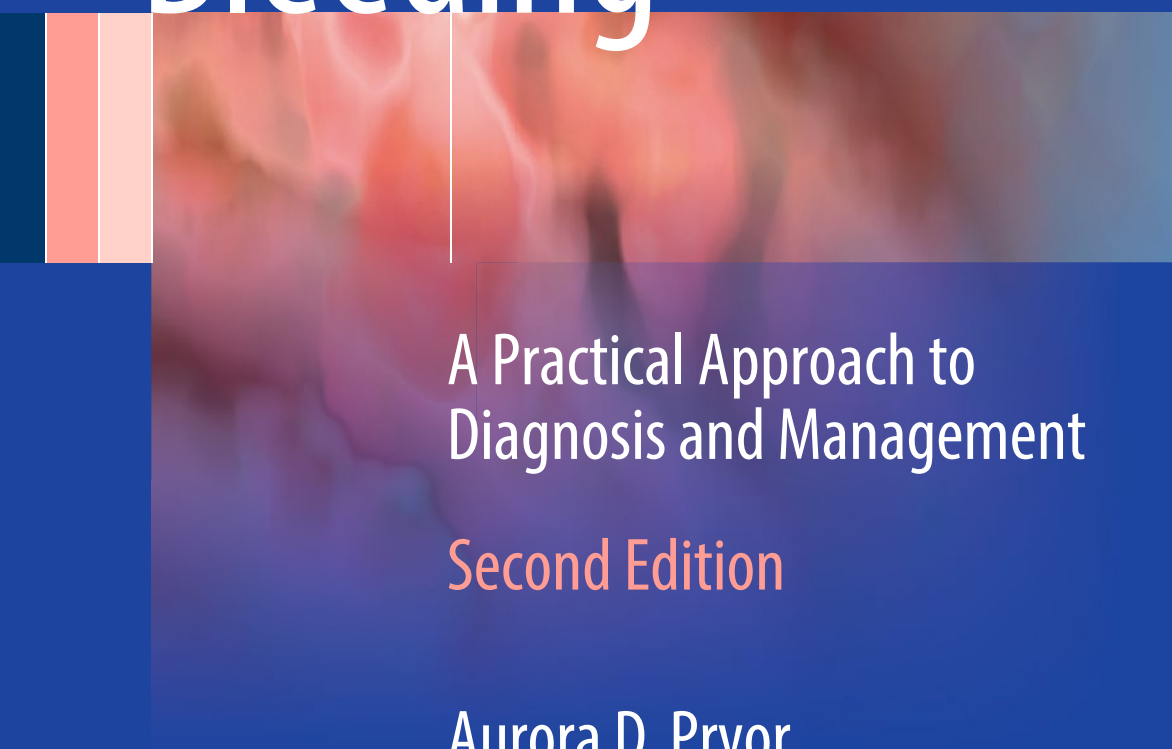
Gastrointestinal Bleeding



A Practical Approach to Diagnosis and Management

Second Edition

Aurora D. Pryor
Theodore N. Pappas
M. Stanley Branch
Editors

Springer

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Preface

Gastrointestinal bleeding is a common medical problem that is managed by clinicians in a variety of medical specialties. Management of upper GI bleeding, in particular, underwent a major transition with the advent of proton pump inhibitor therapy. This transitioned this previously common surgical problem into a predominantly medically managed disease. Newer techniques in gastroenterology and radiology have found utility throughout the gastrointestinal tract and have minimized the necessity for major operations for bleeding. This has also led to major crossover between specialties in the management of GI pathology.

This second edition of *Gastrointestinal Bleeding: A Practical Approach to Diagnosis and Management* provides a foundation for learning for medical students, interns, residents, and practitioners across specialties who encounter these critically ill and difficult to manage patients.

Clinicians who have a common interest in the gastrointestinal tract have collaborated in the construction of this text. This effort has brought together surgeons, gastroenterologists, and radiologists, to carefully chronicle the presentation, diagnosis, and management of modern day causes of gastrointestinal bleeding. These coauthors concentrate on some of the latest innovations in the endoluminal and minimally invasive techniques that characterize the current approaches to these diseases. Emphasis has been placed on minimally invasive diagnostic and therapeutic techniques including capsule endoscopy, double-balloon endoscopy, laparoscopic peptic ulcer surgery, and angiographic diagnosis and management techniques. The text has been written in such a way that the reader can quickly review a specific cause of GI bleeding prior to managing of such a patient. We expect this text will be used with the same immediacy as the diseases present.

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Part I
Upper GI Bleeding

Chapter 1
Stabilization of Patients Presenting with Upper Gastrointestinal Bleeding

C. Cameron McCoy and Mark L. Shapiro

Introduction

Paleopathological evidence and descriptions of upper gastrointestinal bleeds (UGIB), i.e., proximal to the ligament of Treitz, are limited and sometimes inconclusive. The earliest potential reference to UGIB can be traced to the Ebers Papyrus (circa 1550 BC) describing a "blood-nest" in a patient who acutely turned pale and later expired [1]. A more conclusive familiarity of peptic ulcer pathology was noted by Roman scientists during the first century and thus we know that UGIB have been known for at least 2000 years [2]. Risk factors for UGIB were most likely omnipresent and, as such, suffering from UGIB has more than likely always plagued humans.

UGIB are estimated to result in 40–150 episodes per 100,000 population [3], resulting in more than 300,000 hospital admissions [4, 5] and accounting for 1–2 % of all annual US hospital admissions [6]. At least 50 % of UGIB result from peptic ulcer disease [7] (Fig. 1.1), even amongst those with sequelae from advanced liver disease [8]. This diagnosis is followed more than 10 % of the time by variceal bleeding, erosive disease, and Mallory–Weiss tears, and less commonly by diagnoses such as angiodysplasias, posttraumatic, neoplasms, and Dieulafoy lesions [9, 10].

Repetitive vomiting or retching can lead to injury at or near the gastroesophageal junction, known as Mallory–Weiss tears, and has been associated with alcoholic binges, diabetic ketoacidosis, pro-emetic agents, hiatal hernias, and NSAID use [11]. Increased intra-abdominal pressures are thought to result in herniation of the gastric cardia into the chest, resulting in mucosal injury. Boerhaave's syndrome is the result of this process culminating in perforation. Bleeding from Mallory–Weiss

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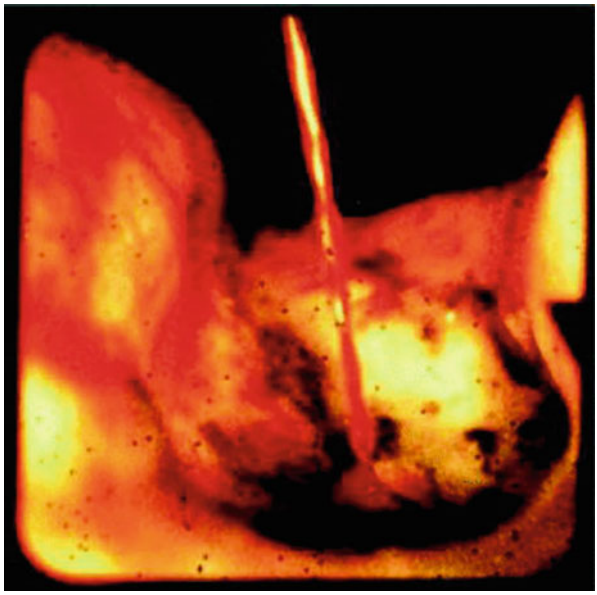


Fig. 1.1 Bleeding ulcer

tears spontaneously ceases in 90 % of cases [12], but persistence is usually associated with bleeding diathesis from other medical comorbidities. Bleeding may be controlled endoscopically and if uncontrolled may require surgery (Fig. 1.2).

Angiodysplasias are acquired lesions with submucosal dilated and tortuous vessels that most commonly occur in the cecum and ascending colon, but can occur in the upper gastrointestinal tract as well. When this occurs they are most commonly noted in the stomach or duodenum. Bleeding from these lesions is intermittent and of varying intensity, but the majority of the bleeds from these lesions spontaneously cease. Uncontrolled bleeding of this source can be severe enough to be catastrophic, and given the intermittent nature of these lesions, they may be missed on endoscopy and therefore must remain in the differential of otherwise unexplained causes of UGIB as oversight can be devastating.

Dieulafoy lesions are congenitally enlarged submucosal arteries that account for approximately 2 % of non-variceal UGIB [13]. The vast majority are less than 5 mm and located 6–10 cm below the gastroesophageal junction on the lesser curvature [14]. Several endoscopic therapies are utilized for bleeding control, but up to 20 % of patients may require surgery for recurrent bleeding [15] (Fig. 1.3).

While UGIB can be both acute and chronic, mortality from the pathology of acute UGIB is much greater than that of chronic UGIB. Large series have estimated that a patient with a UGIB has a mortality rate between 2 and 15 % [16, 17], but that confounding comorbidities such as age, medications, malignancies, and inpatient status may increase this rate to as high as 33 % [17–19]. This takes its toll on society and the health-care system as this diagnosis portends approximately 30,000 deaths [20] and billions of dollars of health-care expenditures annually [21].

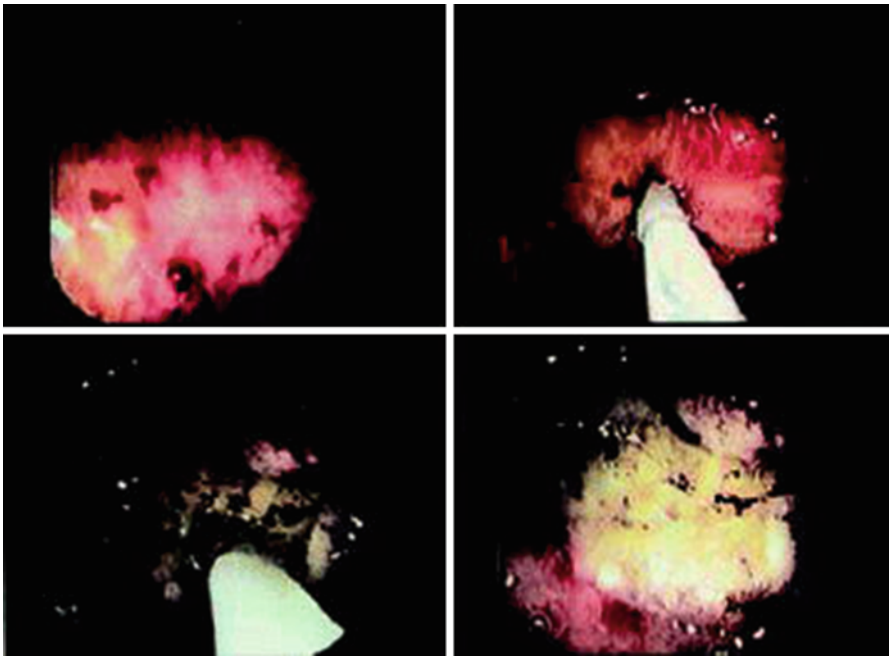
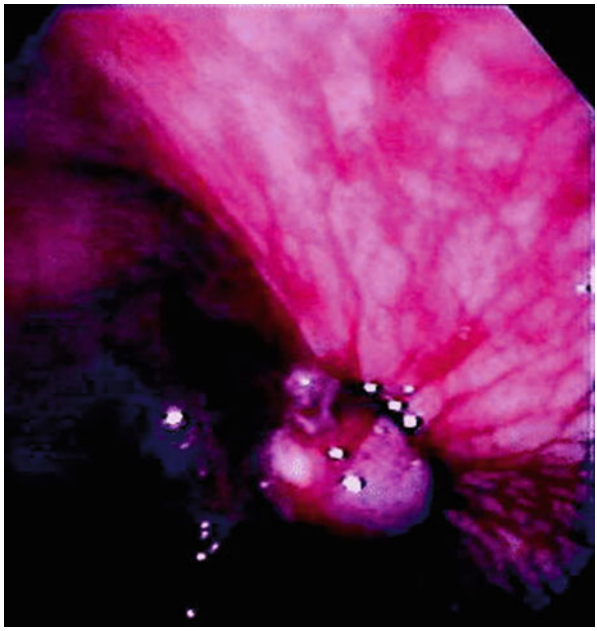


Fig. 1.2 Injection therapy of gastric ulcer

Fig. 1.3 Dieulafoy lesion treated with endoscopic banding



A UGIB may be a life-threatening emergency and requires prompt evaluation, diagnosis, stabilization, and therapeutic measures in a rapid fashion. Management depends on the location and severity of the source and the methodical identification of these. Outcomes are dependent upon time to diagnosis and appropriate management. This chapter focuses on the initial evaluation and management of patients presenting with a UGIB.

Goals of Therapy

Prevention of the morbidity and mortality associated with UGIB should involve assessment and therapy aimed at three approaches: hemodynamic resuscitation, cessation of bleeding source, and prevention of future recurrence. Although each aim is independent, there is inherent overlap and each should proceed in a concurrent manner to achieve the best outcomes.

History

Much information on the etiology of a UGIB can be attained by taking a complete patient history and performing a physical examination. The history should involve inquiring about prior gastrointestinal bleeds, since up to 60 % of UGIB are from the same lesion previously identified [22], as well as alcohol use, liver disease or presence of varices, history of ulcers or symptoms related to them, history of vascular anomalies, prior surgeries or interventions, and the use of certain medications, such as aspirin or non-aspirin NSAIDs. Wilcox et al. noted that the majority of patients presenting with a UGIB had used an aspirin or non-aspirin NSAID in the week prior to presentation and interestingly, 44 % of patients reported non-prescription use [23]. Therefore, history should also include knowledge of the chronic use of over-the-counter medications that might unsuspectingly contain similar products. Cirrhotic patients have a 30 % chance of having a variceal bleed [24]; 60 % of these patients in particular will rebleed within the first year of the index bleed, carrying a 20 % mortality rate per subsequent event [25].

Hemodynamic Resuscitation

It has been demonstrated that, of the modifiable factors affecting outcome, prompt hemodynamic resuscitation affords decreased mortality, as well as morbidity in the form of reduced incidence of myocardial infarction [26]. These authors thus recommend prompt resuscitation of adequate hemodynamic parameters and correction of hematocrit and coagulopathy. We also support this recommendation and thus the

initial evaluation begins with a prompt assessment of hemodynamic instability and aggressive resuscitation afforded within a critical care setting. Delays in resuscitation lead to delays in therapeutic interventions, and thus increased morbidity [26, 27].

The American Society for Gastrointestinal Endoscopy recommends administration of crystalloid fluids to maintain an adequate blood pressure and the use of blood products to meet the demands of ongoing blood loss, significant hemorrhage, or cardiac ischemia [4]. In keeping with these recommendations, we suggest that these patients be treated as seriously as patients who have experienced an acute traumatic injury and have hemodynamic instability. Recommendations include placement of two equal than or larger than 16 gauge intravenous lines and consideration of providing central venous access, especially if the use of a vasoactive drug is anticipated. Administration of a 1 L bolus of crystalloid fluid should then ensue, unless contraindicated by a medical comorbidity. If hemodynamics has not improved, this bolus should be repeated.

If hemodynamic compromise still exists, then blood product transfusion is recommended. For patients requiring large volumes of blood products, massive transfusion protocols have been successfully deployed to treat gastrointestinal bleeding [28]. These protocols are designed to provide oxygen transport in the form of red blood cell transfusion as well as restore coagulation activity from plasma, cryoprecipitate, and platelet transfusion. Coupling massive transfusion with serial laboratory assessments should guide ongoing hemostatic interventions.

Traditional targets for transfusion during upper gastrointestinal bleed have been questioned by recent randomized clinical trials of restrictive transfusion strategies. One of the largest trials enrolled approximately 1000 patients with severe acute upper gastrointestinal bleeding [29]. Patients were randomized to transfusion for hemoglobin below 7 g per deciliter or for hemoglobin below 9 g per deciliter. The restrictive transfusion strategy significantly improved outcomes including 6 week survival and recurrent bleeding.

If a coagulopathy has been detected during resuscitation, the appropriate fractionated blood products should also be administered. During periods of extreme duress, recombinant human factor VIIa (rFVIIa) has been employed. This should only be used in extreme situations as prior investigations continue to question its role in the coagulopathic patient. The largest of these studies did not identify a therapeutic benefit greater than placebo in this setting, although there was a suggestion of potential benefit of reduced therapeutic failure in advanced cirrhosis. However, recently, even this finding was reexamined in a larger population set and not supported [30]. Furthermore, comorbidities such as stroke, pulmonary embolism, and myocardial infarction remain common and severe. Thus a careful, well-balanced risk assessment is necessary prior to the administration of rFVIIa.

Prothrombin complex concentrates (PCC) offer additional means of restoring coagulation function in patients with ongoing bleeding refractory to blood component therapy. These agents have demonstrated efficacy in treating gastrointestinal bleeding in patients on newer therapeutic anticoagulation agents such as direct thrombin inhibitors and direct activated factor X inhibitors [31, 32]. Since direct antidotes are not available, PCCs should be considered for patients on agents such

as dabigatran, rivaroxaban, and apixaban. PCC administration augments drug elimination strategies such aggressive intravenous fluid hydration to promote renal excretion of active metabolites and hemodialysis [33]. Specific coagulation assays such as thrombin time and anti-Xa levels are used to assess residual anticoagulation activity and guide resuscitation as traditional coagulation assays will not accurately measure drug activity [34].

Although blood component therapy has clear survival benefits, utility of antifibrinolytic agents such as tranexamic acid has not been defined. Initial studies demonstrated a beneficial effect on mortality but experienced significant patient drop out [35]. Additional randomized control trials are needed to clarify the role of antifibrinolytics during gastrointestinal bleeding.

During resuscitation efforts, all patients should remain *nil per os*. This will not only aid endoscopic measures but also help protect the patient's airway. If there is any concern for the protection of the patient's airway, either because of potential aspiration or due to mental status, then the patient should be promptly intubated endotracheally.

Cessation of Bleeding

Once the patient has been stabilized by resuscitation efforts, therapeutic measures to control bleeding can be activated. These measures include endoscopic, percutaneous, and surgical. The choice of intervention should be made with the consultation of a multidisciplinary team and consideration of immediately available resources.

Endoscopy

While 80 % of UGIB cease spontaneously, 20 % will recur, and thus the standard of care and first-line therapy is usually upper endoscopy within the first 24 h of an episode [36]. This not only allows visualization of anatomy, source localization, and establishment of predictors of recurrent bleeding (stigmata) but also allows the potential for a therapeutic intervention. The efficacy and safety of achieving endoscopic hemostasis has been reported and carries a high range of both specificity and sensitivity [37–39]. However, the sensitivity is dependent upon both the operator and the endoscopic field. Prior to endoscopy, nasogastric lavage may be performed until lavage fluid is clear or no longer clearing in the case of ongoing hemorrhage. Lavage serves not only as a tool to empty the stomach prior to endoscopy but also as a diagnostic tool for a UGIB, especially in patients with hematemesis [40], though a closed pylorus could result in a negative lavage for a bleeding source distal to the pylorus and proximal to the ligament of Treitz. Intravenous erythromycin (250 mg IV bolus or 3 mg/kg over 30 min) 30–90 min prior to endoscopy may be administered to aid gastric motility and emptying [41, 42].

Numerous studies have addressed the safety of performing endoscopy in the setting of coagulopathy. The risk of ongoing bleeding without endoscopic intervention must be balanced with the risk of iatrogenic bleeding during endoscopy. Current recommendations are to obtain an INR of 1.5 or less prior to endoscopy through the administration of plasma or factor concentrates. Platelet count should be restored to at least 50,000 per microliter by platelet transfusion. In the setting of anticoagulation with high dose aspirin or clopidogrel, platelets should be administered prior to procedure. When severe hemorrhage requires rapid interventions, endoscopy may be performed with simultaneous blood product administration.

Esophageal Tamponade

In patients with uncontrollable esophageal variceal bleeding after failed pharmacologic and endoscopic interventions, balloon tamponade remains a temporary option. The technique was first described by Westphal in 1930 using an esophageal sound for a cirrhotic patient with a variceal bleed [43] and has since spurred the development of three multiluminal nasogastric balloon tubes used for the same purpose. The Sengstaken–Blakemore tube was originally described in 1950 [44] and has a 250 mL gastric balloon, an esophageal balloon, and a gastric suction port. It was later modified to add an esophageal suction port in an effort to decrease the need for parallel insertion of a nasogastric tube for collection of esophageal secretions above the proximal inflated balloon. This modification is known as the Minnesota tube [45]. The third is the Linton–Nachlas tube, which has a 600 mL gastric balloon and both gastric and esophageal aspiration ports. It is used mainly for gastric variceal bleeds. Given that this balloon tamponade has not been shown to be more effective than pharmacological or endoscopic therapy in the long term [46–48] and is frequented by rebleeding after deflating the balloon, as well as a potentially devastating complication of esophageal rupture, balloon tamponade is typically utilized as a temporizing measure until more definitive procedures can be employed.

Percutaneous

The majority of UGIB will either spontaneously cease or be controlled endoscopically. However, in the setting of failed endoscopic therapy, the American College of Radiology has recommended the use of transcatheter-based angiographic interventions, especially in high-risk surgical patients [49]. Angiography is a beneficial tool as it may not only provide diagnostic information in the setting of non-localized lesions but concomitantly be therapeutic through the arterial instillation of vasoactive drugs, arterial embolization, or a combination of the two. Overall this therapy is low risk and may lead to greater than 65 % success [49].

Surgery

Involvement of surgical consultation is necessary for ongoing blood loss despite endoscopic and percutaneous interventions, recurrent bleeding, bleeding related to a prior surgical procedure, or development of an acute abdomen. Any surgical intervention is aimed at providing a procedure predicted to be most effective at achieving hemostasis and preventing future recurrence, while considering its morbidity with the current clinical scenario.

Pharmacological Adjuncts

Octreotide, a somatostatin analogue, is traditionally used to reduce the risk of recurrent variceal bleeding, though recently it has been indicated in non-variceal bleeding, as it not only reduces splanchnic perfusion but also reduces gastric acid secretion and may have a gastric cytoprotective effect and protects renal flow.

Intravenous proton pump inhibitors (PPI) are recommended when a diagnosis of a UGIB is made and one should not wait until confirmation of the source to be a peptic ulcer. Not only does this strategy reduce total length of hospital stay, but it aids the endoscopist as there are fewer actively bleeding ulcers and more ulcers without stigmata of recent bleeding [50]. Opponents of this strategy cite the additional costs associated with this costly therapy in patients without bleeding sources related to acid secretion; however, recent cost analyses have demonstrated this strategy to be more effective pre-endoscopy than afterwards and a less costly treatment strategy for all UGIB [50].

Vasopressin has pharmacological effects which theoretically would aid bleeding cessation. Intravenous vasopressin administration results in mesenteric arteriolar constriction and thus decreased portal venous flow and pressure. Vasopressin used in acute variceal bleeds can have an initial hemostatic rate as high as 80 %, but in a meta-analysis no difference was noted in any major outcome, including mortality reduction. Unfortunately, the vasoconstriction effects of vasopressin may result in systemic end-organ damage, notably of the heart, brain, bowel, and limbs, which can lead to reluctance in its regular use. The same study did demonstrate a 34 % mortality reduction with the use of terlipressin, a vasopressin analogue, suggesting that this analogue may be preferred for vasopressor therapy [51].

Prevention of Recurrence

Both oral and intravenous infusions of PPI have been shown to reduce recurrent bleeding, decrease hospital stay, and reduce the need for blood transfusion. However, the same effect has not been demonstrated with the use of H_2 receptor antagonists, and neither has shown any effect on mortality [36, 51, 52].

Patients with cirrhosis have increased infection rates within the community that are even more greatly elevated when admitted to a hospital. Variceal bleeding disrupts normal mucosal integrity, thus allowing higher rates of bacterial infection. Prophylactic antibiotics in cirrhotic patients hospitalized for UGIB have been demonstrated to reduce overall infections complications, recurrent bleeding, and mortality [53, 54].

Conclusions

Patients presenting with a UGIB undoubtedly represent a serious medical emergency, and outcomes depend on the rapid diagnosis, hemodynamic resuscitation, and successful intervention. The choice of endoscopy, transcatheter-based interventions, or surgery for patients with acute UGIB depends on the site of bleeding being localized or not, patient comorbidities and stability, institutional expertise, and the availability of the aforementioned modalities and resources.

References

1. Brothwell DR, Sandison AT. Diseases in antiquity: a survey of the diseases, injuries, and surgery of early populations. Springfield, lL: Thomas; 1967. xix, 766 p.
2. Majno G. The healing hand: man and wound in the ancient world. Cambridge, MA: Harvard University Press; 1975. xxiii, 571 p., 6 leaves of plates p.
3. Peter DJ, Dougherty JM. Evaluation of the patient with gastrointestinal bleeding: an evidence based approach. Emerg Med Clin North Am. 1999;17(1):239–61. x.
4. Adler DG, Leighton JA, Davila RE, Hirota WK, Jacobson BC, Qureshi WA, et al. ASGE guideline: the role of endoscopy in acute non-variceal upper-GI hemorrhage. Gastrointest Endosc. 2004;60(4):497–504.
5. Hwang JH, Fisher DA, Ben-Menachem T, Chandrasekhara V, Chathadi K, Decker GA, et al. The role of endoscopy in the management of acute non-variceal upper GI bleeding. Gastrointest Endosc. 2012;75(6):1132–8.
6. Zimmerman HM, Curfman K. Acute gastrointestinal bleeding. AACN Clin Issues. 1997;8(3):449–58.
7. Van Dam J, Brugge WR. Endoscopy of the upper gastrointestinal tract. N Engl J Med. 1999;341(23):1738–48.
8. Wilcox CM, Alexander LN, Straub RF, Clark WS. A prospective endoscopic evaluation of the causes of upper GI hemorrhage in alcoholics: a focus on alcoholic gastropathy. Am J Gastroenterol. 1996;91(7):1343–7.
9. Cappell MS, Friedel D. Initial management of acute upper gastrointestinal bleeding: from initial evaluation up to gastrointestinal endoscopy. Med Clin North Am. 2008;92(3):491–509. xi.
10. Czernichow P, Hochain P, Nousbaum JB, Raymond JM, Rudelli A, Dupas JL, et al. Epidemiology and course of acute upper gastro-intestinal haemorrhage in four French geographical areas. Eur J Gastroenterol Hepatol. 2000;12(2):175–81.
11. Kortas DY, Haas LS, Simpson WG, Nickl 3rd NJ, Gates Jr LK. Mallory-Weiss tear: predisposing factors and predictors of a complicated course. Am J Gastroenterol. 2001;96(10):2863–5.
12. Sugawa C, Benishek D, Walt AJ. Mallory-Weiss syndrome. A study of 224 patients. Am J Surg. 1983;145(1):30–3.

