Review Article

Management of upper gastrointestinal bleeding emergencies: evidence-based medicine and practical considerations

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ABSTRACT: Acute upper gastrointestinal (GI) bleeding remains one of the most common encounters in emergency medicine. The increased use of non-steroid anti-inflammatory drugs by the general population and the increased prescription of anti-platelet agents and anti-coagulants after cardiovascular interventions and for prevention of cerebral vascular accidents may have aggravated the situation. Significant progress has been made in the past decade or so in the non-surgical management of acute upper GI bleeding emergencies. This article will review the current standard treatment of the most common upper GI bleeding emergencies in adults as supported by evidence-based medicine with practical considerations from the authors' own practice experience.

KEY WORDS: Emergency medicine; Upper gastrointestinal bleeding; Evidence-based medicine

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GENERAL CONSIDERATIONS

Upper gastrointestinal (GI) bleeding is usually defined by a bleeding source proximal to the ligament of Treitz although some authors may also include a bleeding source in the proximal jejunum. Many upper GI bleeding cases (e.g. erosive gastritis and esophagitis, angiodysplasia, gastric antral vascular ectasia or watermelon stomach, Cameron erosions, portal hypertensive gastropathy and small ulcers) cause iron-deficiency anemia but do not usually present as emergencies. Upper GI bleeding emergencies are characterized by hematemesis, melena, hematochezia (if the bleeding is very massive and brisk) and evidence of hemodynamic compromise such as dizziness, syncope episodes and shock. They are often caused by major hemorrhage from ulcers, varices, Dieulafoy lesions, Mallory-Weiss tears and neoplasms. Rare causes include hemobilia and hemosuccus pancreaticus as well as enteric fistula connecting with major blood vessels. These patients should be admitted to ICU and urgent gastroenterology consult should be requested. Surgery

should also be notified in cases of massive bleeding.^[1-5] Upper endoscopy is the diagnostic modality of choice for acute upper GI bleeding and often the treatment of choice as well.^[6,7] Aggressive resuscitation and stabilization should be started before endoscopic treatment to minimize treatment-associated complications.^[8] Two large caliber (16 gauge or larger) peripheral venous accesses or a central venous line should be placed in the emergency department. Blood transfusion to hemoglobin above 7-8 gm/dL for patients without severe co-morbidities and above 10 gm/dL for patients with severe co-morbidities, correction of coagulopathy (if INR>1.5) and thrombocytopenia (if platelet<50 000/mL) should be initiated. Endotracheal intubation to protect the airway may be necessary in cases of severe hematemesis with mental status change and high risk of aspiration. Empirical treatment with a loading intravenous (IV) dose of a proton pump inhibitor (PPI) followed by an IV drip has been shown to be beneficial.^[9] A quick survey of the past medical history can be very helpful during workup of the potential cause of hemorrhage. For example, a

history of abdominal aortic aneurysm or previous aortic surgery may prompt the need of a CT scan to assess possible aortoenteric fistula formation. For patients who have brisk ongoing hemorrhage further compromising hemodynamic stability, endoscopic treatment may need to be performed simultaneously with resuscitation and stabilization.^[10] The use of IV erythromycin (approximately 3 mg/kg) prior to endoscopy is helpful to empty the stomach of large amount of blood for better endoscopic visualization^[11,12] although it is not routinely recommended for all upper GI bleeding cases.^[10] Empirical use of octreotide or similar agents should be considered in cases highly suspicious of variceal bleeding but it is not routinely recommended for non-variceal bleeding even though it may have some beneficial effect.^[13]

In the next sections, the specific management of the most common upper GI bleeding emergencies will be discussed.

