from their mind). In like manner, we have seen cases in which blood was trickling from the choana into the pharynx and being swallowed, and yet the patient had no history of sneezing or coughing or nasal discharge.

Cats are rare diagnosed with gastric ulceration/erosion. When a cat is found to have gastric ulceration/erosion, it is usually caused by lymphoma. However, we many times never determine the cause of GUE in cats.

Clinical approach to the patient with hematemesis or GI bleeding

There is often something in the history that is suggestive of the cause of the bleeding (e.g., use of NSAIDs, shock, etc). If that is the case, then it is often reasonable to begin appropriate therapy after requesting basic laboratory testing (e.g., CBC, serum chemistry panel) to determine the severity of the bleeding and if there are other diseases (e.g., hepatic disease, renal disease) present. Imaging (especially ultrasound) is typically appropriate but not necessarily imperative at this time. If the cause of the GI bleeding or hematemesis is not obvious, if the patient has not responded to 5-7 days of appropriate therapy, or if the bleeding is severe, then additional diagnostics are important and should be performed promptly.

Diagnostic approach: First, as stated above, it is wise to first eliminate coagulopathy with a platelet count and some measure of clotting factor adequacy. I typically request PT and PTT, but a mucosal bleeding time is a very useful screening test in these patients. Sometimes there is both a mucosal defect and a coagulopathy. In particular, if ehrlichiosis is possible, one must consider the possibility that the patient has what would normally be an insignificant mucosal defect but which is bleeding because of the effects of Ehrlichia spp. upon platelet numbers and their function. After coagulopathy has been eliminated, then imaging should be done if it has not already occurred, and ultrasound is especially important as it may reveal masses that can be aspirated percutaneously, thus avoiding the need for endoscopy/surgery.

If these tests have not revealed the diagnosis, then gastroduodenoscopy is generally performed next. The specific reasons to do gastroduodenoscopy in a patient with GI bleeding are to:

a) determine if this is a case in which surgery can remove a defined number of ulcers (this is for cases that are bleeding and have not responded to medical management or cases that are bleeding so badly that one cannot wait on medical management). In these cases, it is important to be sure that bleeding is not due to widespread erosions that cannot be cured surgically. There is no relationship between the size of the mucosal defect and the amount of bleeding; patients with lots of small erosions often bleed as bad or worse than patients with ulcers. It is also important to determine the number and location of such ulcers as they may be hard to find during a gastroscopy.

b) determine if there is a gastric tumor or some other infiltrate in a patient with GUE that is non-responsive to appropriate therapy.

c) determine the cause in a patient with GUE and no apparent cause on the history, physical examination, or routine blood work.

d) look for a cause of bleeding in a patient with GI blood loss of unknown cause.

It is important to note that endoscopy will not generally allow one to determine if an ulcer will or will not
respond to medical management. In most cases, only by treating and observing the patient will you know.

It is important not to give carafate within 24-36 hr before endoscopy because it will cover the lesions and make evaluation more difficult. It is best if food has been withheld for at least 24 hours. Avoid prokinetics (e.g., metoclopramide). Endoscopy of these patients may be difficult if there is substantial blood present in the stomach. Patience is necessary to flush in water and then aspirate it and the blood over and over again. It is important to be able to view as much of the gastric mucosa as possible. In some cases, there are lots of hugh blood clots that cannot be removed endoscopically, in which case surgery might be necessary. It can be especially easy to miss ulcers that are in the pylorus. The pylorus is typically infiltrated and inflamed, making it more difficult to pass the tip of the scope through that area. Therefore, the endoscopist often does not obtain a good view of this area. One may have to go in and out of the pylorus multiple times to be sure that there is or is not a lesion present. If a cause of upper GI bleeding cannot be found in the stomach or duodenum, strong consideration should be given to examining the trachea, bronchi, and choana while the patient is anesthetized. Patients with hematochezia may benefit from colonoscopy, but patients with hematemesis or melena rarely benefit from lower endoscopy.

If there is substantial upper GI blood loss and these tests do not allow diagnosis, then exploratory surgery is the next step. However, it is very easy to not be able to find the cause of the bleeding in these patients, so warn the owner before doing the procedure.

**Medical management:** If the patient is not exsanguinating, the cause is known or strongly suspected, and the patient has not had 5-7 days of appropriate medical therapy, then medical therapy is often reasonable as opposed to doing a major diagnostic work up. In distinction, if the patient is exsanguinating or if the patient has not shown any appreciable response to 5-7 days of appropriate medical therapy for the ulceration, then it is usually reasonable to surgically resect the ulcerated area. Note – when I say “response”, I am not referring to the patient being cured; I am referring to clear evidence of improvement. If surgery will be considered, it is usually very wise to perform gastroscopy before the surgery to be sure that you find all of the sites of ulceration. It is very easy to fail to detect an ulcer at surgery, and endoscopy usually allows one to easily find all areas of ulceration. Sometimes intraoperative endoscopy is necessary to help the surgeon find the ulcer(s).