13. DiMaio CJ, Stevens PD. Nonvariceal upper gastrointestinal bleeding. Gastrointest Endosc Clin N Am. 2007;17(2):253–72. v.
14. Lee BI, Kim BW, Choi H, Cho SH, Chae HS, Choi MG, et al. Hemoclip placement through a forward-viewing endoscope for a Dieulafoy-like lesion in a duodenal diverticulum. Gastrointest Endosc. 2003;58(5):813–4.
15. Katsinelos P, Paroutoglou G, Mimidis K, Beltsis A, Papaziogas B, Gelas G, et al. Endoscopic treatment and follow-up of gastrointestinal Dieulafoy's lesions. World J Gastroenterol. 2005;11(38):6022–6.
16. Rockall TA, Logan RF, Devlin HB, Northfield TC. Incidence of and mortality from acute upper gastrointestinal haemorrhage in the United Kingdom. Steering Committee and members of the National Audit of Acute Upper Gastrointestinal Haemorrhage. BMJ. 1995;311(6999):222–6.
17. Yavorski RT, Wong RK, Maydonovitch C, Battin LS, Furnia A, Amundson DE. Analysis of 3,294 cases of upper gastrointestinal bleeding in military medical facilities. Am J Gastroenterol. 1995;90(4):568–73.
18. Ferguson CB, Mitchell RM. Nonvariceal upper gastrointestinal bleeding: standard and new treatment. Gastroenterol Clin North Am. 2005;34(4):607–21.
19. Tsoi KK, Lau JY, Sung JJ. Cost-effectiveness analysis of high-dose omeprazole infusion before endoscopy for patients with upper-GI bleeding. Gastrointest Endosc. 2008;67(7):1056–63.
20. Fallah MA, Prakash C, Edmundowicz S. Acute gastrointestinal bleeding. Med Clin North Am. 2000;84(5):1183–208.
21. Jiranek GC, Kozarek RA. A cost-effective approach to the patient with peptic ulcer bleeding. Surg Clin North Am. 1996;76(1):83–103.
22. McGuirk TD, Coyle WJ. Upper gastrointestinal tract bleeding. Emerg Med Clin North Am. 1996;14(3):523–45.
23. Wilcox CM, Shalek KA, Cotsonis G. Striking prevalence of over-the-counter nonsteroidal anti-inflammatory drug use in patients with upper gastrointestinal hemorrhage. Arch Intern Med. 1994;154(1):42–6.
24. Burroughs AK. The natural history of varices. J Hepatol. 1993;17 Suppl 2:S10–3.
25. Bosch J, Garcia-Pagan JC. Prevention of variceal rebleeding. Lancet. 2003;361(9361):952–4.
26. Baradarian R, Ramdhaney S, Chapalamadugu R, Skoczylas L, Wang K, Rivilis S, et al. Early intensive resuscitation of patients with upper gastrointestinal bleeding decreases mortality. Am J Gastroenterol. 2004;99(4):619–22.
27. da Silveira EB, Lam E, Martel M, Bensoussan K, Barkun AN, RUGBE investigators. The importance of process issues as predictors of time to endoscopy in patients with acute upper-GI bleeding using the RUGBE data. Gastrointest Endosc. 2006;64(3):299–309.
28. Young PP, Cotton BA, Goodnough LT. Massive transfusion protocols for patients with substantial hemorrhage. Transfus Med Rev. 2011;25(4):293–303.
29. Villanueva C, Colomo A, Bosch A, Concepcion M, Hernandez-Gea V, Aracil C, et al. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med. 2013;368(1):11–21.
30. Bosch J, Thabut D, Bendtsen F, D'Amico G, Albillos A, Gonzalez Abraldes J, et al. Recombinant factor VIIa for upper gastrointestinal bleeding in patients with cirrhosis: a randomized, double-blind trial. Gastroenterology. 2004;127(4):1123–30.
31. Wychowski MK, Kouides PA. Dabigatran-induced gastrointestinal bleeding in an elderly patient with moderate renal impairment. Ann Pharmacother. 2012;46(4), e10.
32. Dumkow LE, Voss JR, Peters M, Jennings DL. Reversal of dabigatran-induced bleeding with a prothrombin complex concentrate and fresh frozen plasma. Am J Health Syst Pharm. 2012;69(19):1646–50.
33. Abraham NS, Castillo DL. Novel anticoagulants: bleeding risk and management strategies. Curr Opin Gastroenterol. 2013;29(6):676–83.
34. Holster IL, Hunfeld NG, Kuipers EJ, Kruip MJ, Tjwa ET. On the treatment of new oral anticoagulant-associated gastrointestinal hemorrhage. J Gastrointestin Liver Dis. 2013;22(2): 229–31.
35. Bennett C, Klingenberg SL, Langholz E, Gluud LL. Tranexamic acid for upper gastrointestinal bleeding. Cochrane Database Syst Rev. 2014;11:CD006640.

36. Rivkin K, Lyakhovetskiy A. Treatment of nonvariceal upper gastrointestinal bleeding. Am J Health Syst Pharm. 2005;62(11):1159–70.
37. Cook DJ, Guyatt GH, Salena BJ, Laine LA. Endoscopic therapy for acute nonvariceal upper gastrointestinal hemorrhage: a meta-analysis. Gastroenterology. 1992;102(1):139–48.
38. Sacks HS, Chalmers TC, Blum AL, Berrier J, Pagano D. Endoscopic hemostasis. An effective therapy for bleeding peptic ulcers. JAMA. 1990;264(4):494–9.
39. Rollhauser C, Fleischer DE. Current status of endoscopic therapy for ulcer bleeding. Baillieres Best Pract Res Clin Gastroenterol. 2000;14(3):391–410.
40. Witting MD, Magder L, Heins AE, Mattu A, Granja CA, Baumgarten M. Usefulness and validity of diagnostic nasogastric aspiration in patients without hematemesis. Ann Emerg Med. 2004;43(4):525–32.
41. Coffin B, Pocard M, Panis Y, Riche F, Laine MJ, Bitoun A, et al. Erythromycin improves the quality of EGD in patients with acute upper GI bleeding: a randomized controlled study. Gastrointest Endosc. 2002;56(2):174–9.
42. Frossard JL, Spahr L, Queneau PE, Giostra E, Burckhardt B, Ory G, et al. Erythromycin intravenous bolus infusion in acute upper gastrointestinal bleeding: a randomized, controlled, double-blind trial. Gastroenterology. 2002;123(1):17–23.
43. Westphal K. Über eine Kompressionsbehandlung der Blutungen aus Oesophagusvarizen. Deutsch Med Wochenschr. 1930;56(1135):3.
44. Sengstaken RW, Blakemore AH. Balloon tamponage for the control of hemorrhage from esophageal varices. Ann Surg. 1950;131(5):781–9.
45. Boyce Jr HW. Modification the Sengstaken-Blakemore balloon tube. N Engl J Med. 1962;267:195–6.
46. Avgerinos A, Armonis A. Balloon tamponade technique and efficacy in variceal haemorrhage. Scand J Gastroenterol Suppl. 1994;207:11–6.
47. Fort E, Sautereau D, Silvain C, Ingrand P, Pillegand B, Beauchant M. A randomized trial of terlipressin plus nitroglycerin vs. balloon tamponade in the control of acute variceal hemorrhage. Hepatology. 1990;11(4):678–81.
48. Paquet KJ, Feussner H. Endoscopic sclerosis and esophageal balloon tamponade in acute hemorrhage from esophagogastric varices: a prospective controlled randomized trial. Hepatology. 1985;5(4):580–3.
49. Millward SF. ACR Appropriateness Criteria on treatment of acute nonvariceal gastrointestinal tract bleeding. J Am Coll Radiol. 2008;5(4):550–4.
50. Imperiale TF, Birgisson S. Somatostatin or octreotide compared with H2 antagonists and placebo in the management of acute nonvariceal upper gastrointestinal hemorrhage: a meta-analysis. Ann Intern Med. 1997;127(12):1062–71.
51. Ioannou G, Doust J, Rockey DC. Terlipressin for acute esophageal variceal hemorrhage. Cochrane Database Syst Rev. 2003(1):CD002147.
52. Khuroo MS, Yattoo GN, Javid G, Khan BA, Shah AA, Gulzar GM, et al. A comparison of omeprazole and placebo for bleeding peptic ulcer. N Engl J Med. 1997;336(15):1054–8.
53. Ghassemi S, Garcia-Tsao G. Prevention and treatment of infections in patients with cirrhosis. Best Pract Res Clin Gastroenterol. 2007;21(1):77–93.
54. Garcia-Tsao G. Bacterial infections in cirrhosis. Can J Gastroenterol. 2004;18(6):405–6.

Chapter 2
Urgent Workup for Upper Gastrointestinal Bleeding

Mohan K. Mallipeddi and Sandhya A. Lagoo-Deenadayalan

Introduction

Recall that upper gastrointestinal bleeding (UGIB) refers to blood loss originating from within the alimentary tract proximal to the ligament of Treitz. Workup of a patient presenting with an UGIB should proceed down an algorithm based on common sense and evidence based guidelines. First and foremost, the patient should be stabilized and adequately resuscitated. A focused history and physical exam should ensue to help identify the source of bleeding as well as pertinent complicating factors, such as comorbid disease and medications. Scoring systems can be used to risk stratify patients and further direct disposition and diagnostic and/or therapeutic interventions. This chapter addresses the initial workup of patients who present with acute UGIB requiring inpatient management, but many of the same principles apply to other degrees of UGIB.

Initial Assessment

The first priority in managing UGIB is to stabilize and resuscitate the patient. The previous chapter reviews this process in depth. Briefly, the examiner must rapidly assess the airway, breathing, and circulation and be prepared to institute critical care measures such as intubation, insertion of large bore intravenous lines, and goal-directed resuscitation. Concurrently, blood should be drawn to examine cell counts, chemistries (including liver and renal panels), and coagulation markers (INR and aPTT). A type and screen should be obtained in anticipation of transfusion. Basic

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laboratory tests not only help guide goal-directed resuscitation but also provide insight into bleeding diatheses such as liver or renal failure. More specific laboratory tests should be drawn if indicated; for instance, given the high prevalence of *H. pylori* in peptic ulcer disease and the availability of effective treatment regimens, specific testing should be done in patients with bleeding peptic ulcers.

The examiner should also perform a focused history and physical to identify complicating factors and to further clarify the diagnosis/prognosis. The examiner should start by asking about prior bleeding episodes and common underlying causes, such as peptic ulcer disease (31–67 %), gastritis (7–31 %), and varices (4–20 %) [1]. Known liver disease ± alcohol abuse, aortic graft, *H. pylori* infection, and gastroenteric anastomosis should raise the specter of varices, aorto-enteric fistula, PUD, and marginal ulcer, respectively. Moreover, one or more comorbid conditions are present in roughly two-thirds of patients with UGIB. Cirrhosis, renal failure, and coagulopathies are independent risk factors for UGIB. The relative risk of death is higher for hepatic, renal, and malignant disease than for cardiopulmonary disease and diabetes [1]. As noted in the prior chapter, it is important to review medications for NSAIDs, antiplatelet agents, and anticoagulants as well as steroids, acid suppression agents, and beta-blockers.

The physical exam should attempt to reveal stigmata of the underlying disease process and signs of an acute abdomen warranting urgent or emergent surgery. Patients with UGIB may present with postural hypotension, anemia, hematemesis, hematochezia, or melena. Significant hematemesis plus jaundice, ascites, spider angiomata, asterixis, and/or hepatosplenomegaly implicate varices; epigastric tenderness and coffee ground emesis implicate peptic ulcer disease or a Mallory–Weiss tear; cachexia and a palpable mass implicate malignancy.

An integral part of the history and physical is to rule out alternate diagnoses. For instance, epistaxis or red colored food/drink can mimic hematemesis; bismuth medications can mimic melena; and red meat, turnips, and horseradish can produce false-positive fecal occult blood tests. Of course, lower gastrointestinal bleeding should also be on the differential.

Risk Stratification

In addition to guiding resuscitation and diagnosis, the initial assessment should determine interventional needs and immediate disposition. While no single factor can reliably predict the need for intervention there are two commonly employed scoring systems that can identify patients at risk for death, rebleeding, and clinical intervention: the Blatchford Score [2] and the Rockall Score [3]. The Blatchford Score (Table 2.1) was designed to identify patients requiring intervention based on simple clinical and laboratory findings. It does not require endoscopy and can be calculated at an early stage of triage. Patients with a score of 0 can be safely discharged for outpatient management. The Rockall Score

Table 2.1 Blatchford scoring system

Admission risk marker	Score
Blood urea (mmol/L)	
≥6.5 < 8.0	2
≥8.0 < 10.0	3
≥10.0 < 25	4
≥25	6
Hemoglobin (g/L) for men	
≥120 < 130	1
≥100 < 120	3
<100	6
Hemoglobin (g/L) for women	
≥100 < 120	1
<100	6
Systolic blood pressure (mmHg)	
100–109	1
90–99	2
<90	3
Other markers	
Pulse ≥100 (per min)	1
Presentation with melena	1
Presentation with syncope	2
Hepatic disease	2
Cardiac failure	2

Table 2.2 Rockall (full) scoring system

	Score			
Variable	0	1	2	3
Age	<60	60–79	≥80	
Shock	Systolic BP ≥100, pulse <100	Systolic BP ≥100, pulse ≥100	Systolic BP <100	
Comorbidity	No majors		Cardiac failure, ischemic heart disease, other unlisted majors	Renal failure, liver failure, disseminated malignancy
Diagnosis on endoscopy	Mallory–Weiss; none	All other diagnoses	UGI Malignancy	
Major stigmata of recent hemorrhage	None or dark spot only		Blood in UGI tract, adherent clot, visible or spurting vessel	

(Table 2.2) was designed to identify patients at risk of death. The full score can only be calculated after endoscopy but there is a "clinical" or "pre-endoscopy" version as well [4]. Patients with a low Rockall score (0, 1, or 2) have a less than 5 % risk of rebleeding and mortality is virtually zero, even if there is a rebleed. In contrast, patients with a high Rockall score (8 or greater) have a 40 % risk of rebleeding and their mortality is as high as 41 % [3]. While both studies have been validated alone and head-to-head, the quality of evidence is low and therefore neither should supersede clinical acumen.

Nasogastric Lavage

While nasogastric lavage can be used as an adjunct for diagnosis and visualization, it should not delay additional workup and treatment. According to a Canadian UGIB registry, active bleeding or a non-bleeding visible vessel were seen on endoscopy in 45 % of patients with bloody aspirates, 23 % of patients with coffee-ground aspirates, and 15 % of patients with clear/bile-stained aspirates [5]. This confirms the marginal sensitivity of NG lavage as a diagnostic test. However, a prospective randomized study showed patients with bloody aspirate had reduced transfusion requirements and hospital length of stay after early (<12 h of arrival) endoscopy [6]. In other words, frankly bloody aspirate correlates with high risk lesions which should be intervened upon in a timely manner. As for visualization, a small randomized study comparing lavage via a 40 French orogastric tube versus no lavage demonstrated better visualization but no difference in any meaningful clinical endpoints (e.g., hemostasis, recurrent bleeding, death) [7]. Ultimately, insertion of a nasogastric tube is more likely to cause patient discomfort and delay more appropriate care than to provide novel benefits in most patients; that said, lavage may prompt earlier endoscopy in stable patients with occult bleeding.

Esophagogastroduodenoscopy (EGD)

Esophagogastroduodenoscopy is the primary method of evaluating patients with known or suspected UGIB. EGD has a reported sensitivity of 92–98 % and specificity of 30–100 % [8]. The American Society of Gastrointestinal Endoscopy (ASGE) suggests that early upper endoscopy is a critical step in the workup of a patient with UGIB. An early upper endoscopy allows for diagnosis of esophagitis (Fig.2.1), localization and diagnosis of the source of bleeding, risk stratification of recurrence based on the appearance of the lesion, and potential therapy [9].

The consensus amongst major guidelines is that upper endoscopy should be performed within 24 h of presentation [4, 10, 11], but the optimal time point within this window remains under debate. There are numerous clinical trials and observational studies (NB: these studies have disparate inclusion/exclusion criteria, rigor, and end

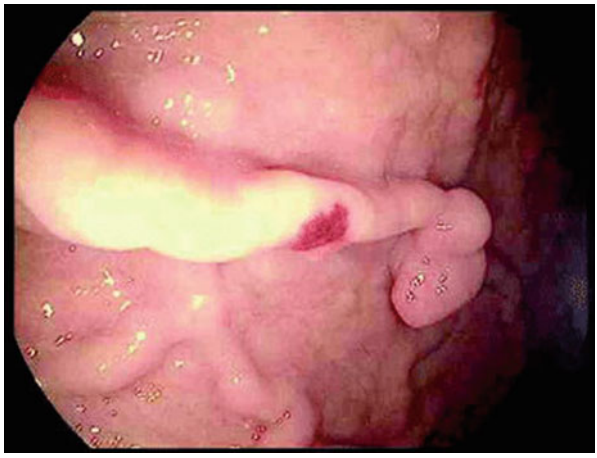

Fig. 2.1 Patient with evidence of esophagitis on EGD

points) that inform this debate, most of which are summarized by two systematic reviews [12, 13]. There is low-level evidence to suggest endoscopy within 12 h of presentation in "high risk" patients lowers mortality and reduces transfusion requirements. There are no clinical benefits—including reduction in rebleeding, length of stay, and additional interventions—to early endoscopy for "low risk" patients. In fact, 40–45 % of low risk patients are candidates for early discharge after endoscopy [10]. However, allocating resources for around-the-clock emergent endoscopy that is unlikely to provide clinical value requires complex financial and behavioral considerations outside the scope of this text. In summary, the current recommendation is to perform EGD in all patients with UGIB within 24 h. In those with persistent bleeding or high risk scores, endoscopy should be performed as soon as it is safe [9].

Patients who experience persistent or recurrent bleeding after initial endoscopy should undergo repeat endoscopy, but routine second-look endoscopy provides no clinical benefit. Up to 24 % of high risk patients will have further bleeding [11] of which 73 % can be successfully treated with repeat endoscopy [14]. Those who progress to surgery for uncontrolled bleeding have a reported postoperative mortality of 30 %, mostly from decompensation of a medical comorbidity or operative complication, such as leak [4]. Therefore, the clinical team should repeat endoscopy or consider interventional radiology in the case of recurrent or uncontrolled bleeding, keeping in mind that failure to achieve control of bleeding will lead to the need for emergent salvage surgery.

In spite of the excellent results with EGD, the procedure is not without complications. It can cause gastrointestinal perforations, further bleeding, aspiration pneumonia, respiratory arrest, and cardiovascular complications [15]. The incidence of complications is low, but it is important to be certain that the benefit of the procedure outweighs the risk.

Table 2.3 Forrest classification of peptic ulcers

Type	Description (prevalence)
Ia	Active spurting bleeding (12 %)
Ib	Active oozing bleeding (included above)
IIa	Non-bleeding but visible vessel (8 %)
IIb	Non-bleeding with adherent clot (8 %)
IIc	Non-bleeding with pigmented ulcer base (16 %)
III	Clean base, no sign of bleeding (55 %)

Endoscopic Findings

During endoscopy the examiner should look for a culprit lesion and associated characteristics that suggest the likelihood of recurrent bleeding. Forrest [16] classified peptic ulcers according to features that were associated with risk of rebleeding (see Table 2.3). They are classified as Ia–III, with lesions in higher groups showing a decrease in risk of recurrence. The first group contains the actively bleeding ulcers (I). This group is further separated into vessels that are either spurting (Ia) or oozing (Ib). The second group includes the non-actively bleeding ulcers. This group is further broken down into three groups: non-bleeding but visible vessel (IIa), ulcer with surface clot (IIb), or ulcer with pigmented spots (IIc). Forrest group III includes ulcers with a clean base [16]. Laine and Peterson looked at thousands of patients with bleeding peptic ulcers and determined their prevalence, rate of further bleeding, and mortality associated with the lesions. They found that most ulcers with a clean base, are associated with a 5 % risk of rebleed and 2 % mortality. Patients with ulcers that have a flat, pigmented spot on endoscopy have a 10 % risk of further bleeding and 3 % mortality. The presence of adherent clots on top of an ulcer is associated with a 22 % risk of further bleeding and 7 % mortality. A visible, non-bleeding vessel is correlated with a 43 % risk of rebleed and 11 % mortality, while actively bleeding vessels have the highest risk of recurrence at about 55 % and a mortality of 11 % [17]. Other lesions such as Mallory–Weiss tears are associated with a low risk (2 %) of further bleeding [18]. These associations suggest that proper evaluation via endoscopy is crucial, as endoscopic findings are directly associated with patients' prognosis and therefore will aid in decisions concerning therapy.

EGD is the first-line diagnostic and therapeutic tool in patients with evidence of UGIB. Endoscopic therapeutic options such as vasoactive injections, sclerotherapy, heat probes, and hemoclipping are discussed in detail in a later chapter.

Arteriography

In 80–90 % of cases an EGD is the only procedure necessary to localize and treat the source of UGI bleeding [19, 20]. The remaining lesions may be elusive to the endoscopist for many reasons, such as structural abnormalities (i.e., strictures or postsurgical

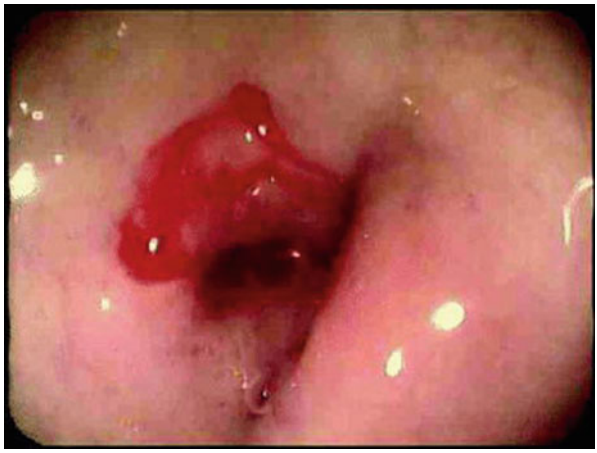

Fig. 2.2 Endoscopy revealing an arteriovenous malformation (AVM)

changes [20]), obscure pathology (i.e., angiodysplasias, arteriovenous malformations, gastric antral vascular ectasias (GAVE), portal hypertensive gastropathy, Dieulafoy lesions [21]), or poor visualization from luminal blood. When an EGD is unable to locate the source of bleeding, a catheter arteriogram is frequently helpful.

Arteriography is an invasive, contrasted radiologic study that can identify briskly bleeding lesions—that is, when the bleeding rate is 0.5–1 mL/min or greater. In the setting of upper GI bleeding, arteriography is positive for extravasation or abnormal mucosal blush in up to 61 % of cases [20]. Some suggest that it has utility in locating structural abnormalities that may not be actively bleeding, such as angiodysplasias, arteriovenous malformations (Fig. 2.2), tumors, or inflammatory lesions [21]. Alternatively, provocative angiography with heparin, thrombolytics, or vasodilators can increase the yield of the study.

In the detection of the source of upper GI bleeding, selective angiography focuses on the celiac axis [20]. Percutaneous access of the femoral artery is obtained via Seldinger technique. A 5F catheter is placed under fluoroscopic guidance into the celiac artery and the superior mesenteric artery. The inferior mesenteric artery is frequently examined to rule out lower gastrointestinal source for bleed as well [20, 21]. Bleeding from the left gastric artery, splenic artery, its closely associated short gastrics, the common hepatic artery, and the gastroduodenal artery can be observed. A positive study is seen as an extravasation of contrast into the bowel lumen or as an abnormal blush. A duodenal ulcer may present as a non-bleeding ulcer (Fig. 2.3) or a bleeding ulcer. Bleeding can occur due to erosion into the gastroduodenal, which may be seen as extravasation around that artery. Embolization of the gastroduodenal artery distal to its take-off from the proper hepatic artery can control bleeding from a duodenal ulcer (Fig. 2.4a, b). Arteriography can also be helpful with the diagnosis of hemorrhagic/stress gastritis, which is a very important diagnosis in ICU patients. On arteriography, one may see multiple small foci of extravasation in a diffusely hypervascular gastric mucosa [19]. A bleeding left gastric artery, associated with a Mallory–Weiss tear, can be seen on arteriogram as well. Once the source of bleeding has been discovered, transcatheter interventions,

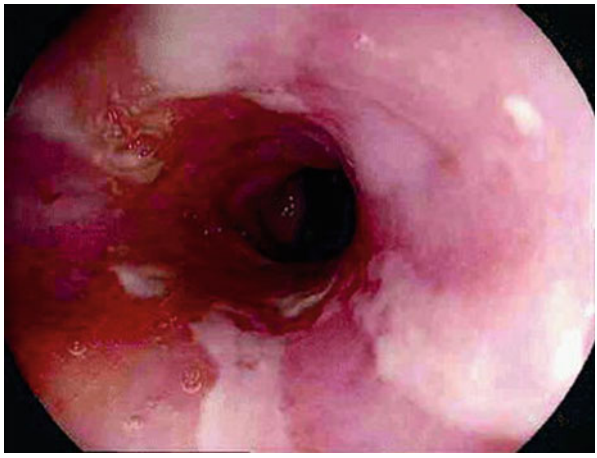

Fig. 2.3 Patient with endoscopic evidence of a non-bleeding duodenal ulcer

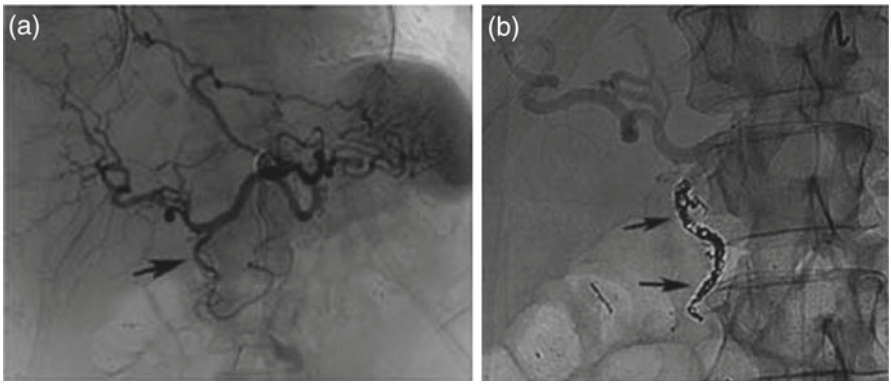

Fig. 2.4 (**a**) Arteriogram of a patient with bleeding from a duodenal ulcer after celiac injection. There was continued bleeding in spite of endoscopic clipping and injection of epinephrine into ulcer bed. The *arrow* indicates gastroduodenal artery with no active extravasation. The clip noticed on fluoroscopy is in the third/fourth portion of duodenum. (**b**) *Arrows* indicate gastroduodenal artery coil embolized using multiple coils. The vessel is occluded just beyond its origin from the proper hepatic artery

such as embolization, can be performed. Figure 2.5a, b shows embolization of the left gastric artery in a patient with a bleeding gastric ulcer.

In spite of the many benefits of arteriography in the detection of occult upper GI bleeding, there is the potential for complications. Arterial injury, contrast reactions, nephrotoxicity, thromboemboli, and hemorrhage are possible but occur quite infrequently. Arteriograms for upper or lower GI bleeding have a complication rate of <5 % [20]. Relative contraindications to catheter directed angiography include severe coagulopathy, congestive heart failure, recent myocardial infarction, renal insufficiency, and pregnancy.