UPPER GI ULCERS

Ulcer hemorrhage remains a common cause of upper GI bleeding.^[1,14] *Helicobacter pylori* (*H. pylori*) infection and nonsteroidal anti-inflammatory agents/analgesics (NSAID) are the most common causes of peptic ulcer diseases.^[3,15] With the increased prevalence of bariatric surgery, anastomotic or ischemic ulcers are becoming more frequent^[16], especially in patients who smoke, have underlying connective tissue diseases or use NSAIDs. Malignant ulcers will be discussed later. Gastric and duodenal ulcers are the most common forms of upper GI ulcers with more gastric ulcers (54.4%) than duodenal ulcers (37.1%) found in a recent population-based study.^[1] Upper GI ulcer bleeding emergencies occur with large and deep ulcers eroding into sizable blood vessels. In addition to aggressive resuscitation and stabilization discussed in the general consideration section, endoscopic examination is almost always indicated in such cases to attempt to stop ongoing bleeding and to prevent recurrent bleeding. High risk stigmata include active bleeding (greater than 90% chance of further bleeding), non-bleeding visible blood vessel (approximately 50% re-bleeding risk) and adherent clot (25%-30% re-bleeding risk).^[17] The most commonly used endoscopic hemostatic interventions include epinephrine injection, thermal coagulation and endoscopic clipping at the ulcer site to constrict, compress and/or destroy the bleeding vessel. Other treatment modalities such as injection with saline, absolute alcohol or fibrin sealant, argon plasma coagulation

(APC) and sclerotherapy are either less effective or too cumbersome to use and therefore not routinely used for bleeding ulcer treatment.^[18-21] Epinephrine injection alone is generally not adequate, as combination with a mechanical or thermal technique has been shown to be more effective than injection alone.^[22] When there is significant ongoing bleeding from an ulcer, a therapeutic double channel endoscope (such as the Olympus GIF 2-T scope), if available, is a better choice than a single lumen endoscope because of the need for constant wash and removal of clots during the procedure. The objective of thermal coagulation is to thoroughly ablate the bleeding blood vessel while minimizing the damage to the underlying and surrounding tissue to prevent complications such as perforation. When the patient is under treatment with anti-platelet agents such as Plavix or has coagulopathy, endoscopic clipping may be a safer technique than thermal coagulation because of less tissue damage caused by clipping. Multiple endoclips can be used if necessary. When endoscopic therapy fails to stop ongoing ulcer bleeding, emergency surgery or angiographic embolization by an interventional radiologist is necessary. For patients who are not good candidates for surgery, transcatheter angiography and intervention is the treatment of choice.^[23] Emergency surgery currently is reserved only for perforations, patients who have failed non-surgical treatment and patients who remain hemodynamically unstable despite aggressive resuscitation.^[24] All patients who have large bleeding ulcers should be tested for *H. pylori* infection and treated to eradicate it if positive. Active bleeding can interfere with the detection of *H. pylori* through biopsy and urease test and serology may be a better choice for actively bleeding patients.^[25] A follow-up upper endoscopy 6-8 weeks after the initial treatment may be indicated for large gastric ulcers to exclude possible underlying malignancy.

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ESOPHAGEAL AND GASTRIC VARICES

Variceal bleeding cases are almost always emergencies because of the potential loss of a large amount of blood causing hemodynamic shock and multi-organ failure and because of the often serious underlying diseases causing the portal hypertension leading to varix formation. In addition, a large amount of hematemesis and gradual loss of consciousness may cause aspiration and suffocation. The large amount of blood in the GI tract can also worsen hepatic encephalopathy as many of these patients also have underlying liver failure. Variceal bleeding from upper GI tract is classified into esophageal variceal bleeding and gastric variceal bleeding (very rarely ectopic varices can also occur in the duodenum) and there are differences in their treatment. While aggressive resuscitation and stabilization including the use of IV octreotide and PPI are necessary for both types of variceal bleeding, esophageal varices are most effectively treated with band ligation with small elastic rubber bands or sclerotherapy with sodium morrhuate or ethanolamine. Fundic gastric varices are more appropriately treated with endoscopic injection of tissue adhesives such as N-butyl-2-cyanoacrylate (Histoacryl) to obturate large variceal complexes, as band ligation and sclerotherapy are not effective. This technique is standard throughout most of the world except for the United States (US), where the technique is only performed at specialized centers in investigational protocols. In the US, transjugular intrahepatic portosystemic shunt (TIPS) is often performed to control gastric variceal bleeding, especially prior to liver transplantation.^[26,27] However, TIPS generally requires follow-up for several years to ensure patency and is often associated with worsening of hepatic encephalopathy. Terlipressin (a synthetic analog of vasopressin, not available in the US) has been shown to be effective in reducing portal hypertension and mortality in variceal bleeding patients and can be used in place of octreotide.^[28]