If medical management is elected, first be sure to remove the cause of the GUE. If the cause is not removed, medical management tends to be far less successful. Next, be sure that the patient is well hydrated; healing of the gut requires or is at least benefitted by adequate perfusion. If there is significant gastroduodenal reflux of bile, metoclopramide or cisapride may be helpful in preventing bile from entering and/or staying in the stomach and augmenting the ulcerogenic process.

H-2 receptor antagonists are commonly used. Cimetidine, ranitidine, and famotidine are good medications for decreasing the gastric hydrogen ion concentration. Cimetidine (5-10 mg/kg) needs to be given 3-4 times per day if you are really serious about decreasing gastric acid secretion. However, famotidine (0.5 mg/kg) only needs to be given once or twice daily. In most patients, cimetidine is more than adequate to allow healing of gastric ulcers. However, the over the counter (OTC) preparations are all oral and some patients are vomiting so vigorously that they must receive parenteral medication. Ranitidine (2.2 mg/kg) is usually effective if given twice daily, but may cause vomiting if given as an IV bolus. There is some evidence that ranitidine is not particularly effective in decreasing gastric acid secretion, but that is not certain at this time. Side-effects of the H-2 receptor antagonists are rare but may include diarrhea, drug eruption, hyperpyrexia, thrombocytopenia, granulocytopenia, and CNS problems including seizures. I think I have seen a couple of dogs in which ranitidine was responsible for large bowel diarrhea or seizures. The primary value of the H-2 receptor antagonists is in treating existing ulcers and erosions. They can be helpful in preventing some types of ulcers, but this is not true with all types of ulcers (e.g., they are not effective in preventing ulcers due to NSAIDs or due to steroids).

Proton pump inhibitors are the most effective antacid drugs we have. Omeprazole, lansoprazole and pantoprazole are the most effective inhibitors of gastric acid secretion we currently have available. Omeprazole is available OTC as Prilosec®. The H-2 receptor antagonists seem quite adequate for GUE except in some animals with gastrinomas and those with esophagitis due to gastroesophageal reflux; these seem to be the main reason for using the PPI’s. The dose of omeprazole is 0.7-1.5 mg/kg qd, although I have often used it at up to 2 mg/kg bid in patients with severe reflux esophagitis or gastrinomas. The dose of lansoprazole (Prevacid), pantoprazole (Protonix), and esomeprazole (Nexium) is 1 mg/kg IV (not approved for use in dogs). It generally takes 2-5 days for a PPI to have maximal efficacy; but, the immediate effects on gastric acid secretion is often still better than that obtained by high dose H-2 receptor blockade. Very rarely, an H-2 receptor antagonist will work better than omeprazole; be prepared to experiment in your difficult cases.
Misonprostatol (Cytotec®) is a prostaglandin E analog which was primarily designed to be a prophylactic drug used to prevent GUE due to NSAIDs. It is also useful in treating existing ulcers, but its higher cost and more plentiful side effects usually make it undesirable as a first line therapy for GUE. It is typically used at a dose of 2-5 ug/kg, 3-4 times daily. It can cause abdominal cramping and diarrhea, but the drug seems relatively safe in dogs. The main disadvantage is that it must be given orally, which is not possible in some vomiting animals. Because it is a prostaglandin analog, it should not be used in pregnant females for fear of causing abortion or miscarriage. It is the best drug available that can be used to prevent NSAID-induced ulceration, but it is not uniformly effective in dogs. The main indications to use it appear to be a) the patient that must have NSAID's to function, but which evidences side-effects from them (e.g., anorexia, vomiting) and b) the patient that seemingly needs to receive NSAID's that have substantial potential for such side-effects (e.g., piroxicam).

Sucralfate seems to be extremely effective in protecting those areas which are already ulcerated and helping them heal. The only common side-effect is constipation. There is minimal absorption from the intestines, but it does have the capacity for adsorbing other drugs (e.g., enrofloxacin). While carafate is effective in treating ulcers, it is not always effective in preventing ulceration. In patients with severe hematemesis and anemia, we sometimes use a large "loading" dose (e.g., 3-6 grams) initially and then decreasing the dose to 1 gram tid to qid. No body know if the loading dose is beneficial or not. My major problem with this drug is that it must be given orally, which does not always work in vomiting dogs. Sometimes you may dissolve the table in water or buy the suspension and have less problem with that being vomited.