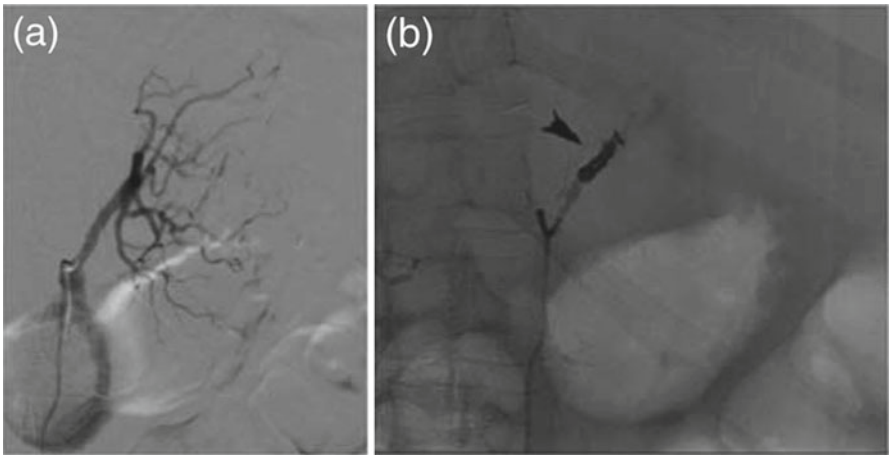

Fig. 2.5 (**a**) Arteriogram of a patient with bleeding from a gastric ulcer. Arteriogram depicts celiac injection with catheter in left gastric artery. (**b**) Left gastric artery occluded with multiple coils

Diagnostic Studies for Obscure Bleeds

Tagged Red Cell Scan

Technetium 99 m-labeled red blood cell scan, also known as tagged red cell scan, can also be used in patients with obscure UGIB. Red blood cells are labeled with technetium 99 and injected into the celiac artery in order to detect upper GI bleeding. This nuclear medicine scan allows for the detection of bleeds that are much slower, with a rate of 0.1–0.4 mL/min.

When compared to the red cell scan, angiography has less sensitivity for slow bleeding but is more precise at the localization of the bleeding site. The red cell scan allows for determination of active bleeding and many prefer to use it as a prelude to angiography [22]. If the red cell scan is positive suggesting current active bleeding, then angiography is more likely to be positive [20, 23]. When the red cell scan is used in conjunction with arteriogram, the sensitivity of the arteriogram increases to 61–72 % from 40 to 78 % [24]. When the red cell scan is negative, then putting the angiogram on hold may be the most effective strategy as it lowers the risk of complications from arteriogram in patients who are unlikely to be positive. Red cell scan has the benefit of allowing the patient to come back later if the bleed was not detected initially. The prolonged bioavailability of the radiolabeled red blood cells allows for continued imaging for up to 24 h [23]. This procedure is therefore well suited for instances when the bleeding is intermittent, which is a common occurrence. Nuclear scintigraphy is therefore recommended before arteriogram in patients with intermittent bleeding [23]. However, angiogram remains the diagnostic tool of choice in patients with obscure, continuous UGIB [20].

CT Angiography (CTA)

CT angiography is a widely available, minimally invasive diagnostic modality capable of quickly identifying active bleeding, its location, and its source when upper endoscopy has failed. At least one study has shown that CTA can detect the source of bleeding in 72 % of patients whose source could not be located via endoscopy [25].

This modality can detect extravasation at rates of 0.3–0.5 mL/min, better than conventional angiography [26]. Even in the absence of active bleeding, skilled radiologists can identify the culprit based on associated clot, angiodysplasia, abnormal mucosal enhancement, or masses; additionally, atypical sources such as hepatic and pancreatic pathology can be assessed. With modern multidetector systems, the sensitivity and specificity of CTA are 85–89 % and 85–92 %, respectively [27, 28].

Although the reported diagnostic yield of initial CT and conventional angiography are similar [29], CTA more readily lends itself to serial investigations to improve the yield; that said, 41 % of patients with a negative CTA for UGIB require further evaluation and treatment to stop bleeding [30]. Ultimately, another modality is required to intervene upon any bleeding source identified by CTA.

Other Modalities

Patients with upper GI bleeding may present with hematemesis, melena, hematochezia, iron deficiency anemia, or hypotension. Many of these signs/symptoms, however, are not exclusive to UGIB sources. The cause of melena, hematochezia, or iron deficiency anemia may be a bleeding source distal to the ligament of Treitz. If an upper GI source cannot be localized, then the rest of the small bowel as well as the large bowel may need examining via imaging studies. Options for further small bowel evaluation include endoscopic studies, such as capsule endoscopy or push enteroscopy, and radiologic imaging, such as small bowel follow-through. Capsule endoscopy is the favored method in most cases [31]. The aforementioned procedures will be discussed in detail in future lower GI bleeding chapters.

Summary

With the improvement of preventive therapy for peptic ulcer disease, there has been a decrease in the frequency of lesions that cause UGIB, but the mortality from UGIB has remained relatively unchanged [17]. UGIB is 60–90 % more common than are lower GI bleeds, and upwards of 75 % of apparently lower GI blood comes from an upper GI source. This leads to a 2–3 times higher mortality for UGIB than LGIB [22]. Patients with signs or symptoms of UGIB require a thorough evaluation

so that lesions at risk of ongoing or recurrent bleeding can be treated in a timely manner. Endoscopy is first line in the diagnosis of UGIB with an overall accuracy of around 80 % [4]. When the source cannot be detected via upper endoscopy, a tagged blood scan and/or conventional angiogram can be performed to find the source of bleeding. For suspected variceal bleeds, endoscopy is the first choice for diagnosis and treatment.

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References

1. Rotondano G. Epidemiology and diagnosis of acute nonvariceal upper gastrointestinal bleeding. Gastroenterol Clin North Am. 2014;43:643–63.
2. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. Lancet. 2000;356(9238):1318–21.
3. Rockall TA, Logan RF, Devlin HB, et al. Risk assessment after acute upper gastrointestinal haemorrhage. Gut. 1996;38(3):316–21.
4. National Institute for Health and Clinical Excellence (NICE). Acute upper gastrointestinal bleeding: management. London, UK: NICE; 2012. p. 23 (Clinical guideline; no. 141).
5. Aljebreen AM, Fallone CA, Barkun AN. Nasogastric aspirate predicts high-risk endoscopic lesions in patients with acute upper-GI bleeding. Gastrointest Endosc. 2004;59(2):172–8.
6. Lin HJ, Wang K, Perng CL, et al. Early or delayed endoscopy for patients with peptic ulcer bleeding. A prospective randomized study. J Clin Gastroenterol. 1996;22(4):267–71.
7. Lee SD, Kearney DJ. A randomized controlled trial of gastric lavage prior to endoscopy for acute upper gastrointestinal bleeding. J Clin Gastroenterol. 2004;38(10):861–5.
8. Lee EW, Laberge JM. Differential diagnosis of gastrointestinal bleeding. Tech Vasc Interv Radiol. 2004;7(3):112–22.
9. Eisen GM, Dominitz JA, Faigel DO, et al. An annotated algorithmic approach to upper gastrointestinal bleeding. Gastrointest Endosc. 2001;53(7):853–8.
10. Laine L, Jensen DM. Management of patients with ulcer bleeding. Am J Gastroenterol. 2012;107:345–60.
11. Hwang JH, Fisher DA, Ben-Menachem T, et al. The role of endoscopy in the management of acute non-variceal upper GI bleeding. Gastrointest Endosc. 2012;75(6):1132–8.
12. Spiegel BM, Vakil NB, Ofman JJ. Endoscopy for acute nonvariceal upper gastrointestinal tract hemorrhage: is sooner better? A systematic review. Arch Intern Med. 2001;161(11):1393–404.
13. Tsoi KK, Ma TK, Sung JJ. Endoscopy for upper gastrointestinal bleeding: how urgent is it? Nat Rev Gastroenterol Hepatol. 2009;6(8):463–9.
14. Lau JY, Sung JJ, Lam YH, et al. Endoscopic retreatment compared with surgery in patients with recurrent bleeding after initial endoscopic control of bleeding ulcers. N Engl J Med. 1999;340(10):751–6.
15. Cappell MS, Friedel D. Acute nonvariceal upper gastrointestinal bleeding: endoscopic diagnosis and therapy. Med Clin North Am. 2008;92:511–50.
16. Forrest JA, Finalyson N, Shearman DJ. Endoscopy in gastrointestinal bleeding. Lancet. 1974;ii:394–7.
17. Laine L, Peterson WL. Bleeding peptic ulcer. N Engl J Med. 1994;331:717–27.
18. Bjorkman D, Zaman A, Fennerty B, et al. Urgent vs. elective endoscopy for acute non-variceal upper-GI bleeding: an effectiveness study. Gastrointest Endosc. 2004;60(1):1–8.

19. Lefkovitz Z, Cappell MS, Kaplan M, et al. Radiology in the diagnosis and therapy of gastrointestinal bleeding. Gastroenterol Clin North Am. 2000;29(2):489–512.
20. Miller M, Smith TP. Angiographic diagnosis and endovascular management of nonvariceal gastrointestinal hemorrhage. Gastroenterol Clin North Am. 2005;34(4):735–52.
21. Concha R, Amaro R, Barkin J, et al. Obscure gastrointestinal bleeding: diagnostic and therapeutic approach. J Clin Gastroenterol. 2007;413:242–51.
22. Burke SJ, Golzarian J, Weldon D, et al. Nonvariceal upper gastrointestinal bleeding. Eur Radiol. 2007;17:1714–26.
23. McKusick KA, Froelich J, Callahan RJ, et al. 99mTc red blood cells for detection of gastrointestinal bleeding: experience with 80 patients. Am J Roentgenol. 1981;137:1113–8.
24. Manning-Dimmitt L, Dimmit SG, Wilson GR. Diagnosis of gastrointestinal bleeding in adults. Am Fam Physician. 2005;7:1339–46.
25. Ettorre GC, Francioso G, Garribba AP, et al. Helical CT angiography in gastrointestinal bleeding of obscure origin. Am J Roentgenol. 1997;168:727–31.
26. Jaskolka JD, Binkhamis S, Prabhudesai V, et al. Acute gastrointestinal hemorrhage: radiologic diagnosis and management. Can Assoc Radiol J. 2013;64(2):90–100.
27. Wu LM, Xu JR, Yin Y, Qu XH. Usefulness of CT angiography in diagnosing acute gastrointestinal bleeding: a meta-analysis. World J Gastroenterol. 2010;16(31):3957–63.
28. García-Blázquez V, Vicente-Bártulos A, Olavarria-Delgado A, Plana MN, van der Winden D, Zamora J, et al. Accuracy of CT angiography in the diagnosis of acute gastrointestinal bleeding: systematic review and meta-analysis. Eur Radiol. 2013;23(5):1181–90.
29. Wang Z, Chen JQ, Liu JL, Qin XG, Huang Y. CT enterography in obscure gastrointestinal bleeding: a systematic review and meta-analysis. J Med Imaging Radiat Oncol. 2013;57(3):263–73.
30. Chan V, Tse D, Dixon S, et al. Outcome following a negative CT Angiogram for gastrointestinal hemorrhage. Cardiovasc Intervent Radiol. 2015;38(2):329–35.
31. Martins NB, Wassef W. Upper gastrointestinal bleeding. Curr Opin Gastroenterol. 2006;22:612–9.

Chapter 3
Management of Esophageal Variceal Bleeding

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Introduction

Variceal bleeding is a devastating complication of portal hypertension, with a mortality rate of 20 % at 6 weeks after hemorrhage in cirrhotic patients with higher mortality rates in those with Child-Turcotte-Pugh (CTP) Class C disease [1]. Although treatments for variceal bleeding were classically surgical in order to divert blood flow from the portal system, there are various medical, endoscopic, and radiologic techniques that currently are pursued prior to any type of definitive surgical management. In 2007, the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of Liver (EASL) held the 6th international single-topic consensus conference on varices and variceal hemorrhage, which helped to develop the most recent guidelines on the prevention and management of variceal bleeding [2].

Pathophysiology

Clinically significant portal hypertension that leads to gastric and esophageal varices is most often associated with cirrhosis, although it can occur without any cirrhosis or liver dysfunction, termed as non-cirrhotic portal hypertension (NCPH)

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[3]. In cirrhosis, there is both an increase in portal venous blood inflow from splanchnic vasodilation and hyperdynamic circulation, and an increased resistance to portal flow. Increased resistance to flow is secondary to intrahepatic vascular resistance from structural changes in the liver architecture, as well as dynamic factors such as an increased vascular tone in the microcirculation secondary to endothelial dysfunction, decreased vasodilators such as nitric oxide, increased vasoconstrictors such as thromboxane A2, increased recruitment of stellate cells in sinusoidal vessels, and irregular growth patterns secondary to angiogenesis [4, 5]. This increase in portal venous resistance leads to the development of porto-systemic collaterals via vascular endothelial growth factor (VEGF) and placental growth factor (P1GF), the most important of which are gastric and esophageal varices [5]. Splanchnic vasodilation and cardiac output both increase to compensate for this diversion of flow, leading to increased portal venous inflow in an already high-resistance portal venous system and therefore exacerbating portal hypertension [4, 5].

Portal hypertension in cirrhosis can be measured by the hepatic venous pressure gradient (HVPG), which is calculated as the difference between the wedged hepatic venous pressure (WHVP) and the free hepatic venous pressure (FHVP) [6]. The pressures are measured with a 7-French balloon-tipped catheter that is placed radiographically into the hepatic vein (HV) via the internal jugular vein (IJV) [6]. The FHVP is measured with the tip of the catheter in the HV, and then the catheter balloon is inflated for 2 min to achieve a stable reading. This wedged pressure reflects the hepatic sinusoidal pressure which is a surrogate for portal venous pressure (PVP) [6]. Elevated HVPG to greater than 10 mmHg is defined as clinically significant portal hypertension, which leads to complications of decompensated liver disease such as the development of ascites and varices [6]. Variceal bleeding does not occur unless HVPG is greater than 12 mmHg, and most of the interventions described in this chapter aim to reduce these pressures to less than 12 mmHg or 20 % below baseline as the risk of variceal bleeding, spontaneous bacterial peritonitis, and overall mortality decrease with a reduction in portal pressures [6, 7].

NCPH is defined as increased portal venous hypertension with a normal or only mildly elevated HVPG. This is usually secondary to a very long list of heterogeneous liver disorders of vascular origin and can be broken down into pre-hepatic (normal HVPG, PV pressure high), hepatic (HVPG normal or high, PVP high), or post-hepatic (HVPG normal or high, PVP high, FHVP high) [3]. Pre-hepatic NCPH includes conditions such as portal vein thrombosis; an example of post-hepatic NCPH includes severe right-sided heart failure [3]. Hepatic causes of NCPH can be even further characterized into pre-sinusoidal (i.e., schistosomiasis), sinusoidal (i.e., amyloidosis), and post-sinusoidal (i.e., Budd-Chiari syndrome).

Once clinically significant portal hypertension develops and leads to rupture and bleeding of esophageal varices, the treatments are often the same as for portal hypertension of cirrhotic and non-cirrhotic origins. The remainder of this chapter focuses on the medical, endoscopic, radiologic, and surgical techniques used to manage bleeding esophageal varices.

Management: Primary Prophylaxis

The best method to treat variceal bleeding is to prevent rupture of varices from even occurring. Gastric and/or esophageal varices are present in about half of cirrhotics, with prevalence increasing along with the CTP class of the patient's liver disease. Patients evolve from no varices to having varices at a rate of 8 % per year, and varices progress from small to large also at a rate of 8 % per year [1]. The overall yearly risk of variceal hemorrhage (5–15 % per year) is related to the size of the varices, as well as the CTP class of the patient and high-risk bleeding stigmata such as red wale marks [8].

In cirrhotic patients, there are established guidelines in the outpatient management of primary prophylaxis of variceal bleeding. The treatment recommendations are based on the CTP class of the patient's liver disease, size of varices, and if there are the presence of any high-risk bleeding stigmata on endoscopy. Primary prophylaxis of varices involves either pharmacologic treatment with a nonselective beta blocker (NSBB) or endoscopic variceal band ligation (EVL) during initial endoscopy. The nonselective beta blockers most commonly used are propranolol and nadolol, with a goal reduction in heart rate of 25 % but not below 55 beats per minute [9]. The mechanism of action is a reduction in portal pressure via two pathways: a decrease in cardiac output secondary to blockade of beta-1 receptors, and splanchnic vasoconstriction secondary to blockade of beta-2 receptors [9].

In cirrhosis of any CTP class, if there are no varices on screening esophagogastroduodenoscopy (EGD), then no pharmacologic treatment with nonselective beta blockade (class III, level B recommendation) is indicated [1]. This recommendation stems from a prospective randomized controlled trial where 213 patients who had cirrhosis (CTP class A and B) without esophageal varices were randomized to placebo versus a nonselective beta-blocker (timolol) and followed for an average of 4.5 years [10]. There were no differences in the primary endpoint of the development of esophageal varices or variceal hemorrhage, but there was an increased and significant rate of adverse events such as fatigue, low blood pressure, heart rate, and even syncope in the timolol group. Expert consensus panels have recommended that these patients with no varices on screening endoscopy should have a repeat EGD in 3 years or yearly if there is any evidence of hepatic decompensation (class I, level C) [1].

Patients with small varices that have never bled and who are without increased risk for variceal bleeding (i.e., CTP class A) can be started on NSBB but there is no long-term data to support or establish treatment (class III, level B) [1]. Patients with small varices that have never bled but are at higher risk for variceal bleeding (i.e., CTP class B/C, red wale signs on endoscopy) should be provided with nonselective beta-blockers for primary prophylaxis of bleeding (class IIa, level C) [1]. A prospective, randomized, single-blinded study trial compared nadolol (with goal heart rate 25 % below baseline or 50 beats per minute) to placebo in 181 patients with cirrhosis and small varices to determine if nonselective beta-blockage had an effect on growth of varices [11]. Patients had endoscopies yearly for 5 years. The placebo group had a significantly greater progression to large varices (OR 4, CI 1.95–8.4)

and the absolute risk reduction of variceal bleeding was 10 % when taking nadolol. Despite these two improvements the overall survival was not different between the two groups [11].

Once patients are on nonselective beta-blockers, unless there is a decompensation of liver disease patients do not need follow-up EGD (class I, level C) [1]. Patients who have small varices but are not on any NSBB (i.e., secondary to symptoms) should have repeat EGD every 2 years (class I, level C) [1].

For patients with cirrhosis and large varices without high-risk bleeding stigmata or risk of hemorrhage (CTP class A), the recommendations suggest nonselective beta blockade as the choice of prophylaxis (see Fig. 3.1a, b) unless there is a contraindication (i.e., intolerance to side effects) and then endoscopic variceal ligation is the method of choice (class I, level A) [1]. There have been several studies comparing nonselective beta-blockers to EVL in the treatment of large varices that have never bled. A large randomized control trial in 2004 compared EVL verses NSBB in 152 patients with large varices without history of bleeding. After a mean follow-up of 34 months, both groups had non-significant differences in the rates of variceal bleeding (25 % EVL vs. 29 % NSBB) and overall mortality (45 % EVL vs. 43 % NSBB) [12]. Thus the recommendations from the AASLD suggest that in patients with large varices who are at higher risk of bleeding (CTP class A/B, red wale signs), NSBB or EVL can be used for primary prophylaxis (class I, level A) [1]. If EVL is used, the recommended strategy is to continue EVL every 1–2 weeks until obliteration, with then a repeat EGD in 1–3 months, and then repeat EGD every 6–12 months thereafter, while if NSBB is used, repeat EGD is not recommended unless decompensation occurs (class I, level C) [1]. Therefore, the decision to perform EVL or NSBB depends on the local expertise, the patient's willingness to follow up, and if patient can tolerate beta blockade.

Surgical portacaval shunting for primary prophylaxis of variceal bleeding is not recommended in the current guidelines. As far back as 1969, the data did demonstrate a decreased rate of bleeding but did not demonstrate any effect on overall survival and therefore prophylactic surgery was not recommended then either [13].

There are no AASLD guideline recommendations for the general approach to primary prophylaxis on non-cirrhotic portal hypertension, although the general treatment for patients who develop varices is similar to the cirrhosis guidelines, unless specific disease states dictate management. For example, in primary biliary cirrhosis (PBC), the AASLD guidelines suggest screening for varices before a diagnosis of cirrhosis is suspected as they can develop portal hypertension without fibrosis secondary to nodular regenerative hyperplasia [14]. A study in 1999 demonstrated that the Mayo Risk Score (a survival probability model utilizing age, bilirubin, albumin, presence of edema, use of diuretics) predicted the likelihood of varices; if the Mayo Risk Score is greater than 4 then a screening endoscopy should be performed [14, 15]. For other NCPH, algorithms suggest treating small varices without high-risk bleeding stigmata with EGD every 2 years, and treating small varices with high-risk bleeding stigmata as well as large varices with either NSBB or EVL [3].

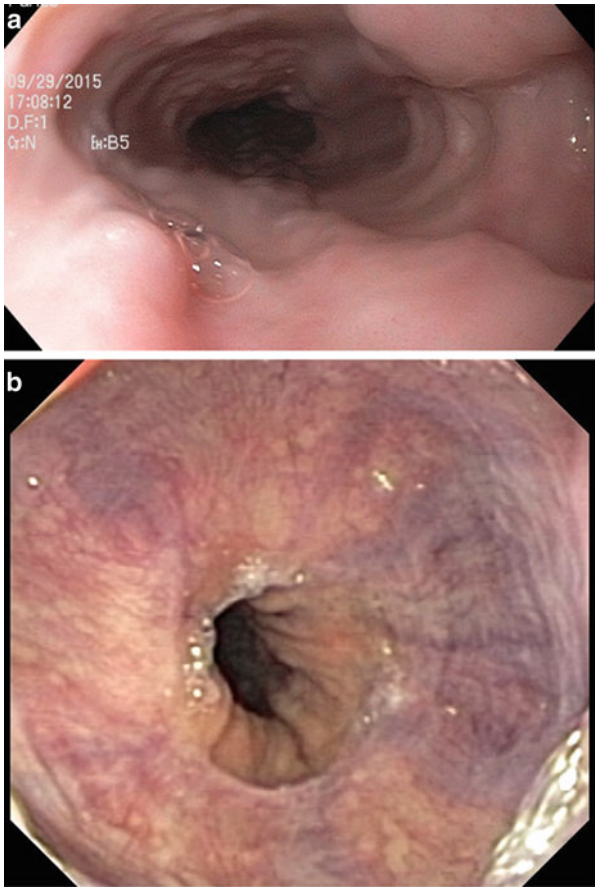

Fig. 3.1 (**a**) Large varices. (**b**) Small varices after NSBB

Management: Variceal Hemorrhage

The initial management of variceal rupture involves aggressive medical management and resuscitation with early endoscopy. Patients should be triaged and managed in a monitored setting such as the intensive care unit with good intravenous access [16]. As with any gastrointestinal bleed, the goal is to maintain tissue perfusion. Although recent studies in non-variceal upper GI bleeding recommend a transfusion goal of 7 g/dL as patients have worse outcomes if a more liberal transfusion strategy is used, based on physiologic studies a goal of 7–8 g/dL in variceal bleeding is used, although this is in order to prevent increased portal pressures and therefore worsened bleeding, unless comorbidities or clinical status dictate otherwise [16–19]. As there is high risk of aspiration during a variceal bleed, endotracheal intubation should be strongly considered, especially in patients who are encephalopathic [1].

The combination of both medical and endoscopic management is the key to decreasing portal pressures and controlling variceal bleeding. Medical management of an acute variceal hemorrhage is a critical part of management. In order to reduce portal pressures via splanchnic vasoconstriction, vasoactive therapy with octreotide, somatostatin, vasopressin, or terlipressin should be given as soon as variceal bleeding is suspected [16]. Currently only octreotide and vasopressin are available in the USA and the most commonly used agent is octreotide [16]. The dosing of octreotide is a bolus of 50 micrograms followed by a rate of 50 micrograms an hour and should be continued for 5 days if variceal bleeding is confirmed [1]. Although beta-blockers are useful in primary prevention, in the event of an acute bleed they can decrease blood pressure and attenuate the body's physiologic response to blood loss and are not recommended [1].

Patients with cirrhosis and variceal bleeding (or any type of upper GI bleeding) have a higher incidence of bacterial infections, likely secondary to gut translocation [1]. A Cochrane review of 12 trials including over a thousand patients demonstrated that prophylactic antibiotics in cirrhotics with upper GI bleeding had significantly less infections, mortality, and even re-bleeding than patients who did not receive antibiotics [20]. A study in 2006 of 111 patients with decompensated cirrhosis and GI bleeding who were given norfloxacin 400 mg orally twice daily verses IV ceftriaxone for 7 days demonstrated that there were more infections (26 % vs. 11 %, $p < 0.03$) and bacteremia (12 % vs. 2 %, $p < 0.03$) in those patients who had norfloxacin vs. ceftriaxone, respectively [21].

Endoscopy for variceal hemorrhage should be performed within the first 12 h of admission [18]. Endoscopic therapy does not alter the pathophysiologic mechanisms that lead to portal hypertension and variceal bleeding; it aims to reduce variceal wall tension by obliterating the varix [18]. Effective endoscopic treatments include variceal band ligation (see Fig. 3.2) and endoscopic sclerotherapy (EST)

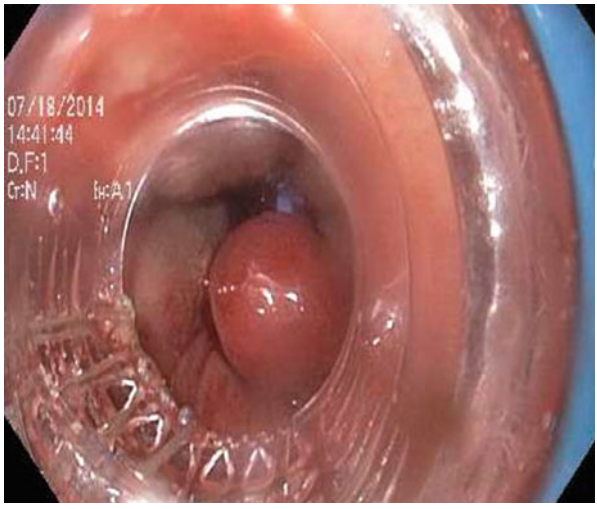

Fig. 3.2 Band ligation

with agents such as ethanolamine oleate or sodium tetrasulfate [18]. Several studies have demonstrated that EVL is superior to EST in both controlling acute hemorrhage and secondary prophylaxis. A prospective randomized controlled trial in 120 cirrhotic patients with acute esophageal variceal bleeding compared ligation versus sclerotherapy (1.5 % sodium tetrasulfate injected into varix). Treatment sessions (6.5 vs. 3.8, $p<0.001$), rates of variceal re-bleeding, (36 % vs. 11 %, $p<0.01$), and complications (19 % vs. 3.3 %, $p<0.01$) were significantly less in the EVL group than the EST group [22].

After successful management of an acute variceal bleed with endoscopic therapy, aggressive secondary prophylaxis needs to take place as there is high risk of re-bleeding and mortality [1]. According to the AASLD guidelines, after an index bleed patients should return for repeat EVL at 1–2-week intervals until complete variceal obliteration; once obliteration is achieved then a repeat EGD is performed in 1–3 months and if no varices then an EGD every 6–12 months (class I, level C) [1]. Data support a combination of both NSBB and EVL for secondary prophylaxis after a variceal bleeding event. In a study looking at 80 cirrhotic patients with variceal bleeding, after hospitalization patients were randomized to either combined therapy or EVL alone. After 16 months of follow-up, the EVL plus nadolol group had a recurrent bleeding rate of 14 % versus 38 % for the EVL-alone group ($p<0.006$). The overall mortality though was not different between the two groups [23]. The findings of this study support the current guidelines which state that a combination of NSBB and EVL is the best option for secondary prophylaxis (class I, level A) [1].