In cases of massive bleeding from esophageal varices, occasionally band ligation may be difficult because the banding device fitted on the tip of the endoscope may interfere with visualization, especially when there is a lot of blood present. Variceal sclerotherapy may be

more convenient because injection of the sclerosant into or outside the bleeding varices can both be effective. However, sclerotherapy does have lower efficacy and higher incidence of complications including ulceration with rebleeding, stricture formation, dysmotility, perforation, sepsis and reportedly an increased mortality compared with band ligation and therefore is not the first choice.^[26,29-31] We have found that placement of bands distal to the bleeding site will generally slow bleeding enough to allow direct banding in these massive bleeding cases. After the patient's airway is protected with intubation, we usually start with a quick surveillance look, preferably using a double-channel therapeutic scope (such as Olympus GIF 2-T) because it is better equipped to clear clots. Once esophageal variceal bleeding is confirmed, a regular upper scope fitted with the banding device is then advanced to the gastroesophageal (GE) junction to start banding any visible varices beginning at the GE junction and working upward the lower esophagus until all visible bleeding and major varices are ligated. This approach may be more practical than trying to band only the bleeding spot because it can be missed and the banded varices can interfere with the further advancement of the scope beyond the banded area. A repeat endoscopy in 2-4 weeks after the initial treatment is recommended to band residual varices and determine the need for further endoscopic treatment. All variceal bleeding patients should receive short-term antibiotics to prevent infection complications and reduce mortality.^[32] The most commonly used antibiotics include oral norfloxacin or IV ciprofloxacin or IV ceftriaxone where quinolone resistance is prevalent. Nonspecific beta-blockers such as propranolol and nadolol are helpful in prevention of recurrent bleeding and should be used for maintenance therapy to reduce portal hypertension if tolerated.^[33,34] When endoscopic treatment fails to stop the active esophageal variceal bleeding, other immediate intervention is necessary. TIPS procedure should be performed emergently when available.^[35] Balloon tamponade with the Minnesota tube may be used for up to 24 hours as a temporizing treatment for patients with uncontrollable bleeding before more definitive treatment such as TIPS is performed; however these tubes are associated with major morbidities such as perforation.^[32] Other endoscopic treatment modalities such as self-expanding stent placement^[36], placement of endoscopic loops and perhaps even endoscopic clipping (personal communication with colleagues) have been reported to be successful but further studies are needed to confirm their effectiveness.

Gastric variceal bleeding emergency is traditionally more difficult to treat endoscopically because of the high risk for recurrent bleeding.^[6,37] While initial hemostasis can be achieved with multiple treatment modalities, more definitive treatment such as TIPS is usually required.^[37] More recently, endoscopic variceal obturation with cyanoacrylate has been reported to have a success rate of up to 93%.^[38-41] However, this technique is not without complications and requires special expertise using standard protocol.^[42] Currently, the use of cyanoacrylate has yet to be approved by US Food and Drug Administration and its use for gastric varices remains experimental in the US. Other treatment modalities such as thrombin injection^[43] and the interventional radiology technique of balloon-occluded retrograde transvenous obliteration (BRTO)^[44] have shown some promises in gastric variceal treatment but the confirmation of their effectiveness still awaits more definitive studies.

Variceal bleeding patients are often treated with PPI to reduce gastric acid secretion but there is no data to support such practice in preventing rebleeding. However, there is data to suggest that over transfusion of blood may be detrimental in these cases and therefore should be avoided.^[45]

DIEULAFOY LESIONS

A Dieulafoy lesion is an abnormal submucosal blood vessel that has eroded the overlying mucosa without the presence of an ulcer. It accounts for approximately 1% of severe upper GI bleeding and tends to occur in patients with cardiovascular diseases, chronic renal insufficiency and NSAID use.^[46] It is most frequently present in the upper stomach along the lesser curvature. Because of the lack of an accompanying ulcer, a Dieulafoy lesion may not be easily identified when it is not actively bleeding. Careful search after thorough irrigation is necessary. Effective treatment modalities include thermal coagulation after epinephrine injection, endoscopic clipping and band ligation.^[47-51] Care should be taken to avoid banding excessive tissue as complications including perforation and death have been reported for band ligation of gastric Dieulafoy lesion.^[50,52] There is a report of APC being effective in treatment of gastric Dieulafoy lesions^[53] and further studies are needed to confirm its effectiveness.