Prior to the advent of therapeutic endoscopy and interventional radiologic techniques, as with most gastrointestinal bleeding, surgery was the mainstay of therapy, with its peak of popularity from the 1960s to 1980s [24]. The mechanism behind surgical management is to reduce portal pressures by creating a portacaval shunt. Total portal systemic shunts decompress the portal system by creating a side-to-side shunt at least 10 mm in diameter between the portal vein and the vena cava (or any of their major tributaries); although these shunts worked well they were fraught with a high rate of encephalopathy [24]. Smaller shunts, called partial portal systemic shunts, are created by placing an 8 mm polytetrafluoroethylene (PTFE) graft between the portal vein and inferior vena cava; these improved the rates of encephalopathy by reducing the diameter of the shunt to 8 mm but still maintain the therapeutic decompression of varices [24]. A randomized controlled trial of 211 cirrhotic patients was randomized to either endoscopic sclerotherapy or emergency surgical portacaval shunt with creation of a side-to-side or end-to-side portal vein and vena cava anastomosis. These patients were triaged and referred to a tertiary medical center from four referring hospitals and treated in an intensive care unit with definitive treatment within 8–12 h of hospital admission. The surgical group had lower rates of primary failure (none vs. 79 %, $p<0.001$) than the endoscopic group, less encephalopathy (35 % vs. 15 %, $p<0.001$), and better overall survival [25]. Another randomized controlled trial of 154 cirrhotic patients was randomized to transjugular intrahepatic portosystemic shunt (TIPS) or emergency surgical portacaval shunt. As with the previous trial, the patients were given definitive treatment within 8–12 h of

hospital admission and treated at the same tertiary referral center. The surgical group permanently controlled bleeding in 97 % of patients while only 22 % of TIPS patients had long-term control of bleeding ($p < 0.001$), lower rates of encephalopathy (21 % vs. 61 %, $p < 0.001$), and again better overall survival [25]. There are some issues with this data prior to recommending surgery as a first-line treatment. Endoscopic therapy with banding of varices and not sclerosants is currently the standard of care. TIPS shunts employ the use of PTFE-covered stents, although in this trial they were uncovered, with a rate of occlusion in 84 % of patients. The study was performed at one tertiary referral center with highly trained experts and may not be feasible or applicable to the widespread medical community. Currently surgery is not recommended in the AASLD guidelines as a first-line treatment for variceal bleeding, instead only as a salvage therapy in patients with preserved hepatic function (see endoscopic treatment failure below) [1].

Although the focus of this chapter is on esophageal variceal bleeding, one cannot talk about the management of esophageal varices without briefly discussing gastric varices. The Sarin Classification has described the various types and combinations of esophageal and gastric varices. Gastroesophageal (GOV) varices are just continuations of esophageal varices into the stomach. Type 1 gastroesophageal varices (GOV-1) run along the lesser curvature of the stomach, while Type 2 gastroesophageal varices (GOV-2) run along the greater curvature [16]. The treatments for these varices are the same as for standard esophageal varices as described throughout this chapter. There are also two types of isolated gastric varices (IGV): IGV-1 are varices located only in the gastric fundus, and IGV-2 are located in the gastric body, antrum, or pylorus [23]. Endoscopic management of gastric varices includes variceal obturation with tissue adhesives such as *N*-butyl-cyanoacrylate [1]. If this endoscopic management fails then patients should be decompressed with a TIPS (see endoscopic treatment failure below) or depending on the variceal venous flow, undergo a balloon-occluded retrograde transvenous obliteration (BRTO). BRTO works by accessing the varices via a gastrocaval shunt, and using an occlusion balloon followed by injection of a sclerosing agent to obliterate the varices [26]. Surgery has also been used to treat gastric varices, with portacaval shunts providing a way to decompress the varices, and if the etiology of gastric varices is secondary to a splenic vein thrombosis then splenectomy is the treatment of choice.

Management: Initial Endoscopic Treatment Failure

Although there are excellent endoscopic and pharmacologic therapies as described above, acute variceal bleeding cannot be controlled in 10–20 % of patients [27]. Factors associated with failure to control an acute hemorrhage include spurting varices, portal vein thrombosis, and high CTP class. The overall risk of re-bleeding after a successful EVL is 8–20 % [27]. According to the Baveno V criteria, failure to control bleeding is defined by evidence of continuous bleeding with either fresh hematemesis or nasogastric aspirate of greater than 100 mL fresh blood 2 h after

therapeutic endoscopy, development of hypovolemic shock, or a decrease in hemoglobin value of greater than 3 g/dL within 24 h of endoscopy [28].

Balloon tamponade is a temporizing measure that can be used as a bridge to more definitive therapies and is effective in temporarily controlling bleeding in over 80 % of patients [1, 27]. As varices lie in the submucosal layer they are amenable to physical tamponade [29]. There are three types of balloons commonly available for tamponade: the Sengstaken–Blakemore tube has esophageal and gastric balloons with a single aspirating port for the stomach, the Minnesota tube has esophageal and gastric balloons with aspiration ports for both the esophagus and stomach, and the Linton–Nicholas tube has only a gastric balloon with aspiration ports in the stomach and esophagus [29]. The downside to balloon tamponade is its many severe and even lethal complications, which include aspiration, esophageal ulceration, necrosis and rupture of the esophagus, balloon migration with asphyxia, and arrhythmias, which occur anywhere from 20 % to even 60 % of the time [30]. Secondary to pressure necrosis, it is not recommended for any of these devices to be inflated for over 24 h [30].

Along the same mechanism as balloon tamponade, there is recent data that demonstrates using fully covered esophageal self-expanding metal stents (FC-SEMS) to be efficacious for mechanical hemostasis in the treatment of refractory variceal bleeding. A randomized controlled trial looking at an FC-SEMS versus balloon tamponade in 28 cirrhotic patients with variceal bleeding refractory to standard endoscopic therapy demonstrated that FC-SEMS was more successful (66 % vs. 20 %, $p=0.025$) with a greater absence of bleeding at 15 days (85 % vs. 47 % $p=0.037$), and less adverse events (31 % vs. 73 %) [30]. This is not currently considered standard of care but with the increased off-label use of FC-SEMS this may become a commonly used backup in the armamentarium of endoscopic therapies for variceal bleeding.

TIPS is a procedure performed by interventional radiologists in patients with portal hypertension for a variety of reasons including refractory ascites, hepatic hydrothorax, and failure of endoscopic therapy in controlling variceal bleeding.

TIPS is a radiologic procedure which reduces the portosystemic pressure as a side-to-side portacaval shunt and successfully reduces the HVPG in over 90 % of cases [31]. To create a TIPS, access to the hepatic veins is gained via a jugular approach with guidewire, and a wedge pressure is obtained to calculate the HVPG. Carbon dioxide is used with balloon occlusion hepatic venography to locate the portal vein. Under fluoroscopic guidance, a needle is then passed via the hepatic vein (usually from the right hepatic vein; however any vein including the inferior vena cava can be used) through the liver parenchyma, and once blood is aspirated a venogram is performed to confirm that the portal vein has been accessed [31]. The tract is dilated with a balloon and a polytetrafluoroethylene-covered stent is deployed, creating the portosystemic shunt. HVPG measurement is repeated to ensure that TIPS is successful.

Although TIPS by a physiologic perspective seems like an uncomplicated procedure, there are many potential complications and patient selection is key. Absolute contraindications for TIPS include congestive heart failure, severe tricuspid regurgitation, and severe pulmonary hypertension; if there is a large shunting of blood to

the right side of the heart after a TIPS, any of these conditions can lead to severe right heart failure [31]. Patients with MELD scores above 18 are not good candidates for TIPS, as they have higher mortality rates 3 months after TIPS placement than those with MELD scores less than 18 [31]. Complications of TIPS include hemorrhage, hemobilia, stent migration, stent stenosis/occlusion, hepatic decompensation, and new or worsened hepatic encephalopathy in 30 % of patients [31]. A study in 1996 evaluated TIPS placement as a definitive therapy in uncontrolled variceal hemorrhage stabilized with balloon tamponade. In 30 patients who met criteria, TIPS was placed successfully in 29 of 30 patients (one failure secondary to portal vein thrombosis) within 12 h after balloon tamponade, and resulted in successful decompression of HVPG to greater than 25 % below baseline in all patients [32]. Most of the patients were severely decompensated CTP class C patients, whose mortality after surgical shunting approaches 90 %. Thirty-day and 6-week survival rates were 63 % and 60 %, respectively. Most complications involved aspiration and when the subgroup without aspiration was analyzed the survival rates approached 90 % [32]. Despite these real complications, TIPS is the only rescue therapy described in this chapter that is supported in the AASLD guidelines for all patients regardless of CTP class, as it is indicated in patients in whom hemorrhage from esophageal varices cannot be controlled despite combined pharmacologic and endoscopic therapy (class I, level C) [1]. The importance of TIPS was studied in a landmark trial published in the *New England Journal of Medicine*. In this study, 63 patients were randomly assigned to EVL/pharmacologic therapy with standard of care medical treatment and follow-up EGD (standard of care) or early TIPS, defined as within 72 h of the endoscopic and pharmacologic therapy for acute bleeding. Re-bleeding or failure to control bleeding occurred in 1 patient in the early TIPS group versus 14 in the standard of care group ($p < 0.001$) [33]. The rates of encephalopathy were not significantly different between the TIPS group and standard of care group (19 % vs. 10 %, $p = 0.8$), but interestingly these rates of encephalopathy were lower than those quoted in the literature for TIPS procedures [33]. Overall survival was better in the TIPS group.

Even though the role of surgery in variceal bleeding has decreased with the advent of alternative endoscopic and radiologic therapies, surgery can be life saving for refractory bleeding [34]. A distal splenorenal shunt (DSRS) is a form of a portacaval shunt where the distal splenic vein is attached to the left renal vein to decompress the portal system and is regarded by most to be the best therapy to prevent re-bleeding in patients with preserved hepatic function that have failed endoscopic therapy [35]. In a randomized controlled trial, 140 patients with CPT class A/B cirrhosis with variceal bleeding refractory to endoscopic therapy were randomized to DSRS or TIPS. Re-bleeding rates (5.5 % DSRS vs. 10.5 % TIPS, $p = 0.29$), encephalopathy (4 % vs. 4 %), and mortality were the same in both groups. Re-intervention rates were higher in the TIPS group than the DSRS group as they required repeated dilations to maintain stent patency (82 % vs. 11 %, $p < 0.001$), although the stents used in the trial were uncovered stents [35]. As both interventions were essentially the same, authors suggested that local expertise and the ability of patients to come for close follow-up care should help determine which intervention is chosen.

The modified Sugiura procedure is another surgical procedure used for salvage therapy and it is indicated in patients with Child CTP A/B cirrhosis when portosystemic shunt placement is not feasible, such as those with extensive thrombosis of the portal, splenic, and superior mesenteric veins, or when TIPS is unavailable or unsuccessful [34]. It involves the complete devascularization of the lesser curvature and the proximal area of the greater curvature of the stomach and transhiatal devascularization of the lower esophagus, with esophageal transection and an end-to-end anastomosis of the esophagus. In retrospective study of 46 patients who had the procedure performed for variceal bleeding refractory to endoscopic therapy, acute bleeding was controlled in all patients. Esophageal leak occurred in five patients (10.8 %) and the postoperative mortality rate was 23.9 % (11 out of 46) with most of those (9 out of 11) being CTP class C patients [34]. Another retrospective review studied the modified Sugiura procedure with and without esophageal transection and found that in terms of bleeding rates, esophageal transection was not necessary once devascularization was achieved as both groups had similar rates of re-bleeding and mortality, with the benefit of less esophageal transection-related morbidity [36].

Conclusion

Variceal bleeding can be a fatal complication of portal hypertension if not prevented or promptly managed. Current treatments aim to decompress varices by resolving portal hypertension and with direct mechanical effects on the varices. With the advent of new techniques, endoscopic therapy with pharmacologic management is considered the first-line treatment. Radiologic therapy with TIPS and surgical therapy with portacaval shunting or devascularization are considered salvage therapies used when endoscopy fails.

References

1. Garcia-Tsao G, Sanyal A, Grace N, Carey W, Shuhart M, Davis G, et al. AASLD practice guidelines: prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology. 2007;46(3):922–38.
2. Garcia-Tsao G, Bosch J, Groszmann R. Portal hypertension and variceal bleeding-unresolved issues. Summary of an American Association for the Study of Liver Diseases and European Association for the Study of the Liver single-topic conference. Hepatology. 2008;47(5):1764–72.
3. Khanna R, Sarin S. Non-cirrhotic portal hypertension-diagnosis and management. J Hepatol. 2014;60(2):421–41.
4. Garcia-Tsao G, Bosch J. Management of varices and variceal hemorrhage in cirrhosis. N Engl J Med. 2010;362(9):823–32.
5. Iwakri Y. Pathophysiology of portal hypertension. Clin Liver Dis. 2014;18(2):281–91.
6. Kumar A, Sharma P, Sarin S. Hepatic venous pressure gradient measurement: time to learn! Indian J Gastroenterol. 2008;27:74–80.

7. Garcia-Pagan J, Patch D. Trials and tribulations: the prevention of variceal bleeding. Gastroenterology. 2015;149(3):528–31.
8. The North Italian Endoscopic Club for the Study and Treatment of Liver Diseases. Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices. N Engl J Med. 1988;319(15):983–9.
9. Garcia-Pagan J, Excorsell A, Moitinho E, Bosch J. Influence of pharmacological agents on portal hemodynamics: basis for its use in the treatment of portal hypertension. Semin Liver Dis. 1999;19(4):427–38.
10. Groszmann R, Garcia-Tsao G, Bosch J, Grace N, Burroghs A, Planas R, et al. Beta-blockers to prevent gastroesophageal varices in patients with cirrhosis. N Engl J Med. 2005;353(21): 2254–61.
11. Merkel C, Marin R, Angeli P, Zanella P, Felder M, Bernardinello E, et al. A placebo-controlled trial of nadolol in the prophylaxis of growth of small esophageal varices in cirrhosis. Gastroenterology. 2004;127(2):476–84.
12. Schepke M, Kleber G, Nurnberg D, Willert J, Koch L, Veltzke-Schlieker W, et al. Ligation versus propranolol for the primary prophylaxis of variceal bleeding in cirrhosis. Hepatology. 2004;40(1):65–72.
13. Conn H. Prophylactic portacaval shunts. Ann Intern Med. 1969;70(4):859–64.
14. Lindor K, Gershwin E, Poupon R, Kaplan M, Bergasa N, Healthcote E, et al. AASLD practice guidelines: primary biliary cirrhosis. Hepatology. 2009;50(1):291–308.
15. Angulo P, Lindor K, Thenaau T, Jorgensen RA, Malinchoc M, Kamath P, et al. Utilization of the Mayo risk score in patients with primary biliary cirrhosis receiving ursodeoxycholic acid. Liver. 1999;19(2):115–21.
16. Hwang JH, Shergill A, Acosta R, Chandrasekhara V, Chathadi K, Decker G, et al. The role of endoscopy in the management of variceal hemorrhage. Gastrointest Endosc. 2014;80(2): 221–7.
17. Villanueva C, Colomo A, Bosch A, Concepcion M, Hernandez-Gea V, Aracil C, et al. Transfusion strategies for upper GI bleeding. N Engl J Med. 2013;368(1):11–21.
18. de Frachis R. Revising consensus in portal hypertension: report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. J Hepatol. 2010;53(4):762–8.
19. Castaneda B, Morales J, Lionetti R, Moitinho E, Andreu V, Perez-Del-Pulgar S, et al. Effects of blood volume restitution following portal hypertensive related bleeding in anesthetized cirrhotic rats. Hepatology. 2001;33(4):821–5.
20. Chavez-Tapia N, Barrientos-Gutierrez T, Tellez-Avila F, Soares-Weiser K, Uribe M. Antibiotic prophylaxis for cirrhotic patients with upper gastrointestinal bleeding. Cochrane Database Syst Rev. 2010;(9) CD002907.
21. Fernandez J, Ruiz del Arbol L, Gomez C, Durandez R, Serradilla R, Guarner C, et al. Norfloxacin vs. ceftriaxone in the prophylaxis of infections in patients with advanced cirrhosis and hemorrhage. Gastroenterology. 2006;131(4):1049–56.
22. Lo G, Lai K, Chen J, Hwu J, Chang C, Chen S, et al. A prospective, randomized trial of sclerotherapy versus ligation in the management of bleeding esophageal varices. Hepatology. 1995;22(2):466–71.
23. Sarin S, Laroti D, Saxena S, Murthy N, Makwana U. Prevalence, classification, and natural history of gastric varices: a long-term follow-up study in 568 portal hypertension patients. Hepatology. 1992;16(6):1343–9.
24. Costa G, Cruz Jr R, Abu-Elmagd K. Surgical shunt versus TIPS for treatment of variceal hemorrhage in the current era of liver and multivisceral transplantation. Surg Clin North Am. 2010;90(4):891–905.
25. Orloff M. Fifty-three years experience with randomized clinical trials of emergency portacaval shunt for bleeding esophageal varices in cirrhosis. JAMA Surg. 2014;149(2):155–69.
26. Sabri S, Saad W. Balloon-occluded retrograde transvenous obliteration (BRTO): technique and intraprocedural imaging. Semin Intervent Radiol. 2011;28(3):303–13.

27. Mihas A, Sanyal A. Recurrent variceal bleeding despite endoscopic and medical therapy. Gastroenterology. 2004;127(2):621–9.
28. Ahn S, Park S, Tak W. Prospective validation of Baveno definitions and criteria for failure to control bleeding in portal hypertension. Hepatology. 2015;61(3):1033–40.
29. Feldman M, Friedman L, Brandt L. Sleisenger and Fordtran's gastrointestinal and liver disease. 9th ed. Philadelphia: Saunders Elsevier; 2012.
30. Escorcell A, Pavel O, Cardenas A, Morillas R, Llop E, Villanueva C, et al. Esophageal balloon tamponade vs. esophageal stent in controlling acute refractory variceal bleeding: a multicenter RCT. Hepatology. 2015. doi:10.1002/hep.28360.
31. Fidelman N, Kwan S, LaBerge J, Gordon R. The transjugular intrahepatic portosystemic shunt: an update. AJR Am J Roentgenol. 2012;199(4):746–55.
32. Sanyal AJ, Freedman A, Luketic VA, Purdum PP, Shiffman M, Tisnado J, et al. Transjugular intrahepatic portosystemic shunts for patients with active variceal hemorrhage unresponsive to sclerotherapy. Gastroenterology. 1996;111(1):138–46.
33. Garcia-Pagan J, Caca K, Bureau C, Laleman W. Early use of TIPS in patients with cirrhosis and variceal bleeding. N Engl J Med. 2010;362(25):2370–9.
34. Voros D, Polydorou A, Polmeneas G, Vassilou I, Melemeni A, Chondrogiannis K, et al. Long-term results with the modified Sugiura procedure for the management of variceal bleeding: standing the test of time in the treatment of bleeding esophageal varices. World J Surg. 2012;36(3):659–66.
35. Henderson J, Boyer T, Kutner M, Galloway J, Rikkers L, Jeffers L, et al. Distal splenorenal shunt versus transjubular intrahepatic portal systemic shunt for variceal bleeding: a randomized trial. Gastroenterology. 2006;130(6):1643–51.
36. Zhang H, Li W, Ye H, Xiao Z. Long term results of the paraesophagogastric devascularization with or without esophageal transection: which is more suitable for variceal bleeding? World J Surg. 2014;38(3):2105–12.

Chapter 4
Management of Dieulafoy's Lesions

Victoria Bendersky and Alexander Perez

Introduction

Dieulafoy's lesion, also referred to as a caliber-persistent artery, gastric aneurysm, or submucosal arterial malformation, is a potentially life-threatening, difficult-to-diagnose, thus perhaps under-recognized, condition of hemorrhage primarily in the gastrointestinal tract with no associated ulceration [1]. Although there are few accounts of the malformation in French medical literature as early as 1884 by Gallard, it was properly distinguished and described by the French surgeon, Paul Georges Dieulafoy (1839–1911) [2]. Due to progress in medicine, particularly the introduction of endoscopy, approaches to diagnose and treat Dieulafoy's lesions have advanced tremendously and the presence of the condition has been broadened to include not only the entire gastrointestinal tract, but also the bronchus [3], eyelid [4], and sciatic area [5]. Although more than a 100 years have passed since Dieulafoy systematically described the lesion, the cause of actual rupture without the ulceration is still not clearly understood [2].

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Pathology

The vascular supply to the stomach and duodenum is quite rich, with many collateral vessels [6]. Vasculature generally branches and narrows in diameter as it traverses closer to the surface of an organ. A Dieulafoy's lesion (DL), however, stays particularly large in diameter for its level of placement, hence the name caliber-persistent artery. The vessel itself is non-aneurysmal and histologic examination usually reveals a large tortuous vessel with no apparent pathology and a minute isolated defect in the mucosa where it protrudes. This abnormally large artery usually occurs at the level of the muscularis mucosa and spans from 0.68 to 2.42 mm, a size more typical of vasculature in the submucosa. The artery may be accompanied by a vein of similar caliber and if perforated, evidence of necrosis in the vessels may be visible [7]. The surrounding tissue generally does not show evidence of an inflammatory response; the absence of an ulcer is characteristic and diagnostic [8] (Fig. 4.1).

Etiology

Acute gastrointestinal bleeding is a common clinical problem in the USA requiring more than 300,000 hospitalizations annually [9]. It is estimated that Dieulafoy's lesion comprises less than 5 % of all gastrointestinal bleeding cases [6]. In adults it presents twice more in men than women [10], and can surface in any age group [11];

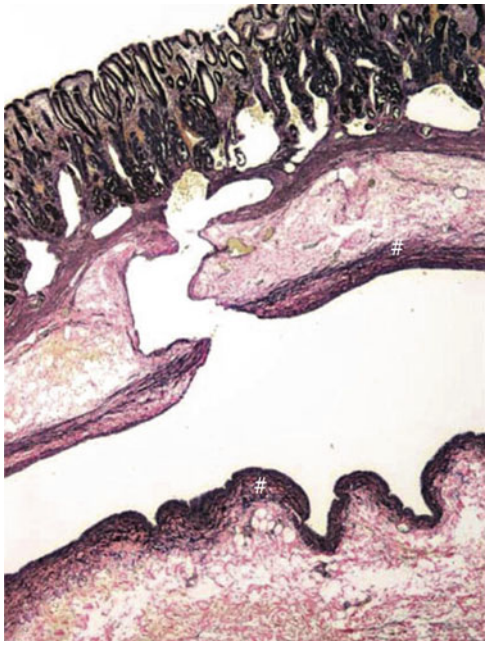

Fig. 4.1 Image obtained from Senger et al. demonstrating a Dieulafoy's lesion in the submucosa. Elastin stain (objective lens ×10) confirms the presence of elastin in the wall (#) alluding to the vessel's arterial origination [2]

however it more commonly affects those that are 50 and older [8]. Curiously, this twofold higher rate of occurrence in males does not extend to the pediatric population. Equal gender distribution of Dieulafoy's lesions in children followed by a marked preference for males in adulthood may suggest hormonal connections; however more studies are needed [2]. Comorbidities are present in a majority of patients with most frequent reports of cardiopulmonary dysfunction, ischemic heart disease, hypertension, diabetes mellitus, liver disease, and chronic renal failure [12]. Comorbidities may be more of an artifact of aging than predictive of DL.

Medical literature suggests several theories on the reasons for Dieulafoy's lesions. The presence of pediatric cases alludes to a possible congenital component [11, 13]. No family linkage has been established, but risk factors such as the usage of nonsteroidal anti-inflammatory drugs (NSAIDs), alcohol, tobacco, or history of peptic ulcer disease have been suggested [2]. The theories of what causes the erosion or an injury to the vessel to initiate the rupture vary; the most prominent three are the following: pulsations of the abnormally large artery may disrupt the mucosa and expose the artery to the gastric contents which in turn may lead to rupture, gastric "wear and tear" promotes thrombosis within the artery leading to necrosis, and age-related atrophy [14].

Location

In his initial description, Dieulafoy prescribed the lesions to the stomach; in 75–95 % of cases this holds true with a particular preference for the proximal stomach within the first 6 cm of the gastroesophageal junction on the lesser curve [8, 12]. However, Dieulafoy's lesions have also been described in the duodenum, jejunum, ileum, cecum, appendix, colon, and rectum. Non-gastrointestinal Dieulafoy's lesions have been reported in the bronchus [3], as well as in the eyelid [4], and sciatic area [5]. The preponderance of lesions to the lesser curve of the proximal stomach is hypothesized to be a product of the vascular architecture in that area with the vessels arising from an arterial chain on the lesser curve [15].

Presentation

Dieulafoy's lesions classically present similar to many other types of GI bleeds, should be carefully considered in the differential, and are a challenge to diagnose endoscopically. As an arteriolar vessel is implicated, Dieulafoy's lesions result in massive hemorrhage that can be intermittent or persistent. Thus, in addition to GI symptoms patients may present with symptoms associated with acute or chronic blood loss. Patients predominantly report melena (44 %), hematemesis (30 %), both melena and hematemesis (18 %), hematochezia (6 %), and iron-deficiency anemia (1 %) [14].

GI symptoms at presentation allude to the location of the lesion. Bright red blood in vomit with dark tarry stools indicates the lesion in the upper GI tract. Dark brown, coffee-ground emesis may implicate an upper GI lesion that has slowed or stopped bleeding and has been exposed to gastric acid. Melena alludes to a source in the upper GI tract, small bowel, or colon. About 100–200 mL of blood in the upper GI tract usually produces melena. Interestingly, it has been suggested that an elevated blood urea nitrogen implies the location in the upper GI source [9]. Diagnostically, hematemesis usually calls for upper GI endoscopy, hematochezia for colonoscopy, and melena calls for both to rule out the massive upper GI bleed.

Diagnostics

Gross examination of a Dieulafoy's lesion consists of a large serpiginous vessel protruding from a small defect in non-inflamed mucosa. Upper/lower endoscopy is the path of choice for diagnosis of the Dieulafoy's lesion (although not exclusive). About 70 % of patients are diagnosed with DL through initial endoscopy [14]. However, for 6 % of patients with intermittent bleeding, multiple endoscopies may be required to establish a definitive diagnosis [14]. Diagnosing DL is difficult as the lesion may present with excess blood (44 %), be subtle and difficult to pinpoint (56 %) [14], or retract altogether [6]. Due to such challenges and the likelihood of erroneously attributing the bleed to ulcerous lesions or varices, Dy et al. established a set of endoscopic visual criteria in 1995 [16]. The parameters are described in Table 4.1.

Direct means of visualization via endoscopy allow for concomitant treatment if the defect is readily located, thereby possibly avoiding other intervention. Even if the defect could not be clearly seen, endoscopy aids in assessing the urgency and planning the approach of subsequent tests; for example: a generalized localization obtained through endoscopy guides which artery to cannulate first at angiography [6].

If endoscopy fails to determine the location of lesion, endoscopic ultrasonography, push enteroscopy, wireless capsule endoscopy, or double/single-balloon enteroscopy may prove necessary to locate the source of obscure bleeding. Following endoscopy, angiography, preceded by nuclear scintigraphy, seems to be the preferred method of localization. Loffroy et al. described the typical presentation of a candidate for angiography and findings are summarized in Table 4.2 [6].

Table 4.1 Endoscopic visual criteria for diagnosing Dieulafoy's lesion by Dy et al. [16]

• Active arterial spurting or micropulsatile streaming from a mucosal defect <3 mm or through normal surrounding mucosa
• Visualization of protruding vessel with or without bleeding, within a minute mucosal defect or through normal surrounding mucosa
• The appearance of fresh, densely adherent clot with a narrow point of attachment to a minute mucosal defect or to normal-appearing mucosa form of hematemesis, melena, fresh bleeding per rectum, or hematochezia

Table 4.2 Indications for angiography [6]

• Massive bleeding (requiring transfusion of at least 4 U of blood/24 h) or hemodynamic instability (hypotension with systolic pressure <100 mmHg and heart rate of 100 bpm or clinical shock secondary to blood loss)
• Bleeding that has failed to respond to conservative medical therapy such as volume replacement, antacids, H2-receptor blocking agents, or proton pump inhibitors
• Bleeding that has failed to respond to at least one attempt at endoscopic control

Endoscopy and angiography are the preferred methods as they in many cases allow for immediate attempts at treatment, whereas the other methods (such as capsule endoscopy) serve purely diagnostic purposes. However, as none of the methods mentioned are foolproof, for obscure bleeding, a combination of diagnostics approaches most likely may be necessary with several repeat cycles.

Laboratory workup should include complete blood count, renal function, and coagulation parameters and should be performed before the patient reaches treatment [6]. Optimal pre-procedural laboratory parameters include a serum creatinine < 1.5 mg/dL with an estimated glomerular filtration rate > 60, an international normalized ratio < 1.5, and a platelet count > 50,000/dL. If necessary, blood products should be transfused before or during the procedure [6].

Therapy/Treatment

As in diagnostics, endoscopy seems to be the first method of treatment for Dieulafoy's lesion, as it is minimally traumatic for the patient and allows for an immediate attempt at hemostasis and tattoo marking for a possible recurrence and surgical planning [17]. Therapeutic endoscopic treatments are classified into three groups: injection therapy-epinephrine and/or sclerotherapy, mechanical method-hemoclipping and band ligation, and thermal-electrocoagulation, heat probe coagulation, and argon plasma coagulation [18].

Injection therapy involves a regional epinephrine injection (dilution, 1:10,000) into four quadrants with 2.5 mL initially with repetition as necessary [18]. It is relatively inexpensive and widely available. Sclerotherapy using sclerosing agents (ethanol, polidocanol) can also be used in injection therapy. Mechanical method involves the usage of hemoclips and endoscopic band ligation. Both are highly effective in achieving hemostasis with less chance for rebleeding [18]. However, it is difficult to apply hemoclips at certain angles and conditions, or after a previous incorrect hemoclip attempt thus requires an experienced endoscopist (Fig. 4.2). Band ligation (EBL) is easier to use but also has disadvantages and may provide difficulty in a possible re-intubation [18]. Thermal coagulation is classified as contact—bipolar and heater probe, or noncontact—argon plasma coagulation.

Multiple studies show that endoscopic treatment in itself frequently requires a combination of methods for maximum efficacy and adjuvant therapy is almost always preferred to minimize rebleeding [1, 8, 14, 19–22]. Frequently, although not

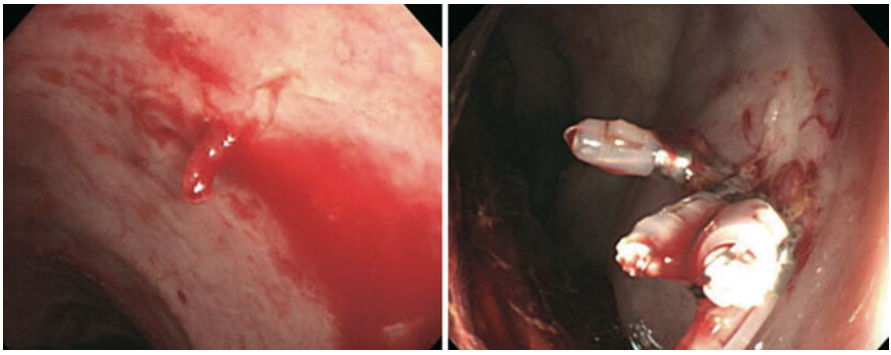

Fig. 4.2 Dieulafoy lesion in the colon prior to and following hemoclip application

universally, an epinephrine injection precedes other definitive treatments [17, 22]. Each modality has its advantages and disadvantages. Table 4.3 illustrates the outcomes of several studies using various treatment approaches.

Two of the studies mentioned above directly compared the efficacy of monotherapy versus combined therapy (Cui et al. and Kanth et al.). Both support the efficacy of combined modalities: Kanth et al. demonstrated that 14 % rebleed from monotherapy and 7 % from a combined modality, while Cui et al. demonstrated that an average 26 % rebleed from monotherapy and 3 % from combined modality [20, 21].

Since it is currently undetermined which combination of endoscopic treatment modalities yields the highest success rate, and mechanical methods cause less damage to the surrounding tissue, perhaps it should serve as the first (of several) steps in management of Dieulafoy's lesion [14, 18]. A novel endoscopic approach has been reported using an over-the-scope clip in management of small bleeds [26] and endoscopic ultrasonography (EUS) may increase treatment options in this area [18].

Secondary to endoscopy, recent developments in catheter-based techniques and newer embolic agents, as well as recognition of minimally invasive treatments as a viable option, the role of interventional radiology has expanded in treating Dieulafoy's lesion [6].

Injection of 2-cyanoacrylate (liquid tissue adhesive NBCA) has been used to successfully arrest bleeding and achieve hemostasis after other methods have failed [6, 27]. In urgent situation using NBCA or a similar adhesive liquid in experienced hands yields a faster time than using other techniques [6]. The use of glue is of particular interest in hemodynamically unstable patients with underlying coagulopathy [6]. Hemostatic powders such as TC-325 (Hemospray™) and EndoClot™ [28] have also been used, but some of these treatment modalities have not yet been approved in the USA, although they show promise in other countries.

Surgical management of Dieulafoy's lesion has been replaced by endoscopy and angiography and is considered as the last step in achieving hemostasis in uncontrolled recurrent obscure bleeding [18]. Within surgery, wedge resection has proven more effective than the oversewing of a vessel. Recent developments in laparoscopy and minimally invasive wedge resection combined with endoscopy is the desired

Table 4.3 Results of therapies for Dieulafoy's lesion

Study	Technique	Patient no.	Initial homeostasis	Recurrent bleeding	Refractory treatment	Deaths
Cui et al. [20]	Ethoxysclerol	46	46	13 (28)	9 Hemoclip	0
					4 Surgery	
	Hemoclip	31	31	7 (23)	4 Ethoxysclerol	0
					3 Surgery	
	Ethoxysclerol + hemoclip	30	30	1 (3)	1 Surgery	0
Lara et al. [23]	Injection	62	58	4 (6)	1 Surgery	3
Dulic-Lakovic et al. [24]	APC/hemoclip	10	10	2 (20)	2 Surgery	0
Ahn et al. [25]	Hemoclip	34	34	5 (15)	0	0
	EBL	32	32	1 (3)	0	0
Kanth et al. [21]	Thermal (bipolar electrocoagulation)	31	31	7 out of 52 for monotherapy (14)	N/A	0
	Injection (Epin)	8	8			
	Mechanical (EBL/hemoclip)	12	12			
	Thermal + injection (Epin)	18	18	4 out of 56 for ≥ 2 modes of therapy (7)	N/A	0
	Thermal + mechanical	14	14			
	Injection (Epin) + mechanical	10	10			
	Thermal + mechanical + injection (Epin)	14	14			
	Surgery	2	2	0	0	0

Values are present as number (%)

APC argon plasma coagulation, *EBL* endoscopic band ligation, *Epin* 1:10,000 epinephrine solution

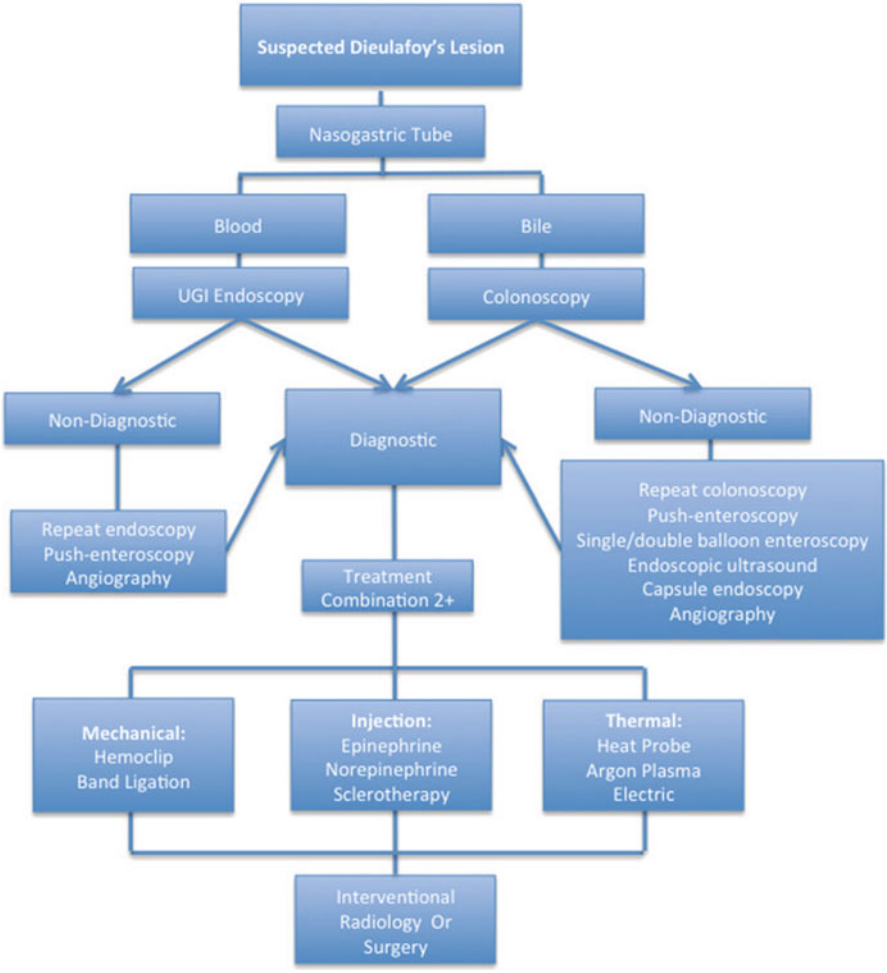

Fig. 4.3 Diagnostic and treatment approach to Dieulafoy's lesion

course of action, although it depends on the physician as the clear guidelines for surgical criteria for Dieulafoy's lesion have not been outlined [1, 2, 17, 18]. The adjacent flowchart illustrates a diagnostic/treatment algorithm for the Dieulafoy's lesion (Fig. 4.3):

Conclusion

Due to continuous developments in the fields of gastrointestinal endoscopy, interventional radiology, and surgery, Dieulafoy's lesions are being identified more accurately and managed with much greater success. Mortality rate has been reduced

from 80 to 8 % [18]. Endoscopic treatment is the standard at the present time; however, advances in interventional radiology are very promising. Surgery is reserved for the very complicated, previously failed attempts at hemostasis and it also is increasingly moving from open to minimally invasive procedures.

References

1. Faes SK, Untch BR, Edwards C, Turner J, Poleski M, Tyler DS. Management of Dieulafoy's lesions. Gastrointestinal bleeding. New York: Springer; 2010. p. 31–7.
2. Senger JL, Kanthan R. The evolution of Dieulafoy's lesion since 1897: then and now—a journey through the lens of a pediatric lesion with literature review. Gastroenterol Res Pract. 2012;2012:432517. doi:10.1155/2012/432517.
3. Gharagozloo F, Rennert D, Margolis M, Tempesta B, Schwartz A, Cole V. Dieulafoy lesion of the bronchus: a review of the literature and report of the 13th case. J Bronchol. 2008;15:38–40.
4. Wong KK, Roberts F, Cauchi P, Diaper C. Caliber persistent artery of the eyelid. Graefes Arch Clin Exp Ophthalmol. 2011;249(9):1395–7. doi:10.1007/s00417-011-1685-x.
5. Futamata H, Kawate T, Sakamoto H, Kitami Y, Takeda S. Large-caliber persistent sciatic artery with aneurysm. Anat Sci Int. 2008;83(4):301–6. doi:10.1111/j.1447-073X.2008.00228.x.
6. Loffroy RF, Abualsaud BA, Lin MD, Rao PP. Recent advances in endovascular techniques for management of acute nonvariceal upper gastrointestinal bleeding. World J Gastrointest Surg. 2011;3(7):89–100. doi:10.4240/wjgs.v3.i7.89.
7. Rouse RV. Dieulafoy lesion/caliber persistent artery. Stanford University School of Medicine, Stanford CA. 2009. http://surgpathcriteria.stanford.edu/gi/dieulafoy-caliber-persistent/. Accessed 25 Feb 2015.
8. Schmulewitz N, Baillie J. Dieulafoy lesions: a review of 6 years of experience at a tertiary referral center. Am J Gastroenterol. 2001;96(6):1688–94. doi:10.1111/j.1572-0241.2001.03922.x.
9. Elta GH, Takami M. Approach to the patient with gross gastrointestinal bleeding. Principles of clinical gastroenterology. Wiley-Blackwell; 2009. p. 122–51.
10. Garg R. Bleeding from a gastric Dieulafoy lesion. Emerg Med J. 2007;24(7):520. doi:10.1136/emj.2006.040667.
11. Avlan D, Nayci A, Altintas E, Cingi E, Sezgin O, Aksoyek S. An unusual cause for massive upper gastrointestinal bleeding in children: Dieulafoy's lesion. Pediatr Surg Int. 2005;21(5):417–8. doi:10.1007/s00383-005-1389-6.
12. Lee YT, Walmsley RS, Leong RW, Sung JJ. Dieulafoy's lesion. Gastrointest Endosc. 2003;58(2):236–43. doi:10.1067/mge.2003.328.
13. Itani M, Alsaied T, Charafeddine L, Yazbeck N. Dieulafoy's lesion in children. J Pediatr Gastroenterol Nutr. 2010;51(5):672–4. doi:10.1097/MPG.0b013e3181ee9f89.
14. Baxter M, Aly EH. Dieulafoy's lesion: current trends in diagnosis and management. Ann R Coll Surg Engl. 2010;92(7):548–54. doi:10.1308/003588410X12699663905311.
15. Veldhuyzen van Zanten SJ, Bartelsman JF, Schipper ME, Tytgat GN. Recurrent massive haematemesis from Dieulafoy vascular malformations—a review of 101 cases. Gut. 1986;27(2):213–22.
16. Dy NM, Gostout CJ, Balm RK. Bleeding from the endoscopically-identified Dieulafoy lesion of the proximal small intestine and colon. Am J Gastroenterol. 1995;90(1):108–11.
17. Hoffman A, Kunert A, Lahat A, Volkov A, Zmora O, Rosin D. Laparoscopic resection of gastric Dieulafoy lesion following preoperative tattooing. Isr Med Assoc J. 2011;13(3):187–8.
18. Jeon HK, Kim GH. Endoscopic management of Dieulafoy's lesion. Clin Endosc. 2015;48(2):112–20. doi:10.5946/ce.2015.48.2.112.

19. Blecker D, Bansal M, Zimmerman RL, Fogt F, Lewis J, Stein R, et al. Dieulafoy's lesion of the small bowel causing massive gastrointestinal bleeding: two case reports and literature review. Am J Gastroenterol. 2001;96(3):902–5. doi:10.1111/j.1572-0241.2001.03641.x.
20. Cui J, Huang LY, Liu YX, Song B, Yi LZ, Xu N, et al. Efficacy of endoscopic therapy for gastrointestinal bleeding from Dieulafoy's lesion. World J Gastroenterol. 2011;17(10):1368–72. doi:10.3748/wjg.v17.i10.1368.
21. Kanth R, Mali P, Roy PK. Outcomes in Dieulafoy's lesion: a 10-year clinical review. Dig Dis Sci. 2015;60(7):2097–103. doi:10.1007/s10620-015-3568-1.
22. Kasapidis P, Georgopoulos P, Delis V, Balatsos V, Konstantinidis A, Skandalis N. Endoscopic management and long-term follow-up of Dieulafoy's lesions in the upper GI tract. Gastrointest Endosc. 2002;55(4):527–31.
23. Lara LF, Sreenarasimhaiah J, Tang SJ, Afonso BB, Rockey DC. Dieulafoy lesions of the GI tract: localization and therapeutic outcomes. Dig Dis Sci. 2010;55(12):3436–41. doi:10.1007/s10620-010-1385-0.
24. Dulic-Lakovic E, Dulic M, Hubner D, Fuchssteiner H, Pachofszky T, Stadler B, et al. Bleeding Dieulafoy lesions of the small bowel: a systematic study on the epidemiology and efficacy of enteroscopic treatment. Gastrointest Endosc. 2011;74(3):573–80. doi:10.1016/j.gie.2011.05.027.
25. Ahn DW, Lee SH, Park YS, Shin CM, Hwang JH, Kim JW, et al. Hemostatic efficacy and clinical outcome of endoscopic treatment of Dieulafoy's lesions: comparison of endoscopic hemoclip placement and endoscopic band ligation. Gastrointest Endosc. 2012;75(1):32–8. doi:10.1016/j.gie.2011.08.038.
26. Gomez V, Kyanam Kabir Baig KR, Lukens FJ, Woodward T. Novel treatment of a gastric Dieulafoy lesion with an over-the-scope clip. Endoscopy. 2013;45 Suppl 2:71. doi:10.1055/s-0032-1326073.
27. Kurek K, Baniukiewicz A, Swidnicka-Siergiejko A, Dabrowski A. Application of cyanoacrylate in difficult-to-arrest acute non-variceal gastrointestinal bleeding. Wideochir Inne Tech Maloinwazyjne. 2014;9(3):489–93. doi:10.5114/wiitm.2014.44169.
28. Barkun A. New topical hemostatic powders in endoscopy. Gastroenterol Hepatol. 2013;9(11):744–6.

Chapter 5
Management of Bleeding Peptic Ulcer Disease

Brian Ezekian and Alexander Perez

Introduction

Peptic ulcer disease is the most common cause of upper gastrointestinal bleeding, accounting for almost half of all cases. While the majority of patients with bleeding peptic ulcers will have spontaneous resolution of bleeding [1], a subset of patients is at high risk of recurrence that requires endoscopic management. If initial endoscopy fails, repeated endoscopy, angiographic embolization, or surgery will be required to prevent fatal hemorrhage.

Epidemiology

PUD is a prevalent disease that remains a major source of morbidity and healthcare-associated costs in developed countries. PUD was responsible for greater than 300,000 deaths in 2013 [2]. It is estimated that expenditures related to the PUD including work loss, hospitalization, and outpatient care amount to $5.65 billion dollars per year in the USA [3]. In addition, the lifetime risk of developing a peptic ulcer is around 10 % [4].

The complications of PUD vary geographically, but the most common complication by far in the USA is bleeding, composing 73 % of all complications [5]. Certain risk factors dramatically increase the risk of bleeding from PUD, namely chronic

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use of nonsteroidal anti-inflammatory drugs (NSAIDs), infection with *H. pylori*, and old age. Use of NSAIDs is the most commonly identified risk factor for bleeding from PUD and is both drug and dose specific. NSAID use confers a relative risk ranging from approximately 3 to 33 depending on the study [6]. Multiple studies have also proven *H. pylori* to be implicated in bleeding from PUD. Intuitively, NSAID use in patients with *H. pylori* infection imparts a synergistic risk [7]. Finally, bleeding from PUD is most commonly seen in elderly patients. Sixty percent of patients are above the age of 60 years and 20 % are over the age of 80 years [8]. In addition, the incidence of bleeding from PUD is 13-fold higher in individuals >70 years as compared with those <40 years [9].

Fortunately, a recent large database analysis found an approximate 30–40 % decrease in hospitalization for complications of PUD between 1993 and 2006 [5]. This overall trend reflects the complex interplay and change over time in risk factors causing PUD. For example, rates of *H. pylori* infection have dramatically fallen in developing countries due to the improved socioeconomic and hygienic conditions following World War II [10]. Contrarily, NSAID use has burgeoned, especially in the elderly, which may account for the slower decline in rates of PUD than expected. Modern-day pharmacological advances including widespread proton pump inhibitor use and effective antibiosis for *H. pylori* have also made significant contributions. None the less, gastrointestinal bleeding from PUD remains a prevalent problem, with estimates showing as high at 57 cases per 100,000 individuals [6].

Pathophysiology

A peptic ulcer is a defect in the gastric or duodenal wall that extends through the muscularis mucosa. While conceptually simple, the pathophysiology of ulcers is quite intricate. The acidic environment of the stomach is predominantly an effect of intraluminal hydrogen ion gradient produced by the parietal cell. Contrarily, stomach epithelial cells secrete both mucus and bicarbonate that form a protective barrier that does not mix with the bulk luminal contents of the stomach. As a result, the pH in the lumen of the stomach generally ranges from 1 to 2, but is near neutral in the immediate vicinity of surface mucosal cells [11]. Peptic ulcer disease occurs when the injurious effects of the acidic environment overwhelm the mucosal barrier.

Prostaglandins stimulate the secretion of mucus and bicarbonate, making the mucosal barrier increasingly robust. The mechanism of NSAID-induced ulcerogenesis is thought to be a result of their inhibitory effects on prostaglandin synthesis [12]. *H. pylori* is highly adapted to the gastric environment. This bacterium adheres to (but does not invade) the gastric epithelial tissue and resides within or underneath the mucus barrier. Disruption of this barrier along with release of enzymes and toxins then renders the underlying mucosa more vulnerable to damage from stomach acids [13]. In addition, the host inflammatory response against the bacteria multiplies this injury.

General Approach to Upper GI Bleeding

Patients with bleeding peptic ulcers generally present with hematemesis or melena similar to other etiologies of upper gastrointestinal bleeding, as these symptoms imply disease proximal to the ligament of Treitz. Initial efforts should be focused towards stabilizing the patient from a hemodynamic standpoint including airway protection, establishing reliable peripheral access, and beginning resuscitation with crystalloid and blood as needed. Subsequently, if possible, a thorough history and physical examination should be obtained. Laboratory evaluation including a complete blood count, serum chemistries, liver function tests, and coagulation studies should be obtained. Particular attention may be paid towards the BUN:creatinine ratio, which has been shown to be elevated and predictive in the cases of upper GI bleed [14, 15].

Routine use of nasogastric tube (NGT) lavage is a matter of controversy. This debate is largely due to the fact that studies have not shown a benefit with regard to outcomes [16]. However, useful clinical information can be derived from this procedure. The presence of red blood or coffee ground material in the NGT aspirate confirms an upper GI source of bleeding. Contrarily, the presence of bilious, non-bloody aspirate demonstrates an open pylorus with no evidence of bleeding distal to the pylorus. In addition, NGT lavage has been associated with shorter time to endoscopy [16] and may ultimately allow clearance of particulate and clots that may obscure endoscopic visualization of the pathology [17].

Treatment of Bleeding Peptic Ulcer Disease

With clinical suspicion of PUD as the source of upper GI bleeding, immediate administration of acid suppression should be instated. The traditional treatment has been a bolus of 80 mg of a proton pump inhibitor (typically pantoprazole or esomeprazole) followed by an 8 mg/h infusion. However, there is mounting evidence that lower bolus and infusion doses may be just as effective [18, 19]. Furthermore, higher dose oral PPIs may also produce comparable results [20]. PPIs have shown a significant reduction in the risk of recurrent bleeding and the need for surgery when compared to H2 histamine receptor antagonists. A recent trial randomized patients admitted with upper GI bleeding to IV omeprazole or placebo at the time of admission, with both arms subsequently undergoing endoscopy the following day. Patients that received IV omeprazole were less likely to have signs of active bleeding or require hemostatic therapy [21]. Another study randomized patients with bleeding ulcers to IV omeprazole or placebo following endoscopic hemostasis. This trial showed that recurrent bleeding was significantly decreased in the omeprazole group, causing early termination of the trial [22].

Somatostatin and octreotide are more infrequently used agents in bleeding from PUD. Their theoretical benefits include reduction in splanchnic blood flow, decreased gastric acid secretion, and increased gastric mucus production [23]. A meta-analysis

of trials that looked at these agents showed efficacy in reducing the risk of continued bleeding [24]. The role of these agents seems to be limited to when endoscopy is unsuccessful, contraindicated, or unavailable [25].

After beginning medical management, the next key step in treating bleeding from PUD is endoscopy. This intervention can both confirm the diagnosis and be therapeutic. Endoscopic treatment is generally performed in patients thought to be at high risk for recurrent bleeding including those with active bleeding, a non-bleeding but visible vessel, or an adherent clot. The standard approaches are thermal coagulation and hemoclip placement. Thermal coagulation involves using a contact probe to compress the area of bleeding and subsequently coagulate it with a heat source, resulting in sealing (coaptation) [26]. Hemoclips function similarly to surgical ligation. Placement of hemoclips can be valuable even if they are unable to achieve hemostasis, as they can serve as a marker for subsequent IR or surgical intervention.

Injection therapy with dilute epinephrine results in tamponade and local vasospasm [27], which provides temporary hemostasis and may permit a cleaner and more visible target field. The role of injection therapy is in conjunction with thermal coagulation and hemoclip placement. Injection monotherapy is not performed because this has been associated with a higher rate of rebleeding when compared with thermal coagulation alone, hemoclip placement alone, or combination therapy [28, 29]. There is no role for injection of sclerosants after epinephrine injection [30].

The role of planned second-look endoscopy is debated. Consensus recommendations from 2010 do not recommend this as a routine practice [31]. Meta-analysis data that looked at over 900 patients across eight randomized trials found that second-look endoscopy was associated with lower rates of rebleeding and surgery, but not mortality [32]. In general, the role of second-look endoscopy is limited to when the endoscopist feels that the initial round of endoscopy was suboptimal in terms of visualization or treatment.

H. pylori infection is associated with the majority of all acute episodes of bleeding from PUD and is considered a major etiologic factor [33]. A recent Cochrane review found that although maintenance anti-secretory therapy was used most commonly in patients to prevent recurrent bleeding, eradication of *H. pylori* in infected individuals was actually more efficacious [34]. Therefore, testing patients with complicated PUD for this bacterium and treating infected individuals with subsequent eradication therapy are necessary.

The European Society of Gastrointestinal Endoscopy has proposed a set of guidelines for the management of non-variceal upper gastrointestinal hemorrhage which are listed below [35]:

- Hemodynamic status assessment and volume replacement with crystalloid fluids.
- Restrict transfusions for target hemoglobin 7–9 g/dL.
- Assessment for transfusion and endoscopic management.
- Proton pump inhibitors (80 mg then 8 mg/h) before endoscopy.
- No routine use of nasogastric or orogastric aspiration/lavage.
- Intravenous erythromycin (250 mg given 30–120 min) prior to endoscopy.
- Early (≤24 h) upper GI endoscopy.