MALLORY-WEISS TEARS

Mallory-Weiss tears are lacerations in the lower esophagus and gastric cardia because of forceful retching.^[54] Small Mallory-Weiss tears may be incidentally found on endoscopy in patients with nausea and vomiting and do not necessarily cause bleeding.^[55] Most bleeding Mallory-Weiss tears are also minor and self-limited. Only a very small percentage of Mallory-Weiss tears present with massive hemorrhage that requires endoscopic treatment, angiographic embolization or surgery.^[56,57] The classic presentation of a Mallory-Weiss tear bleeding is the turning of vomitus from initially non-bloody to bloody. Hiatal hernia, chronic alcoholism and portal hypertension are predisposing factors for Mallory-Weiss tear bleeding.^[57,58] Endoscopic treatment modalities are similar to those for Dieulafoy lesions although care should be exercised using thermal coagulation to prevent perforation of the thin esophageal wall.^[59-62] Thermal coagulation is also contraindicated in patients who have underlying portal hypertension and varices because of the potential risk of worsening bleeding under those circumstances. However, band ligation is generally successful for tears in the setting of portal hypertension and sclerotherapy reportedly has been used successfully as well.^[60,63]

NEOPLASMS

Both intrinsic and metastatic neoplasms of the upper GI tract can cause hemorrhage. The intrinsic neoplasms include gastric and esophageal cancers, GI stromal tumor (GIST), lymphoma, carcinoid tumor, Kaposi's sarcoma, leiomyoma and leiomyosarcoma. Metastatic tumors from the breast, lung and melanoma are also occasionally seen in the upper GI tract.^[64] Massive hemorrhage from malignancies in the upper GI tract is usually not amenable to endoscopic treatment because such bleeding is usually caused by tumor tissue necrosis that does not respond well to routine endoscopic hemostatic treatment which, at best, provides only very temporary hemostasis.^[65] APC, if available, can be tried. Surgery and transcatheter angiographic embolization are generally required.

HEMOBILIA AND HEMOSUCCUS PANCREATICUS

Hemobilia is bleeding from the hepatobiliary tract while hemosuccus pancreaticus is bleeding from the pancreatic duct. Both present with bleeding from the duodenal papilla endoscopically but can easily

be overlooked without active bleeding during the endoscopy. Hemobilia is often caused by trauma to the liver and biliary tract including liver biopsy, TIPS procedure, percutaneous transhepatic cholangiogram (PTC) and hepatic artery aneurysm rupture.^[66-71] Its classic presentation is the triad of biliary colic, obstructive jaundice and acute and often occult GI bleeding.^[72] Hemosuccus pancreaticus is often related to pancreatic pseudocysts and tumors. Erosion of a pseudocyst into surrounding blood vessels may cause massive hemorrhage. Iatrogenic trauma to the pancreatic duct as in stone removal and pancreatic duct stenting is another cause of hemosuccus pancreaticus.^[73-76] Abdominal contrast CT scan, endoscopy with a side view scope to examine the duodenal papilla or ERCP are helpful in establishing the diagnoses. Treatment, however, is usually through interventional radiology and, if that fails, surgery.

AORTOENTERIC FISTULA

Aortoenteric fistula carries an extremely high mortality rate and should be suspected in all patients with massive or repeated upper GI bleeding and a history of aortic aneurysm or aortic vascular surgeries.^[77,78] The classic triad of abdominal pain, palpable pulsatile mass and GI bleeding occurs only in 11% cases.^[78] Endoscopy with distal duodenal and possibly proximal jejunal examination is essential to exclude other bleeding etiologies and to look for possible evidence of enteric fistula because the most frequent sites of occurrence for aortoenteric fistula is the distal duodenum and proximal jejunum.^[77] Abdominal contrast CT scan is useful in confirming the diagnosis.^[79,80] Treatment is invariably surgical and broad spectrum antibiotics should be used right away to prevent complications.^[77-81]

The common upper GI bleeding emergencies and the highlights of their management have been reviewed. This is by no means meant to be comprehensive. Special occasions can always occur to turn an otherwise non-emergency into an emergency and vice versa. For example, a bleeding from a gastric angiodysplasia usually causes iron-deficiency anemia but does not present as an emergency. However, such a bleeding in a patient with severe coagulopathy and other serious comorbidities may indeed result in a bleeding emergency. Discretion should be exercised by emergency department physicians to decide whether an upper GI bleeding is an emergency or not based on the specific patient's situation.

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