- Treat ulcers with spurting or oozing bleeding or with visible vessel.
- Consider removing adherent clot from ulcers.
- Do not endoscopically treat ulcers with a flat pigmented spot.
- Epinephrine injection therapy should not be used as endoscopic monotherapy.
- Proton pump inhibitors (8 mg/h) for 72 h post-endoscopy.
- No routine second-look endoscopy.
- Investigate *Helicobacter pylori*.
- Restart aspirin in patients with high-risk CAD and low rebleeding risk.

Risk Factors and Treatment of Recurrent Bleeding

Fortunately, a majority of bleeding ulcers can be controlled by endoscopy [36]. Recurrent bleeding can be defined as follows [37]: hematemesis or bloody NGT aspirate more than 6 h post-endoscopy, melena or hematochezia after normalization of stool color, hemoglobin drop >2 points after two stable hemoglobin values, or hemodynamic instability in the absence of other causes.

Several factors have been identified that increase a patient's risk for recurrent bleeding including ulcer location, appearance and size of the ulcer, and presence of comorbidities. Ulcers located along the lesser curvature of the stomach and posterior wall of the duodenum are closer in proximity to large arteries (the left gastric and gastroduodenal arteries, respectively) and increase the risk for high volume or recurrent bleeding [37]. In terms of ulcer appearance during endoscopy, the Forrest classification has been developed to stratify the risk of mortality and rebleeding (see Table 5.1). Ulcers measuring >2 cm are an independent risk factor for endoscopic failure [36]. Patients with end-stage renal disease on dialysis have a higher risk for recurrent bleeding [39]. A visible vessel larger than 2 mm has been associated with rebleeding in patients who undergo endoscopic control of bleeding with clipping [40].

In general, a first episode of recurrent bleeding is treated with repeat endoscopy. The therapeutic strategy used may be the same that was used initially or a different endoscopic modality (e.g., failed thermal coagulation may be repeated or substituted for hemoclip placement). This approach was validated by a randomized trial in which long-term control of recurrent bleeding was achieved in 73 % of patients undergoing repeated endoscopic therapy [41].

Table 5.1 Forrest classification of bleeding peptic ulcers [38]

Grade	Endoscopic picture	Risk of rebleeding
I	Active hemorrhage	
Ia	Spurting	60–100 %
Ib	Oozing	25 %
II	Sings of recent hemorrhage	
IIa	Visible vessel	50 %
IIb	Adherent clot	30 %
IIc	Hematin-covered flat spot	<10 %
III	No hemorrhage-clean ulcer bed	<3 %

For a second episode of recurrent bleeding the trend has shifted from immediate surgical management to attempts at angiographic embolization where skilled interventional radiologists are available. Angiographic embolization has shown to be a viable option in this scenario, in particular for patients deemed high-risk surgical candidates, such as those who were older and with multiple comorbidities. One study demonstrated that these high-risk-type patients were more likely selected to undergo an angiographic embolization than surgery. While there was not a statistically significant difference there was a trend toward a lower 30-day mortality rate seen in the angiographic embolization group compared to the surgery group (3 % vs. 14 %) [42]. Patients with bleeding peptic ulcers refractory to less invasive means of therapy may require surgery as the final and most definitive means of hemorrhage control. Approximately 5 % of patients will require surgical management for bleeding peptic ulcers that recur or are refractor to non-surgical methods [43]. This significant reduction is most likely due to the contemporary widespread use of proton pump inhibitor medications, *H. pylori*-directed diagnosis and eradication, and successful application of endoscopic and angiographic approaches.

When surgery is required three main techniques have primarily been used. The most common is local oversewing of the bleeding ulcer alone. The other two include controlling the bleeding source and add a vagotomy as an acid suppression procedure. In addition to the vagotomy a drainage procedure (pyloroplasty) may be added to avoid delayed gastric emptying or a resection (antrectomy) may be added an additional method to not only remove the ulcer if located in the antrum but also to reduce gastrin production, which stimulates acid secretion.

Most patients (64 %) that have required surgery have undergone just the local oversewing of the bleeding ulcer. The remaining group of patients underwent a vagotomy as an additional acid-suppressing procedure. The benefit of this additional procedure is difficult to clearly define in the era of widespread use of proton pump inhibitor medications and *H. pylori* eradication. Bleeding ulcer size and location may favor a particular surgical technique, such as vagotomy and resection for a large antral ulcer.

Patients with preoperative overall health assessments that are poor (higher American Society of Anesthesiologists physical health score or ASA score), those requiring more blood transfusions, and those presenting under more urgent circumstances appeared to undergo drainage procedure more often than resection procedures [44]. While overall postoperative morbidity, incidence of rebleeding, or reoperation did not differ significantly amongst these groups, there was a significantly higher incidence of deep or organ space surgical site infections in the resection group compared to the local oversewing and vagotomy with drainage procedure group (8 % vs. 4 % and 2 %, respectively). In addition, patients undergoing a vagotomy and resection had a longer median length of hospital stay compared to those who underwent a local oversewing or vagotomy with drainage procedure (13 vs. 10 days) [45].

A summary of the rates of rebleeding, morbidity, and mortality amongst the most commonly used technical approaches in the management of bleeding peptic ulcer disease is seen in Table 5.2. The following flowchart illustrates a diagnostic/treatment algorithm for the bleeding peptic ulcer disease, Fig. 5.1.

Table 5.2 Comparison of various therapeutic approaches to bleeding peptic ulcer disease

Intervention	Rebleed	Morbidity	Mortality	References
EGD (clip)	8–10 %	0–0.5 %	0.3–3 %	[40, 46, 47]
EGD (sclerosis)	4–20 %	0.5–3 %	0.5–3 %	[46–48]
Angiographic embolization	9–28 %	8–10 %	17–27 %	[49, 50]
Local oversewing	20 %	61 %	21 %	[45]
Vagotomy and drainage	11–17 %	53–65 %	9–18 %	[44, 45]
Vagotomy and resection	11–16 %	50–66 %	17 %	[44, 45]

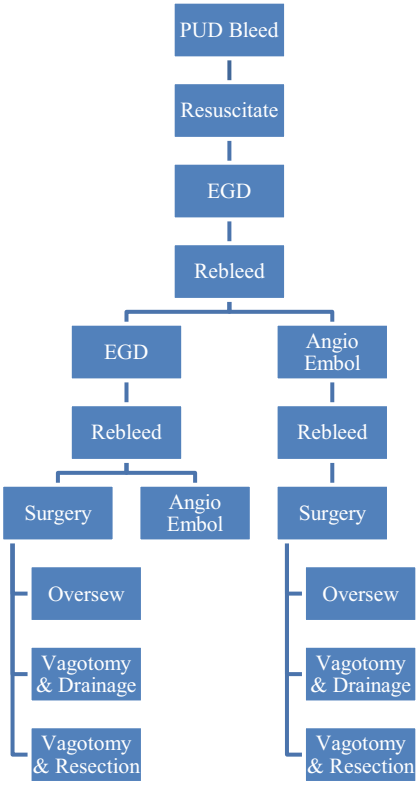

Fig. 5.1 Diagnostic and treatment approach to bleeding peptic ulcer disease

Bleeding Marginal Ulcer

A review of the management of bleeding peptic ulcers would not be complete without mentioning a related pathology: bleeding margin ulcers. These result from the exposure of the acid-rich stomach to the vulnerable small intestine. Marginal ulcers, resulting from exposure of the small intestinal portion of a gastroenterostomy to the acid-rich gastric environment, which can arise from the creation of a gastroenterostomy have been well described, dating back nearly a century: “Bearing upon this

thought of situation of peptic ulcer, in the series quoted in this article, the usual position was in the posterior wall of the stomach near the opening, or its posterior edge, in the lower portion of the jejunal surface of anastomosis, and in that portion of the jejunum distal to the anastomosis, i.e., in the normal course of the jejunal peristalsis." [51]

Gastroenterostomies performed for the primary indication of peptic ulcer disease have nearly disappeared due to an enhanced understanding of the pathophysiology behind peptic ulcer disease and the use of proton pump inhibitors and *H. pylori*-directed therapy. There has however been a significant increase in the creation of these types of anastomoses due to increased use of the Roux-en-Y gastric bypass to manage morbid obesity and gastroenterostomies during procedures such as a pancreaticoduodenectomy or partial gastrectomy for tumor resection.

The management of bleeding from this type of ulcer is managed similarly to that of the native stomach and duodenum in the acute setting primarily via an endoscopic [52] and/or angiographic approach [53]. Additional tools that have shown to be beneficial to favor ulcer healing and reduce the future bleeding in this particular setting include revision of the anastomosis [54] and vagotomy that due to abdominal adhesions may be more efficiently and effectively managed via a thoracic approach [55].

Conclusion

The incidence of bleeding peptic ulcer disease is decreasing thanks to a better understanding and successful pharmacologic directed therapy for this disease. Patients who require an intervention usually are successfully managed with endoscopic hemostasis as their first line of therapy. Patients who continue to bleed may require angiographic or surgical control of the bleeding ulcer. Access to these specialized services and overall health status of the patient will dictate subsequent lines of therapy, need for additional procedures, morbidity, and mortality.

References

1. Katschinski B, Logan R, Davies J, Faulkner G, Pearson J, Langman M. Prognostic factors in upper gastrointestinal bleeding. Dig Dis Sci. 1994;39(4):706–12.
2. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015;385(9963):117–71.
3. Sonnenberg A, Everhart JE. Health impact of peptic ulcer in the United States. Am J Gastroenterol. 1997;92(4):614–20.
4. Snowden FM. Emerging and reemerging diseases: a historical perspective. Immunol Rev. 2008;225:9–26.
5. Wang YR, Richter JE, Dempsey DT. Trends and outcomes of hospitalizations for peptic ulcer disease in the United States, 1993 to 2006. Ann Surg. 2010;251(1):51–8.

6. Lau JY, Sung J, Hill C, Henderson C, Howden CW, Metz DC. Systematic review of the epidemiology of complicated peptic ulcer disease: incidence, recurrence, risk factors and mortality. Digestion. 2011;84(2):102–13.
7. Huang JQ, Sridhar S, Hunt RH. Role of Helicobacter pylori infection and non-steroidal anti-inflammatory drugs in peptic-ulcer disease: a meta-analysis. Lancet. 2002;359(9300):14–22.
8. Sung JJ, Tsoi KK, Ma TK, Yung MY, Lau JY, Chiu PW. Causes of mortality in patients with peptic ulcer bleeding: a prospective cohort study of 10,428 cases. Am J Gastroenterol. 2010;105(1):84–9.
9. Lin KJ, Garcia Rodriguez LA, Hernandez-Diaz S. Systematic review of peptic ulcer disease incidence rates: do studies without validation provide reliable estimates? Pharmacoepidemiol Drug Saf. 2011;20(7):718–28.
10. Sonnenberg A. Temporal trends and geographical variations of peptic ulcer disease. Aliment Pharmacol Ther. 1995;9 Suppl 2:3–12.
11. Yeomans ND. The ulcer sleuths: the search for the cause of peptic ulcers. J Gastroenterol Hepatol. 2011;26 Suppl 1:35–41.
12. Rainsford KD. Mechanisms of NSAID-induced ulcerogenesis: structural properties of drugs, focus on the microvascular factors, and novel approaches for gastro-intestinal protection. Acta Physiol Hung. 1992;80(1–4):23–38.
13. Logan RP. Adherence of Helicobacter pylori. Aliment Pharmacol Ther. 1996;10 Suppl 1:3–15.
14. Richards RJ, Donica MB, Grayer D. Can the blood urea nitrogen/creatinine ratio distinguish upper from lower gastrointestinal bleeding? J Clin Gastroenterol. 1990;12(5):500–4.
15. Mortensen PB, Nohr M, Moller-Petersen JF, Balslev I. The diagnostic value of serum urea/creatinine ratio in distinguishing between upper and lower gastrointestinal bleeding. A prospective study. Dan Med Bull. 1994;41(2):237–40.
16. Pallin DJ, Saltzman JR. Is nasogastric tube lavage in patients with acute upper GI bleeding indicated or antiquated? Gastrointest Endosc. 2011;74(5):981–4.
17. Aljebreen AM, Fallone CA, Barkun AN. Nasogastric aspirate predicts high-risk endoscopic lesions in patients with acute upper-GI bleeding. Gastrointest Endosc. 2004;59(2):172–8.
18. Songur Y, Balkarli A, Acarturk G, Senol A. Comparison of infusion or low-dose proton pump inhibitor treatments in upper gastrointestinal system bleeding. Eur J Intern Med. 2011;22(2):200–4.
19. Andriulli A, Loperfido S, Focareta R, Leo P, Fornari F, Garripoli A, et al. High- versus low-dose proton pump inhibitors after endoscopic hemostasis in patients with peptic ulcer bleeding: a multicentre, randomized study. Am J Gastroenterol. 2008;103(12):3011–8.
20. Laine L, Shah A, Bemanian S. Intragastric pH with oral vs intravenous bolus plus infusion proton-pump inhibitor therapy in patients with bleeding ulcers. Gastroenterology. 2008;134(7):1836–41.
21. Leontiadis GI, Sharma VK, Howden CW. Systematic review and meta-analysis of proton pump inhibitor therapy in peptic ulcer bleeding. BMJ. 2005;330(7491):568.
22. Lau JY, Sung JJ, Lee KK, Yung MY, Wong SK, Wu JC, et al. Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. N Engl J Med. 2000;343(5):310–6.
23. Bloom SR, Mortimer CH, Thorner MO, Besser GM, Hall R, Gomez-Pan A, et al. Inhibition of gastrin and gastric-acid secretion by growth-hormone release-inhibiting hormone. Lancet. 1974;2(7889):1106–9.
24. Imperiale TF, Birgisson S. Somatostatin or octreotide compared with H2 antagonists and placebo in the management of acute nonvariceal upper gastrointestinal hemorrhage: a meta-analysis. Ann Intern Med. 1997;127(12):1062–71.
25. Choudari CP, Rajgopal C, Elton RA, Palmer KR. Failures of endoscopic therapy for bleeding peptic ulcer: an analysis of risk factors. Am J Gastroenterol. 1994;89(11):1968–72.
26. Llach J, Bordas JM, Salmeron JM, Panes J, Garcia-Pagan JC, Feu F, et al. A prospective randomized trial of heater probe thermocoagulation versus injection therapy in peptic ulcer hemorrhage. Gastrointest Endosc. 1996;43(2 Pt 1):117–20.

27. Lai KH, Peng SN, Guo WS, Lee FY, Chang FY, Malik U, et al. Endoscopic injection for the treatment of bleeding ulcers: local tamponade or drug effect? Endoscopy. 1994;26(4): 338–41.
28. Calvet X, Vergara M, Brullet E, Gisbert JP, Campo R. Addition of a second endoscopic treatment following epinephrine injection improves outcome in high-risk bleeding ulcers. Gastroenterology. 2004;126(2):441–50.
29. Vergara M, Bennett C, Calvet X, Gisbert JP. Epinephrine injection versus epinephrine injection and a second endoscopic method in highrisk bleeding ulcers. Cochrane Database Syst Rev. 2014;(10):Cd005584.
30. Chung SC, Leong HT, Chan AC, Lau JY, Yung MY, Leung JW, et al. Epinephrine or epinephrine plus alcohol for injection of bleeding ulcers: a prospective randomized trial. Gastrointest Endosc. 1996;43(6):591–5.
31. Barkun AN, Bardou M, Kuipers EJ, Sung J, Hunt RH, Martel M, et al. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med. 2010;152(2):101–13.
32. El Ouali S, Barkun AN, Wyse J, Romagnuolo J, Sung JJ, Gralnek IM, et al. Is routine second-look endoscopy effective after endoscopic hemostasis in acute peptic ulcer bleeding? A meta-analysis. Gastrointest Endosc. 2012;76(2):283–92.
33. Henriksson AE, Edman AC, Held M, Wadstrom T. Helicobacter pylori and acute bleeding peptic ulcer. Eur J Gastroenterol Hepatol. 1995;7(8):769–71.
34. Gisbert JP, Khorrami S, Carballo F, Calvet X, Gene E, Dominguez-Munoz JE. H. pylori eradication therapy vs. antisecretory non-eradication therapy (with or without long-term maintenance antisecretory therapy) for the prevention of recurrent bleeding from peptic ulcer. Cochrane Database Syst Rev. 2004;(2):Cd004062.
35. Gralnek IM, Dumonceau JM, Kuipers EJ, Lanas A, Sanders DS, Kurien M, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy. 2015;47(10):1–46.
36. Wong SK, Yu LM, Lau JY, Lam YH, Chan AC, Ng EK, et al. Prediction of therapeutic failure after adrenaline injection plus heater probe treatment in patients with bleeding peptic ulcer. Gut. 2002;50(3):322–5.
37. Laine L, Spiegel B, Rostom A, Moayyedi P, Kuipers EJ, Bardou M, et al. Methodology for randomized trials of patients with nonvariceal upper gastrointestinal bleeding: recommendations from an international consensus conference. Am J Gastroenterol. 2010;105(3):540–50.
38. de Groot NL, van Oijen MG, Kessels K, Hemmink M, Weusten BL, Timmer R, et al. Reassessment of the predictive value of the Forrest classification for peptic ulcer rebleeding and mortality: can classification be simplified? Endoscopy. 2014;46(1):46–52.
39. Cheung J, Yu A, LaBossiere J, Zhu Q, Fedorak RN. Peptic ulcer bleeding outcomes adversely affected by end-stage renal disease. Gastrointest Endosc. 2010;71(1):44–9.
40. Ishikawa S, Inaba T, Wato M, Takashima S, Mizushige T, Izumikawa K, et al. Exposed blood vessels of more than 2 mm in diameter are a risk factor for rebleeding after endoscopic clipping hemostasis for hemorrhagic gastroduodenal ulcer. Dig Endosc. 2013;25(1):13–9.
41. Lau JY, Sung JJ, Lam YH, Chan AC, Ng EK, Lee DW, et al. Endoscopic retreatment compared with surgery in patients with recurrent bleeding after initial endoscopic control of bleeding ulcers. N Engl J Med. 1999;340(10):751–6.
42. Eriksson LG, Ljungdahl M, Sundbom M, Nyman R. Transcatheter arterial embolization versus surgery in the treatment of upper gastrointestinal bleeding after therapeutic endoscopy failure. J Vasc Interv Radiol. 2008;19(10):1413–8.
43. Quan S, Frolkis A, Milne K, Molodecky N, Yang H, Dixon E, et al. Uppergastrointestinal bleeding secondary to peptic ulcer disease: incidence and outcomes. World J Gastroenterol. 2014;20(46):17568–77.
44. de la Fuente SG, Khuri SF, Schifftner T, Henderson WG, Mantyh CR, Pappas TN. Comparative analysis of vagotomy and drainage versus vagotomy and resection procedures for bleeding peptic ulcer disease: results of 907 patients from the Department of Veterans Affairs National Surgical Quality Improvement Program database. J Am Coll Surg. 2006;202(1):78–86.

45. Schroder VT, Pappas TN, Vaslef SN, De La Fuente SG, Scarborough JE. Vagotomy/drainage is superior to local oversew in patients who require emergency surgery for bleeding peptic ulcers. Ann Surg. 2014;259(6):1111–8.
46. Laine L, McQuaid KR. Endoscopic therapy for bleeding ulcers: an evidence-based approach based on meta-analyses of randomized controlled trials. Clin Gastroenterol Hepatol. 2009;7(1):33–47.
47. Sung JJ, Tsoi KK, Lai LH, Wu JC, Lau JY. Endoscopic clipping versus injection and thermocoagulation in the treatment of non-variceal upper gastrointestinal bleeding: a meta-analysis. Gut. 2007;56(10):1364–73.
48. Kim JW, Jang JY, Lee CK, Shim JJ, Chang YW. Comparison of hemostatic forceps with soft coagulation versus argon plasma coagulation for bleeding peptic ulcer—a randomized trial. Endoscopy. 2015;47(8):680–7.
49. Larssen L, Moger T, Bjornbeth BA, Lygren I, Klow NE. Transcatheter arterial embolization in the management of bleeding duodenal ulcers: a 5.5-year retrospective study of treatment and outcome. Scand J Gastroenterol. 2008;43:217–22.
50. Loffroy R, Guiu B, D'Athis P, Mezzetta L, Gagnaire A, Jouve JL, et al. Arterial embolotherapy for endoscopically unmanageable acute gastroduodenal hemorrhage: predictors of early rebleeding. Clin Gastroenterol Hepatol. 2009;7(5):515–23.
51. Erdmann JF. Marginal, gastrojejunal or peptic ulcer subsequent to gastroenterostomy. Ann Surg. 1921;73(4):434–40.
52. Azagury DE, Abu Dayyeh BK, Greenwalt IT, Thompson CC. Marginal ulceration after Roux-en-Y gastric bypass surgery: characteristics, risk factors, treatment, and outcomes. Endoscopy. 2011;43(11):950–4.
53. Sidani S, Akkary E, Bell R. Catastrophic bleeding from a marginal ulcer after gastric bypass. JSLS. 2013;17(1):148–51.
54. Moon RC, Teixeira AF, Goldbach M, Jawad MA. Management and treatment outcomes of marginal ulcers after Roux-en-Y gastric bypass at a single high volume bariatric center. Surg Obes Relat Dis. 2014;10(2):229–34.
55. Hunter J, Stahl RD, Kakade M, Breitman I, Grams J, Clements RH. Effectiveness of thoracoscopic truncal vagotomy in the treatment of marginal ulcers after laparoscopic Roux-en-Y gastric bypass. Am Surg. 2012;78(6):663–8.

Chapter 6
Management of Unusual Sources of Upper GI Bleeding

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Upper gastrointestinal bleeding is an important clinical condition managed routinely by endoscopists; however, at times needs surgical intervention. Diagnostic and therapeutic options vary immensely based on the source of bleeding and it is important to be cognizant of both common and uncommon etiologies. In this chapter, we discuss the diagnosis and management of Cameron lesions, Dieulafoy lesions, gastric antral vascular ectasia (GAVE), hemorrhagic gastritis, duodenal varices, hemosuccus pancreaticus and hemobilia, aortoduodenal fistula (ADF), and arteriovenous malformation (AVM).

Cameron Lesions

Initially described by Philemon Truesdale in 1924 and then further expanded on in a case series published by Cameron in 1976, these lesions are best described as linear erosions or ulcerations (Fig. 6.1) found at the distal end of a hiatal hernia sac in close proximity to the diaphragmatic hiatus [1]. The prevalence of these lesions has been estimated to be between 3 and 5 % in the presence of any hiatal hernias and is directly related to the size of the hernia [1]. Patients with a hiatal hernia larger than 5 cm have reported a prevalence greater than 12 %. In a recent study from 2013, the prevalence of Cameron's ulcers was 3.8 % in patients hospitalized for obscure causes of GI bleeding [2]. They can present as frank hematemesis, melena, or iron-deficiency anemia. The mechanism for the formation of Cameron lesions is not clearly defined and it is thought that they occur in patients with hiatal hernias as a

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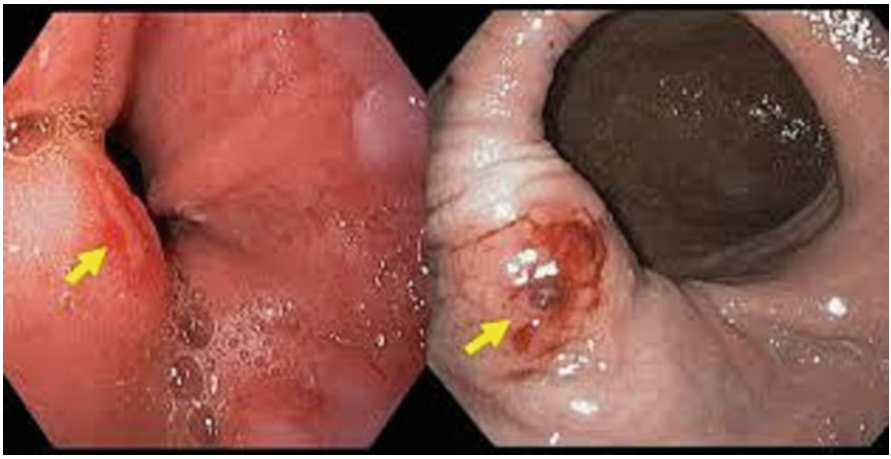

Fig. 6.1 Cameron lesion

result of mechanical trauma and repetitive movement of the hernia sac against the diaphragm causing ischemia. Other reports in the literature show that Cameron lesions can result from acid reflux, ischemia, *Helicobacter pylori* infection, and gastric and vascular stasis.

Cameron lesions are often a source for both overt and obscure GI bleeding. They can present as frank hematemesis, melena, or iron-deficiency anemia. The hernia neck and sac should be meticulously evaluated during esophagogastroduodenoscopy (EGD) specifically in retroflexed views because they are difficult to visualize. Bleeding from theses lesions is exacerbated by both acid exposure and nonsteroidal anti-inflammatory drug use. It is particularly important for Cameron lesions to be considered in the differential diagnosis because Cameron lesions can come and go and be missed on initial endoscopy.

Treatment of Cameron lesions should be individualized to their presentation. Oftentimes, simple acid-suppressive therapy with proton pump inhibitors may be sufficient. In overt GI bleeding due to Cameron lesions, endoscopic therapy with band ligation has been reported to be successful. Alternate methods of endoscopic hemostasis, such as injection of epinephrine, thermal-contact therapy, and clipping, may be difficult to perform for technical reasons. Furthermore, thermal-contact therapy and heat probe or electrocoagulation can result in deep ulcers or perforations because of the thin mucosal wall in this area and the lack of underlying fibrous tissue. However, when patients present with recurrent or life-threatening bleeding or with persistent and severe iron-deficiency anemia from Cameron lesions, surgical intervention may be necessary. Surgery will usually entail a wedge or partial gastrectomy of the Cameron ulcer and repair of the large hiatal hernia, thus correcting a major underlying pathogenic mechanism of disease.

Dieulafoy Lesion

This vascular lesion was originally referred to as *exulceratio simplex* in 1898 by the French surgeon Paul Georges Dieulafoy because he thought that it was the first stage of a gastric ulcer [3]. A Dieulafoy lesion is a vascular abnormality where persistently large-caliber arteries are present in the submucosa and occasionally the mucosa itself with a small overlying defect. Constant pressure or trauma to a singular area of mucosa ultimately leads to erosions and breakdown of tissue. The most common location where a Dieulafoy lesion can be found is along the lesser curvature of the stomach within 6 cm from the GE junction in the gastric cardia. Other locations where these lesions have been described include the duodenum (14 %), the colon (5 %), surgical anastomoses (5 %), the jejunum (1 %), and the esophagus (1 %) [4].

The clinical presentation of this lesion is usually major coffee ground emesis, hematemesis, or melena without any preceding symptoms. This presentation is followed by recurrent intermittent bleeding that can last for several days. Before the advent of endoscopy, these lesions carried an 80 % rate of mortality; however, with current endoscopic and angiographic techniques, this rate has been reduced to 13 % or less [5]. Diagnosis is made during endoscopy and requires high index of clinical suspicion. Finding a nonbleeding Dieulafoy lesion is very challenging because the mucosal defect is often small and can be hidden between gastric folds and the vessel itself can be constricted and retracted after a bleeding episode and impossible to visualize. The lesion may also be covered in clot, thus making it hard for identification. Majority of Dieulafoy lesions can be treated endoscopically with multiple different interventions and possible need for angio-embolization. Endoscopists should also be asked to tattoo the lesion, so if recurrent bleeding were to occur, repeat endoscopic management for surgical wedge resection may be necessary.

GAVE: Gastric Antral Vascular Ectasia

Another unusual entity of upper gastrointestinal bleeding is gastric antral vascular ectasia (GAVE). GAVE is a rare disorder characterized by visible columns of fiery red ectatic vessels and mucosa radiating longitudinally from the pylorus toward the antrum of the stomach After the initial description of this condition by Ryder et al. in 1953, early observers dubbed the condition “watermelon stomach” because the striped pattern made by the erythematous columns resembled the stripes on a watermelon [6]. Although not common, GAVE is an important cause of upper GI bleeding, accounting for almost 4 % of all non-variceal hemorrhages from an upper gastrointestinal source [6].

While the pathophysiology of GAVE remains poorly understood, the underlying chronic disease is thought to be related to its development. GAVE is often associated with systemic illness, most commonly hepatic cirrhosis and portal

hypertension—which are present in 30 % of GAVE patients. These patients have a mean age of 65 and are predominantly male. In non-cirrhotic patients, GAVE is most commonly associated with autoimmune disorders, including connective tissue disorders (62 %), Raynaud's phenomenon (31 %), and scleroderma (19 %) [6]. Other less common conditions associated with GAVE include bone marrow transplantation, chronic renal failure, ischemic heart disease, valvular heart disease, familial Mediterranean fever, and acute myeloid leukemia. In contrast to cirrhotic patients, these non-cirrhotic patients are typically older and predominantly female.

The link between cirrhosis and the development of GAVE is poorly understood. While scattered reports of the complete resolution of mucosal damage after liver transplant have supported a causal link between cirrhosis and GAVE, they have provided little insight into the mechanism [6]. Portal hypertension does not appear to cause the vascular ectasia in GAVE, and GAVE should not be confused with portal gastropathy. Unlike portal gastropathy, a reduction of portal pressures in cirrhotic patients does not improve the process or reverse the gastric mucosal damage. Also incompletely understood is the development of GAVE in the setting of autoimmune disease. Some studies have linked GAVE to elevated levels of gastrin or prostaglandin E2, both of which have vasodilatory properties. Others have emphasized the role of mechanical stress on the development of the disorder based on increased antral area half-time on motility studies in these patients [6, 7].

A wide spectrum of initial presentations have been described for GAVE including severe acute upper GI hemorrhage and iron-deficiency anemia secondary to occult blood loss. Patients may also complain of intermittent melena or hematemesis. Many are transfusion dependant despite iron supplementation. The diagnosis of GAVE is made on endoscopy and confirmed by gastric mucosal biopsy. The classic striped "watermelon" or "tiger" pattern of erythematous mucosa is found in the antrum. Non-cirrhotic patients are more likely to possess this typical pattern while cirrhotic patients may have more diffuse disease (Fig. 6.2). A primary difficulty in diagnosing cirrhotic patients stems from the fact that GAVE is not easily differentiated from portal hypertensive gastropathy (PHG). The correct diagnosis is all the more important, however, as GAVE will not respond to reduction in portal pressure [6, 8]. Distribution of the vascular changes may help: GAVE is typically limited to the antrum while PHG is associated with changes to the fundus and corpus, although, as noted above, cirrhotic patients with GAVE are less likely than autoimmune patients to have this typical distribution. Histologically, GAVE is characterized by mucosal vascular ectasia, fibrin thrombi, hyalinosis, and proliferation of spindle cells. Active bleeding may not be immediately apparent on endoscopy, but often occurs spontaneously after strong antral contractions. In PHG, active bleeding is obvious on endoscopy and recent bleeding is often characterized by variceal stigmata.

Management of GAVE involves the treatment of symptoms of acute or chronic bleeding and prevention of future bleeding. For symptomatic blood loss from GAVE, initial management includes fluid resuscitation and transfusion for acute episodes, along with iron supplementation for chronic anemia. To stop active bleeding and prevent future episodes, endoscopic ablation is the first-line therapy as well as treating underlying medical comorbidities. When endoscopic measures fail,

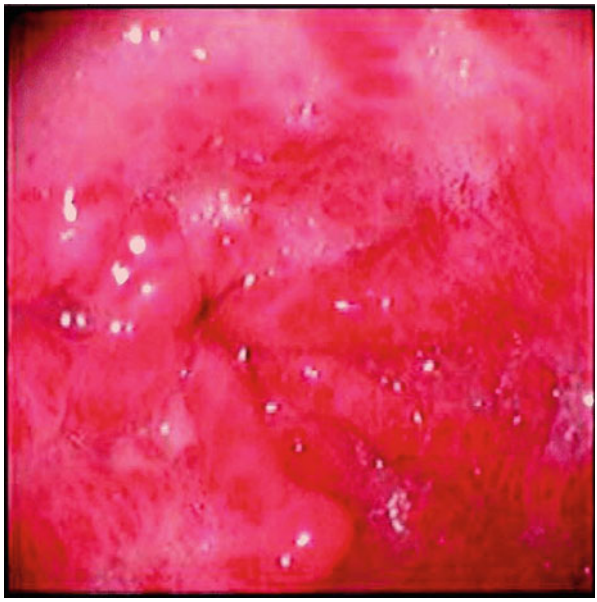

Fig. 6.2 Endoscopic findings of portal hypertensive gastropathy (PHG) and gastric antral vascular ectasia (GAVE) syndrome

pharmacological therapy may reduce chronic blood loss. Several case studies have reported positive results through estrogen, progesterone, tranexamic acid, and chronic octreotide injections in controlling bleeding associated with GAVE [9–11]. For GAVE unresponsive to any of the above therapies, surgical resection (antrectomy) may be necessary; however, in the setting of a cirrhotic patient with portal hypertension, the mortality of an antrectomy is quite high. TIPS has been shown to reduce portal pressures but does not appear to affect transfusion requirements in GAVE [6].

Hemorrhagic Gastritis

Finally, acute hemorrhagic gastritis is the classic term used to describe the superficial, diffuse lesions of the gastric mucosa associated with epithelial cell damage and regeneration resulting in moderate-to-massive upper GI bleeding [12]. Acute hemorrhagic gastropathy is the more accurate histological term as the mucosal injury is usually not associated with inflammation (implying *Helicobacter pylori* infection, autoimmune disorders, or hypersensitivity reactions) although rare cases have been reported [13, 14]. Instead, acute hemorrhagic gastritis is more frequently caused by irritants which can directly damage the gastric mucosa, including NSAIDs, bile acid from bile reflux, alcohol, cancer chemotherapy, and accidentally ingested caustic substances, or by mucosal hypoxia induced by trauma, burns, sepsis, or, rarely, long-distance running [12, 15]. In many patients, acute hemorrhagic gastritis is multifactorial with several of these predisposing gastric insults present. Once

compromised, the acids, proteases, and bile acids penetrate the lamina propria causing vascular injury and release of inflammatory mediators.

Recognizing the risk factors in the patient's history and awareness of any recent physiologic stress may lead to the diagnosis of acute hemorrhagic gastritis quickly. Trauma, burn, and severely ill patients in intensive care units are at increased risk for this condition, although recent emphasis on stress ulcer prevention may help decrease the incidence of acute hemorrhagic gastritis among critically ill patients. Bleeding from hemorrhagic gastritis begins suddenly and without other symptoms, although nausea, vomiting, and abdominal pain may develop. The diagnostic modality of choice for acute hemorrhagic gastritis is upper endoscopy, which reveals multiple petechial hemorrhages and small erosions. In acute hemorrhagic gastritis induced by physiologic stress, lesions are often concentrated in the fundus and near the GE junction, while in cases associated with alcohol or NSAID use, they are more widespread [12].

Any discussion of the management of acute hemorrhagic gastritis begins with prevention. In all high-risk patients, including critically ill patients and those on chronic NSAID therapy, prophylactic acid blocking therapy should be given [12, 16–18]. In the severely ill population, aggressive treatment of the underlying disease is crucial in preventing and managing acute hemorrhagic gastritis. Multiple studies have suggested that risk of bleeding from mucosal damage is proportional to the acuity of the underlying illness. Patient prognosis is also more closely associated with disease progression or regression than degree of mucosal injury. Once acute hemorrhagic gastritis has developed, the principles of management are to discontinue any offending agent (NSAIDs, alcohol, etc.), aggressively treating underlying medical problems, correct any coagulation abnormalities, and neutralizing gastric acid (with H_2-blocker or proton pump inhibitor therapy). Aggressive medical management leads to improvement in 80 % of patients [12].

Patients with massive or persistent hemorrhage can be managed endoscopically with electrocoagulation, laser, or use of sclerosing agents. Arteriography with embolization may be required if endoscopy fails. For most causes of acute hemorrhagic gastritis, surgery is reserved for patients with severe, persistent hemorrhage or perforation and is associated with a high mortality. Although there are no prospective data on the operation of choice for acute hemorrhagic gastritis, vagotomy/pyloroplasty/oversewing areas of bleeding have a higher rate of rebleeding than gastric resection with vagotomy. For patients with bile reflux with a history of surgically altered anatomy, surgical intervention (typically a Roux-en-Y revision) may be necessary for definitive treatment.

Duodenal Varices

Variceal bleeding is a well-understood complication of portal hypertension of any cause, and the most common sites where this occurs are in the esophagus or the stomach. Occasionally, varices develop at alternative sites throughout the body

including the small intestine, colon, rectum, and peristomal pouch. Although a rare cause, bleeding from ectopic varices should be considered in all patients with known portal hypertension with overt GI bleeding without an obvious source noted in the esophagus or stomach. Duodenal varices make up 17 % of cases of bleeding from ectopic varices [19]. Duodenal varices most commonly occur in the bulb or in the second portion of the duodenum.

Once a bleeding duodenal varix is identified on endoscopic evaluation, cyanoacrylate therapy can achieve hemostasis without any further evidence of recurrent bleeding. Much of the present management is based on data for gastric varices where initial therapy with cyanoacrylate injection has been shown to be superior to endoscopic band ligation in head-to-head trials. In cases where primary endoscopic management fails, it is important to remember that most duodenal varices have an afferent venous supply from either the portal vein or the superior mesenteric vein with an outflow tract directly into the inferior vena cava; thus, transjugular intrahepatic portosystemic shunt (TIPS) and balloon retrograde transvenous obliteration procedures are possible (Fig. 6.3).

Hemosuccus Pancreaticus/Hemobilia

Hemosuccus pancreaticus is an exceptionally rare and life-threatening source of upper GI bleeding that has a reported incidence of less than 1 in 1500 patients admitted for GI bleeding [21]. The clinical entity of bleeding through the ampulla of Vater from a pancreatic source was first described by Lower and Farrell in a report of bleeding as a result of a splenic artery aneurysm in 1931 [22]. In 1970, Sanblom coined the term “hemosuccus pancreaticus” in a case series of patients with bleeding noted from the ampulla [23]. Hemosucus pancreaticus occurs as a consequence of numerous clinical conditions that are specifically associated with structural disorders of the pancreas or with its vascular supply.

Diagnosis of hemosuccus pancreaticus can be quite challenging because it can present with intermittent and infrequent bleeding. Patients will typically present with abdominal pain radiating to the back with intermittent bleeding manifesting as melena, hematemesis, and possible hematochezia. Pain occurs from transient increases in intraductal pancreatic pressure by formation of blood clots and improves after bleeding episodes due to passage of the clots. Other clinical features include nausea, vomiting, acute pancreatitis, icterus from retrograde obstruction of bile ducts, anorexia, weight loss, and a palpable or pulsating epigastric mass.

Direct visualization of bleeding from the ampulla of Vater during endoscopy is uncommon because of the intermittent nature of bleeding. Contrast-enhanced CT scan with angiography and MRI can be helpful in further characterization of the local anatomy and can help lead to the diagnosis in more than 90 % cases [22]. Occasionally, CT angiography can identify active bleeding if the rate of bleeding is at least 0.4 mL/min. On precontrast CT, the characteristic finding of clotted blood in the pancreatic duct, known as the sentinel clot, is seldom seen. ERCP can be used

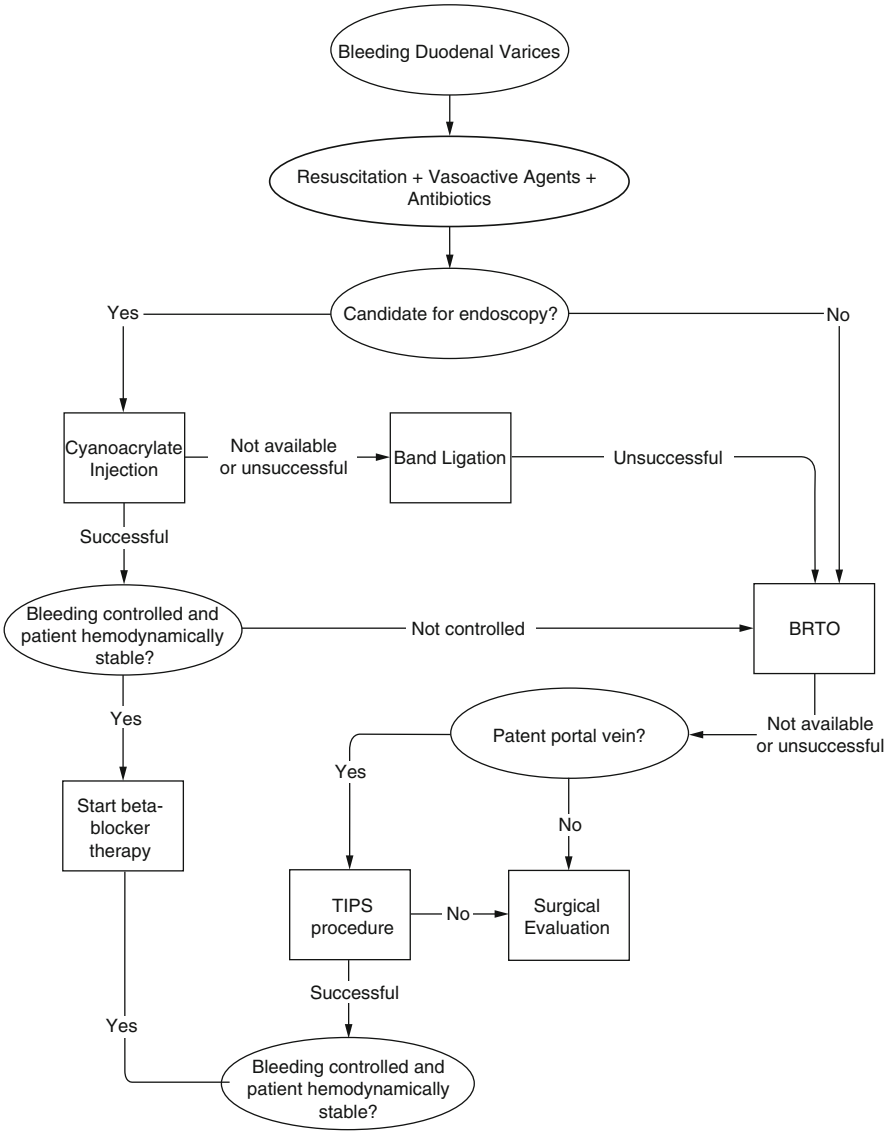

Fig. 6.3 Algorithm for the management of GI bleed from duodenal varices [20]

to show extravasation of contrast, but carries increased inherent risk, including worsening of bleeding, post-ERCP pancreatitis, and disruption of the pancreatic duct. The gold standard to establish the diagnosis of hemosuccus pancreaticus includes selective arteriography of the celiac trunk and the superior mesenteric artery, where opacification of the pancreatic duct at angiography provides a definitive diagnosis of hemosuccus pancreaticus and has a reported sensitivity of 96 % [22]. Pseudoaneurysms of the splanchnic arteries can present as hemosuccus

pancreaticus in 20 % of total cases [24]. These pseudoaneurysms have been reported to involve the splenic, gastroduodenal, pancreaticoduodenal, and hepatic arteries.

Management of hemosuccus pancreaticus depends on the underlying cause and in most cases treatment is surgical or with interventional radiology for selective arterial embolization. The surgical management of the various causes of hemosuccus pancreaticus depends on underlying pathology and range from duodenotomy with suture of bleeding site to the need for a pancreaticoduodenectomy.

Hemobilia, meaning bleeding from the biliary system, is a rare cause of upper GI bleeding, but should be suspected in patients with recent biliary tract or hepatic parenchymal instrumentation or trauma. Hemobilia was initially described with the classic triad consisting of obstructive jaundice, right upper quadrant abdominal pain, and either occult or overt GI bleeding [25]. However, manifestation of all three signs at the time of presentation is uncommon. In fact most patients have atypical presentations which include cholestasis without jaundice, ascending cholangitis, coffee ground emesis, hematemesis, melena, pancreatitis, or even cholecystitis. The rate of bleeding may lead to clot formation in various sections of the biliary ductal system and occlusion of specific locations can lead to the abovementioned presentations. Diagnosing hemobilia can be quite challenging and, as with hemosuccus pancreaticus, bleeding can be intermittent and difficult to visualize with standard forward-viewing endoscopes. Various radiological procedures have been suggested as being helpful, including tagged red blood cell scan, CT angiography, and mesenteric angiography with coil embolization. If minimally invasive techniques using endoscopy or angiography fail to resolve the underlying cause of bleeding, definitive management commonly involves surgical intervention specific to the cause of hemobilia.

Aortoenteric Fistula

An aortoenteric fistula is a direct connection between the abdominal aorta and the bowel, most commonly the retroperitoneal portion of the distal duodenum lying anterior to the aorta. However, other sites of fistulae are possible (Fig. 6.4). The spontaneous development of a connection between the GI tract and the abdominal aorta is referred to as a *primary aortoenteric fistula* and is an uncommon event (0.04–0.07 % incidence at autopsy) [26]. The majority of primary aortoduodenal fistulas (ADFs) are associated with existing abdominal aortic aneurysms (AAA). Inflammation and irritation of the fixed retroperitoneal portion of duodenum that lies adjacent to the expanding aneurysm may eventually result in the development of a fistula. Infectious aortitis, mycotic aneurysms, trauma, radiation, metastases, ulcers, gallstones, diverticulitis, and appendicitis can also be rare causes of primary ADFs.

In the USA, *secondary aortoduodenal* fistula is much more prevalent than primary ADF. Secondary ADF is an infrequent but feared complication of open and rarely endovascular AAA repair, with an incidence ranging from 0.6 to 1.6 % after

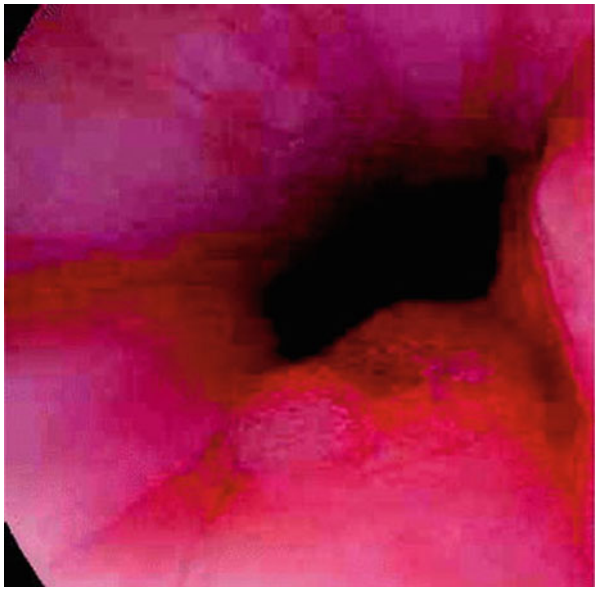

Fig. 6.4 Aortoesophageal fistula

open repair (the incidence after endovascular repair is unknown but believed to be less than 0.5 % from available reports) [27, 28]. Secondary ADF usually occurs at the site of the proximal anastomosis and is caused by pressure erosion from an anastomotic aneurysm, anastomotic suture line, or the vascular prosthesis itself. Although intuitively there would seem to be little risk of this complication after endovascular repair, at least 20 reports in the literature describe this complication [27]. Most of these secondary ADFs occur as a result of either device malfunction (such as stent fracture) or endo-leak. The median time from aneurysm repair to GI hemorrhage from ADF is 3 years following open repair or 16 months following endovascular repair, although bleeding may occur within days to weeks of the initial operation [28, 29].

The classic clinical triad for ADF is an upper GI bleed, abdominal pain, and pulsatile abdominal mass; however, the complete triad may be present in as few as 11 % of patients with acute hemorrhage from an ADF. Clinical suspicion is essential for timely diagnosis and management [30]. Aortoduodenal fistula usually presents with an initial episode of GI bleeding (the "herald bleed") that subsides temporarily but is followed in hours, days, or weeks by catastrophic hemorrhage. Patients may give a history of intermittent hematemesis or hematochezia and may report back pain or fever. The "herald bleed" most likely represents initial hemorrhage that is temporarily sealed by thrombus and bowel contracting around the fistulous tract. After the initial bleed has subsided, the risk of a subsequent exsanguinating hemorrhage is high.

Delayed or missed diagnosis of ADF carries a high mortality and morbidity. Since most delays in diagnosis occur in hemodynamically stable patients with atypical presentations, any patient with a history of AAA presenting with upper GI

bleeding or significant melena should be suspected of having an ADF until proven otherwise. In an actively bleeding patient with suspected ADF, management starts with rapid assessment of hemodynamic stability. An unstable patient or the presence of massive hemorrhage in any patient requires a rapid initial assessment, placement of large-bore resuscitation lines (located with potential vascular reconstruction in mind), immediate fluid and non-typed blood resuscitation, and eventual typing and cross-matching of blood. These patients will most likely require urgent laparotomy for control of bleeding for survival. More commonly, a hemodynamically stable patient will present after one or more self-limited episodes of GI bleeding, allowing for a more comprehensive diagnostic workup with imaging studies that can confirm the diagnosis of ADF and allow for operative planning. It is important to note that laboratory values may or may not show a low hemoglobin/hematocrit depending on the chronicity of GI bleeding. Also, a mild-to-moderate leukocytosis (white blood cell count $>10 \times 10^9$ per L) may result from a contaminated prosthetic graft and, potentially, bacteremia. In these patients, blood cultures should be sent and broad-spectrum coverage should be started empirically against the most common pathogens documented in these circumstances: *Escherichia coli, Staphylococcus aureus*, and *Staphylococcus epidermidis.* Although rare, fungal infections leading to secondary ADF have been reported, so initiating empiric antifungal therapy is reasonable [28, 31].

In a patient that is hemodynamically stable, the classic diagnostic study is an upper endoscopy (EGD). EGD should be carried out to the fourth portion of the duodenum. Active bleeding into the duodenum may be visualized. If not, the fistula may be detected by the presence of clot, ragged mucosa, purulent material inside the bowel, or exposed graft material. If no evidence of fistula is seen, EGD may be useful in searching for other sources of bleeding; however, it lacks the sensitivity or specificity to conclusively rule out ADF. More recent reviews in the literature have advocated for initial screening with a CT scan of the abdomen including arterial and portal phase intravenous contrast. CT is less invasive and carries less of a risk of dislodging a thrombus than EGD [28, 31]. A CT can provide both the diagnosis of ADF and important information on the location and nature of the fistula. This anatomic information is essential in operative planning. Loss of a distinct aneurismal wall, obliteration of the fat plane between the aorta and duodenum, and retroperitoneal air are the radiologic signs of ADF. Detection rates with all modalities have traditionally been low. In a recent review, CT alone had a 61 % detection rate for ADF compared with 25 % and 26 % for EGD and angiography, respectively. However, EGD detection rates are dependent on the skill and experience of the endoscopist. In studies of known ADF patients undergoing preoperative EGD, detection rates varied from under 25 % to as high as 80 %. While an abnormality is identified in nearly 50 % of ADF patients undergoing EGD, it is nonspecific and is diagnostic in only 25 %. Although CT has a higher sensitivity for ADF, its specificity for the diagnosis is also low [28, 32, 33].

Angiography has less value in the diagnosis of ADF since extravasation of contrast from the aorta into the bowel lumen is rarely seen. However, angiography remains useful for the evaluation of arterial anatomy in preparation for the required

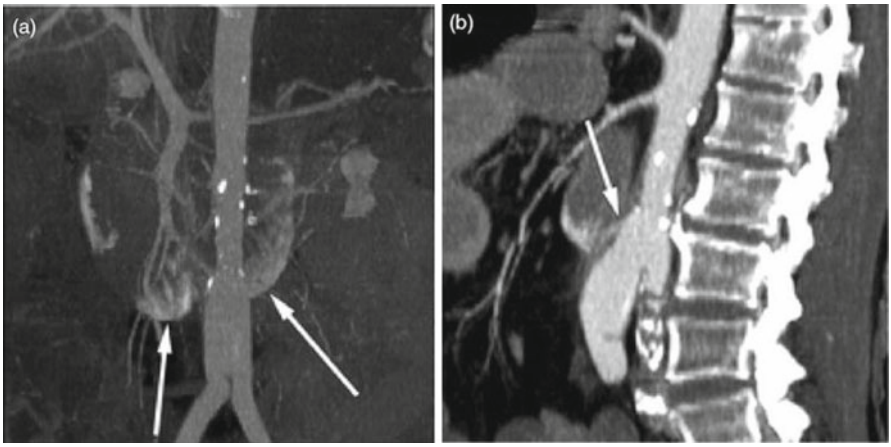

Fig. 6.5 Aortoduodenal fistula in a 70-year-old man 10 years after aortoiliac graft implantation: (**a**) contrast-enhanced axial CT with extravasation of contrast into duodenum; (**b**) contrast-enhanced sagittal view showing location of fistula. From Frauenfelder et al. [34]

intraoperative arterial reconstruction that results from removing the graft and closing the ADF (Fig. 6.5a, b). Given their low yield, MR, tagged white blood cell scans, and upper/lower GI series have little role in the diagnosis of ADF, especially in the acute setting. Awaiting these tests can inappropriately delay patient care without significant benefit [27, 29]. Clinical suspicion remains the key factor in timely diagnosis and management of ADF. The clinical factors most associated with poor outcomes in patients following ADF repair are delays in therapy longer than 24 h, greater number of diagnostic tests prior to operative intervention, and hypotension preoperatively [35].

Once in the operating room, the operative management for a hemodynamically unstable patient begins with prepping and draping widely, including the chest, axilla, and groins. The initial incision is a large midline incision in order to gain proximal control of the aorta. If there are too many adhesions to rapidly gain control of the supraceliac aorta, an anterolateral thoracotomy via the left chest will gain access to the supra-abdominal aorta. Once proximal control is obtained, dissection is carried to the level of the fourth portion of the duodenum. A medial visceral rotation from the right will expose both the vena cava and the aorta-duodenal junction. Once the fistula is identified, careful dissection around the aorta and involved segment of bowel can be carried out. Once distal control is obtained, the bowel defect can be closed in two layers unless the extent of the defect necessitates segmental resection with anastomosis. For primary ADF, aneurysmorrhaphy may be attempted, especially for a saccular or posttraumatic aneurysm. More commonly, repair involves replacement of the involved aorta with prosthetic graft after closure of the enteric defect. Extra-anatomic reconstruction may also be considered.

For secondary ADF, operative management is initially approached similar to that of a primary ADF, with control of the aorta prior to dissection of the fistula. For the

subsequent repair, two approaches have been well described. The first involves removal of the infected graft with thorough debridement of aorta and perigraft structures with in situ graft replacement or, more commonly, extra-anatomic bypass. Mortality rates for this procedure range from 30 to 40 % due to bleeding, sepsis, acute lung injury, and multi-organ system failure [28]. The second widely used approach involves closure of the enteric defect, complete graft removal, aortic stump closure, and extra-anatomic bypass through uninvolved tissue planes. However, this approach is associated with significant complications (including aortic stump rupture and limb loss). Even with recent advances, including wide debridement of tissue beds and staging the extra-anatomical bypass and graft excision to reduce periods of lower body ischemia, the procedure still carries significant mortality with many series reporting rates of 40–50 % [29]. In either approach, copious irrigation and separation of the new prosthesis or aortic stump from the overlying bowel by interposition of viable tissue may help reduce complications or recurrent fistula. Although some analyses have found improved outcomes with the in situ repair, other reviews have found no statistical difference in long-term outcome between the two approaches.

In patients not hemodynamically stable enough for an open repair or poor candidates due to other comorbidities, endovascular stent grafting over the fistula site has been done with reasonable success. There are also reports of injecting the fistula tract with *N*-butyl-2-cyanoacrylate, fibrin glue, or coil remobilization of the fistula prior to placing the stent graft. The potential advantages of endovascular repair include rapid control of catastrophic hemorrhage; avoiding operating in an inflamed, hostile field [36, 37]; and avoiding the complications of a prolonged anesthetic and open abdominal procedure.

Complications after repair include graft re-infection, aortic stump blowout, and graft failure. Recurrent ADFs are rare with only scattered case reports in the literature; their outcomes are generally poor [35].

Arteriovenous Malformation

Another unusual entity, arteriovenous malformations (AVMs) of the upper GI tract are an important source of upper GI bleeding. These vascular malformations include lesions described as angiodysplasia, vascular ectasia, vascular dysplasia, and mucosal vascular abnormalities. Although most frequently associated with the colon since the first description in 1956, GI AVMs have been found throughout the GI tract, including the stomach (1.4 %), duodenum (2.3 %), and pancreas (0.9 %) [38]. These upper GI AVMs may account for up to 5–7 % of upper GI bleeding [18, 19, 21, 22] (Fig. 6.6). The pathogenesis of AVMs is not well understood. Although the lesions have been found in patients of all ages, symptomatic AVMs are more often found in patients 60–80 years old. Whether these are congenital lesions exacerbated by increased intraluminal pressure over time or acquired lesions of aging as a result of a similar process is unclear [39].

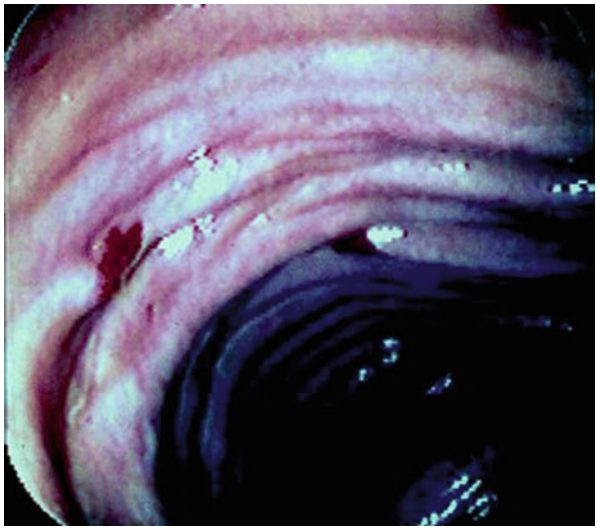

Fig. 6.6 Small-bowel arteriovenous malformations

The diagnosis of gastroduodenal AVMs can be made by observing the bright red, fern-like lesions on endoscopy which range in size from 1 to 7 mm. Lesions beyond the duodenal bulb are easily missed via routine endoscopy because the scope is often not advanced far enough. Determining whether an AVM visualized on endoscopy is the actual source of upper GI bleeding may be more of a challenge than finding the lesion. The classic endoscopic criteria for a bleeding AVM are (1) active bleeding from the lesion, (2) clots at the site of the lesion or in the vicinity, and (3) the absence of other potential sources [40, 41]. When blood filling the stomach or prominent mucosal folds complicates identification of the lesions, endoscopic ultrasound has been used in some series to detect abnormal submucosal blood flow [40]. Angiography and tagged red blood cell scans have limited success in diagnosis [40].

Endoscopy is diagnostic as well as therapeutic for bleeding gastroduodenal AVMs. Electrocoagulation and laser ablation are first-line therapies that have been described and have demonstrated a significant decrease in transfusion requirements in patients with significant upper GI bleeds from AVMs. Recurrences can be managed with repeat endoscopy or hormonal therapy (estrogen–progesterone combination). Although the mechanism of hormonal therapy is not entirely clear, there is some evidence to suggest that hormonal therapy reduces frequency and intensity of bleeding episodes [28, 41, 42]. Surgical resection is rarely needed and should be reserved for treatment failures.

Pancreatic AVMs are a very rare cause of upper GI bleeding, but the bleeding they cause is often catastrophic (Fig. 6.7a, b). Since their first description in 1968, numerous cases have been reported in the literature to date, with the diagnoses increasing as imaging techniques improve. Pancreatic AVMs are either congenital or acquired, resulting from trauma or inflammation. The most frequent symptom associated with pancreatic AVMs is upper GI bleeding, which usually results from the associated portal hypertension. Abdominal pain and jaundice may also be present. Angiography has been the primary diagnostic modality, showing dilated, tortuous feeding arteries with early venous filling and early disappearance of the

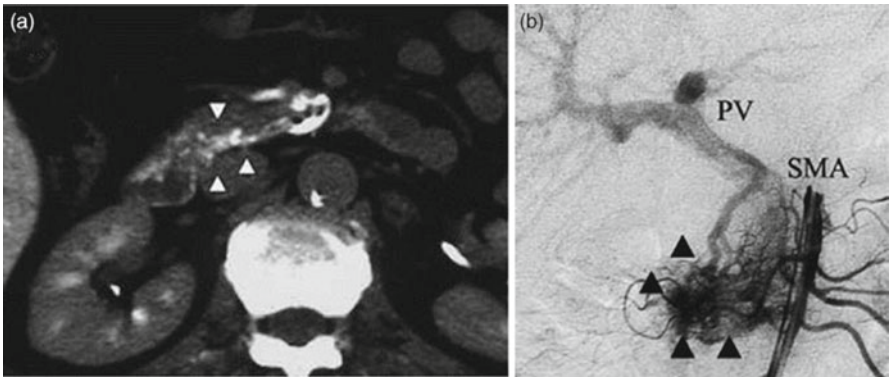

Fig. 6.7 (**a**) Contrast-enhanced CT of a pancreatic arteriovenous malformation showing the hypervascular lesion. (**b**) Angiography of pancreatic arteriovenous malformation shows vascular proliferation and early filling of the portal vein in the arterial phase. From Uchida et al. [43]

pancreatic stain [44]; however, noninvasive imaging including Doppler ultrasound and multi-slice CT have recently demonstrated their utility in the diagnosis of pancreatic AVMs [43–45]. The lesions are hypoechoic on ultrasound with a mosaic-like structure on color Doppler. CT findings include a conglomeration of hypervascular spots and early contrast filling of the portal vein on arterial phase.

Anatomic considerations complicate the management of pancreatic AVMs. Embolization has been successful in some reports; however, the multiple feeding arteries make a complete cessation of blood flow to the AVM difficult. Recurrent bleeding has been reported in over one-third of pancreatic AVMs treated by embolization alone, necessitating repeat embolization or surgical resection [44, 46].

Summary

There are several unusual but important causes of upper GI bleeding. Although their incidence is relatively low compared to bleeding peptic ulcers and esophageal varices, these conditions may require quick recognition and intervention, even though they may be difficult to distinguish from other sources of bleeding. Those caring for patients with an acute GI bleed should include unusual sources of GI bleeding on their differential diagnosis so that they are aware of the classic presentation, endoscopic and imaging findings, and management of these conditions.

References

1. Truesdale PE. Recurring hernia of the diaphragm. Ann Surg. 1924;79:751–7.
2. Cameron AJ. Incidence of iron deficiency anemia in patients with large diaphragmatic hernia. A controlled study. Mayo Clin Proc. 1976;51:767–9.

3. Lee YT, Walmsley RS, Leong RW, et al. Dieulafoy's lesion. Gastrointest Endosc. 2003;58:236–43.
4. Fockens P, Meenan J, van Dullemen HM, et al. Dieulafoy's disease: endosonographic detection and endosonography-guided treatment. Gastrointest Endosc. 1996;44:437–42.
5. Nesje LB, Skarstein A, Matre K, et al. Dieulafoy's vascular malformation: role of endoscopic ultrasonography in therapeutic decision-making. Scand J Gastroenterol. 1998;33:104–8.
6. Selinger CP, Ang YS. Gastric antral vascular ectasia (GAVE): an update on clinical presentation, pathophysiology and treatment. Digestion. 2008;77(2):131–7.
7. Sebastian S, O'Morain CA, Buckley MJ. Review article: current therapeutic options for gastric antral vascular ectasia. Aliment Pharmacol Ther. 2003;18(2):157–65.
8. Burak KW, Lee SS, Beck PL. Portal hypertensive gastropathy and gastric antral vascular ectasia (GAVE) syndrome. Gut. 2001;49(6):866–72.
9. Manning RJ. Estrogen/progesterone treatment of diffuse antral vascular ectasia. Am J Gastroenterol. 1995;90(1):154–6.
10. McCormick PA, Ooi H, Crosbie O. Tranexamic acid for severe bleeding gastric antral vascular ectasia in cirrhosis. Gut. 1998;42(5):750–2.
11. Nardone G, Rocco A, Balzano T, Budillon G. The efficacy of octreotide therapy in chronic bleeding due to vascular abnormalities of the gastrointestinal tract. Aliment Pharmacol Ther. 1999;13(11):1429–36.
12. Chamberlain CE. Acute hemorrhagic gastritis. Gastroenterol Clin North Am. 1993;22(4): 843–73.
13. Carpenter HA, Talley NJ. Gastroscopy is incomplete without biopsy: clinical relevance of distinguishing gastropathy from gastritis. Gastroenterology. 1995;108(3):917–24.
14. Yardley JH, Hendrix TR. Acute hemorrhagic erosive gastropathy and chronic chemical gastropathy. In: Basow D, editor. UpToDate. Waltham: UpToDate; 2008.
15. Choi SC, Choi SJ, Kim JA, et al. The role of gastrointestinal endoscopy in long-distance runners with gastrointestinal symptoms. Eur J Gastroenterol Hepatol. 2001;13(9):1089–94.
16. Dellinger RP, Levy MM, Carlet JM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med. 2008;36(1): 296–327.
17. Menguy R. The prophylaxis of stress ulceration. N Engl J Med. 1980;302(8):461–2.
18. Priebe HJ, Skillman JJ, Bushnell LS, et al. Antacid versus cimetidine in preventing acute gastrointestinal bleeding. A randomized trial in 75 critically ill patients. N Engl J Med. 1980;302(8):426–30.
19. Henry Z, Uppal D, Saad W, et al. Gastric and ectopic varices. Clin Liver Dis. 2014;18:371–88.
20. Parikh K, Akbar Ali M, Wong R. Unusual causes of upper gastrointestinal bleeding. Gastrointest Endo Clin North Am. 2015;25:583–605.
21. Rammohan A, Palaniappan R, Ramaswami S, et al. Hemosuccus pancreaticus: 15-year experience from a tertiary care GI bleed centre. ISRN Radiol Feb 28;2013:191794.
22. Etienne S, Pessaux P, Tuech JJ, et al. Hemosuccus pancreaticus: a rare cause of gastrointestinal bleeding. Gastroenterol Clin Biol. 2005;29:237–42.
23. Pham KD, Pedersen G, Halvorsen H, et al. Usefulness of endoscopic ultrasound for the diagnosis of hemosuccus pancreaticus. Endoscopy. 2014;46:528.
24. Akpinar H, Dicle O, Ellidokuz E, et al. Hemosuccus pancreaticus treated by transvascular selective arterial embolization. Endoscopy. 1999;31:213–4.
25. Bloechele C, Izibicki JR, Rashed MY, et al. Hemobilia: presentation, diagnosis, and management. Am J Gastroenterol. 1994;89:1537–40.
26. Lemos DW, Raffetto JD, Moore TC, Menzoian JO. Primary aortoduodenal fistula: a case report and review of the literature. J Vasc Surg. 2003;37(3):686–9.
27. Bergqvist D, Bjorck M, Nyman R. Secondary aortoenteric fistula after endovascular aortic interventions: a systematic literature review. J Vasc Interv Radiol. 2008;19(2 Pt 1):163–5.

28. Montgomery RS, Wilson SE. The surgical management of aortoenteric fistulas. Surg Clin North Am. 1996;76(5):1147–57.
29. Kim LT, Heldmann M, Turnage RH. Acute gastrointestinal hemorrhage. In: Michael WM, editor. Greenfield's surgery. Philadelphia: Lippincott, Williams, and Wilkins; 2006. p. 1062–5.
30. Sears SJ, Scheltinga MR. Primary aortoenteric fistula. Br J Surg. 2005;92:143–52.
31. Witz M, Lehmann JM, Shnaker A, et al. Secondary aortoduodenal fistula. Isr Med Assoc J. 2002;4(10):824.
32. Busuttil RW, Rees W, Baker JD, Wilson SE. Pathogenesis of aortoduodenal fistula: experimental and clinical correlates. Surgery. 1979;85(1):1–13.
33. Kiernan PD, Pairolero PC, Hubert Jr JP, et al. Aortic graft-enteric fistula. Mayo Clin Proc. 1980;55(12):731–8.
34. Frauenfelder S et al. Nontraumatic emergent abdominal vascular conditions: advantages of a multidetector row CT. Radiographics. 2004;24(2):481–96.
35. Goshtasby P, Henriksen D, Lynd C, Fielding LP. Recurrent aortoenteric fistula: case report and review. Curr Surg. 2005;62(6):638–43.
36. Burks Jr JA, Faries PL, Gravereaux EC, et al. Endovascular repair of bleeding aortoenteric fistulas: a 5-year experience. J Vasc Surg. 2001;34(6):1055–9.
37. Shapiro M, Addis MD, Ellozy SH, et al. Successful endovascular treatment of bleeding aortoenteric fistula: a case report. Ann Vasc Surg. 2006;20(6):817–9.
38. Gunnlaugsson O. Angiodysplasia of the stomach and duodenum. Gastrointest Endosc. 1985;31(4):251–4.
39. Katz PO, Salas L. Less frequent causes of upper gastrointestinal bleeding. Gastroenterol Clin North Am. 1993;22(4):875–89.
40. Moreto M, Figa M, Ojembarrena E, Zaballa M. Vascular malformations of the stomach and duodenum: an endoscopic classification. Endoscopy. 1986;18(6):227–9.
41. Szilagyi A, Ghali MP. Pharmacological therapy of vascular malformations of the gastrointestinal tract. Can J Gastroenterol. 2006;20(3):171–8.
42. Van Cutsem E, Piessevaux H. Pharmacologic therapy of arteriovenous malformations. Gastrointest Endosc Clin North Am. 1996;6(4):819–32.
43. Uchida E, Aimoto T, Nakamura Y, et al. Pancreatic arteriovenous malformation involving adjacent duodenum with gastrointestinal bleeding: report of a case. J Nippon Med Sch. 2006;73(6):346–50.
44. Nishiyama R, Kawanishi Y, Mitsuhashi H, et al. Management of pancreatic arteriovenous malformation. J Hepatobiliary Pancreat Surg. 2000;7(4):438–42.
45. Hirai T, Ohishi H, Yamada R, et al. Color Doppler flow imaging of pancreatic arteriovenous malformation. J Ultrasound Med. 1995;14(5):393–8.
46. Ogawa H, Itoh S, Mori Y, et al. Arteriovenous malformation of the pancreas: assessment of clinical and multislice CT features. Abdom Imaging. 2008;32:215–23.

Chapter 7
Mallory–Weiss Syndrome

Joshua P. Spaete and M. Stanley Branch

Introduction

While Quincke described bleeding from a gastroesophageal laceration in 1879, Mallory and Weiss first described the eponymous syndrome of gastrointestinal hemorrhage due to gastroesophageal tears as a result of retching and emesis in alcoholic patients in 1929 [1, 2]. Since that time, longitudinal mucosal lacerations, associated with forceful retching, have become a well-known cause of upper gastrointestinal bleeding. The prevalence of Mallory–Weiss Syndrome is generally accepted to be approximately 5 %; however, it has been reported as low as 3 % and as high as 15 % in one series [3–5]. Mortality associated with Mallory–Weiss tears has been shown to be similar to gastric and duodenal ulcers in at least one series [6].

Etiology and Pathogenesis

The pathogenesis of Mallory–Weiss tears is thought to be a result of a large transient increase in the transmural pressure gradient between the intragastric pressure and the intrathoracic pressure, which leads to a tear [3]. Forceful emesis is the most common etiology, but straining, lifting, childbirth, hiccupping, blunt abdominal trauma, and iatrogenic etiologies, such as nasogastric tube placement, upper endoscopy, or polyethylene glycol administration, have also been reported [3, 7–9]. Despite frequent interventions, iatrogenic causes of Mallory–Weiss tears are infrequent [8–10]. Bleeding from Mallory–Weiss tears occurs when the laceration involves either the esophageal arteries or the venous plexus. Most frequently, the tears are single, but may be multiple in up to one-quarter of patients [3, 11].

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Alcohol use, NSAID use and hiatal hernias are the main risk factors identified for the development of Mallory–Weiss tears. Heavy alcohol use associated with emesis has been noted in up to 75 % of Mallory–Weiss syndrome [3, 11–13]. Similarly, hiatal hernia has been found in the same percentage of patients with bleeding, although some studies have not reported such a high prevalence [14, 15]. The majority of Mallory–Weiss tears occurs in patients aged 30 to 50 with a male predominance [3, 13]. It does appear that age may be a predisposing factor for iatrogenic tears after endoscopy, likely due to atrophic mucosa [8].

Presentation

The majority of patients present with hematemesis, often associated with epigastric, chest, or back pain. Classically, patients will give a history of antecedent non-bloody emesis or retching, but a significant minority will give a history of bleeding with the initial emesis [12]. In the majority of cases, bleeding is self-limited, but in those with life-threatening hemorrhage requiring blood transfusion or hymodynamic support an endoscopic or operative intervention may be required. Active bleeding at the time of endoscopy has consistently been shown to be a risk factor for rebleeding and a complicated course [14–16].

Diagnosis

Early endoscopy is the diagnostic modality of choice with Mallory–Weiss tears, as it is both diagnostic and offers an opportunity for therapeutic interventions. Most lesions will heal within 48 h, and delayed esophagoscopy may be of limited diagnostic yield. Endoscopically, Mallory–Weiss tears appear as longitudinal lacerations through the mucosa, occasionally exposing the muscular layer of the esophagus (Fig. 7.1). These tears can be non-bleeding, actively bleeding, or covered in clotted blood.

Treatment

While many patients with Mallory–Weiss syndrome ultimately require blood transfusion, 90 % of lacerations heal spontaneously [11, 14]. As with any patient with gastrointestinal bleeding, large-bore intravenous access should be obtained and adequate intravenous fluid resuscitation should be instituted. Anticoagulation should be held and coagulopathy should be reversed, with the appropriate agent as indicated. Patients should be closely monitored for hemodynamic changes. Initiation of a proton pump inhibitor is recommended; however, the effect on Mallory–Weiss

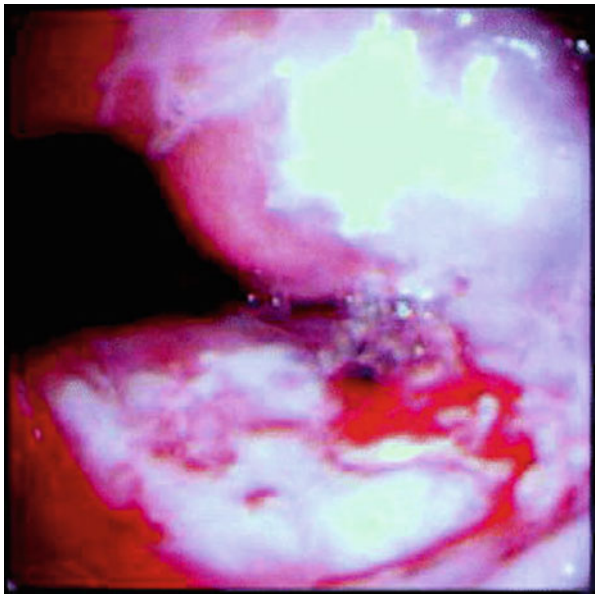

Fig. 7.1 Endoscopic image of Mallory–Weiss tear

tears has not been evaluated. Additionally, patients should be put on bowel rest during their initial observation.

Patients should be risk stratified and if high risk, undergo endoscopy within 24 h [17, 18]. If, on endoscopy, active bleeding is not observed, no endoscopic therapy is indicated and the patient can be observed for rebleeding for 24–48 h. If bleeding is observed, endoscopic therapy (such as injections, electrocautery, banding, clipping, or a combination of these modalities) is the first-line treatment of patients with Mallory–Weiss tears. Injection of epinephrine, ethanol, or other sclerosing agents is commonly used as treatment (Fig. 7.2). Epinephrine (1:10,000) with an additional sclerosing agent (such as polidocanol) appears to be very effective with an approximate 5 % rebleeding rate versus 25 % in controls [19, 20]. Epinephrine (1:10,000) and saline alone do not appear to be as effective, and epinephrine should not be used as a single agent [21]. Thermal coagulation with either bipolar or multipolar electrocautery (Fig. 7.3) has also been described [22]. Although this treatment modality may be used, caution must be exhibited as the esophagus lacks a serosal layer and coagulation may cause a full thickness injury and perforation. Thermal coagulation should be avoided in patients with esophageal varices, as this could worsen bleeding and may be life threatening. Electrocautery is best indicated in small, limited lesions, where minimal electrocautery can be used.

Multiple small trials have reported excellent results with the application of hemoclips (Figs. 7.4 and 7.5) to Mallory–Weiss tears with complete hemostasis and minimal to no rebleeding [23–26]. Despite this, a recent meta-analysis of endoscopic clipping for acute non-variceal upper gastrointestinal bleeding reported that clipping alone was not superior to other endoscopic modalities [27]. These results may be slightly skewed due to the fact this analysis contained a majority of patients

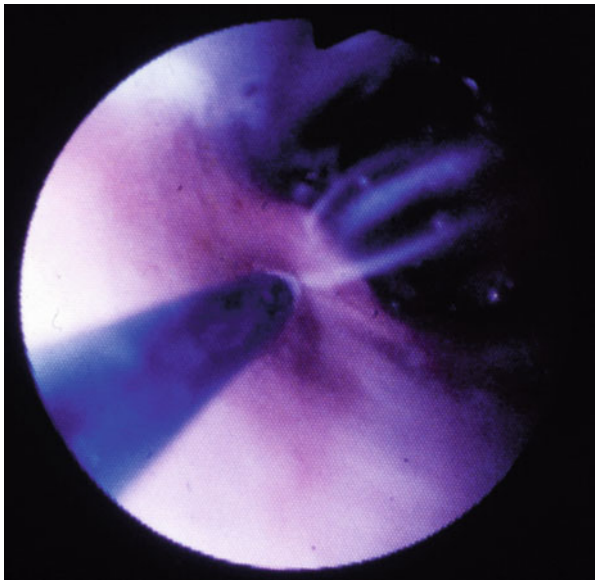

Fig. 7.2 Injection of epinephrine via needle catheter in esophagus

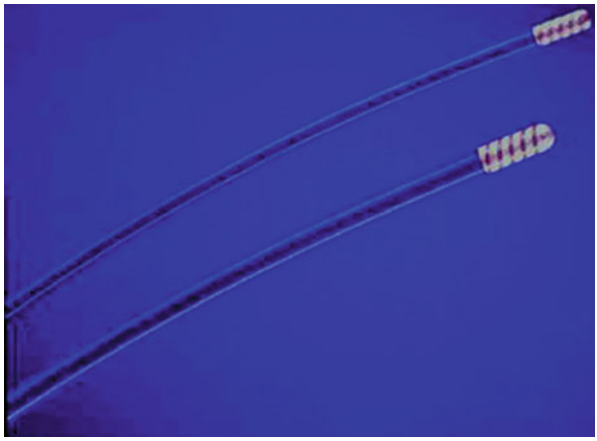

Fig. 7.3 Multipolar electrocautery catheter (Bicap)

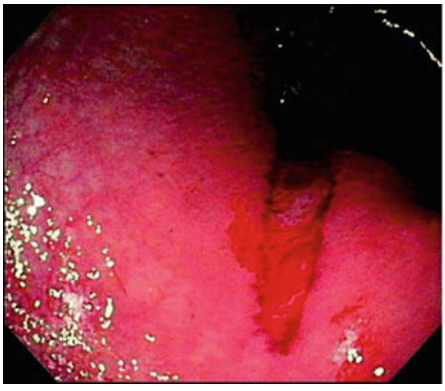

Fig. 7.4 Mallory–Weiss tear in patient with acute bleeding

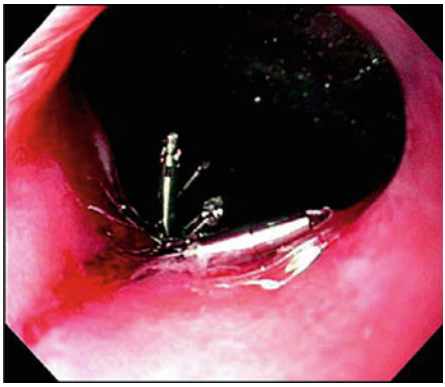

Fig. 7.5 Multiple endoclips applied to Mallory–Weiss tear

with lesions other than Mallory–Weiss tears. While the success rates have been high, clip placement at the gastroesophageal junction can be difficult and is technically more challenging than injection therapy or band ligation.

Endoscopic band ligation has been reported for treatment of Mallory–Weiss tears with excellent results [23, 28, 29]. In one recent study comparing endoscopic band ligation to hemoclips plus epinephrine injection, no recurrence was observed in the band ligation group, as compared with an 18 % recurrence rate in the hemoclip and epinephrine injection group [28]. Endoscopic band ligation does not pose the technical challenges that can be seen with hemoclip placement.

Other novel methods have been reported for treatment of Mallory Weiss tears. Successful closure of a large Mallory–Weiss tear with hemoclips and an endoloop has been described [30]. The use of the over the scope clip has also been reported; however, while technical hemostasis was achieved, it was not clinically successful [31].

Just as with treatment of bleeding ulcers, multiple endoscopic therapeutic techniques have been shown to be effective and the technique used should be dependent upon the experience and comfort level of the endoscopist.

Rebleeding is treated with repeat endoscopic treatment. Patients with refractory bleeding can be treated with angiographic embolization, as well as intravenous infusion of vasopressin [32, 33]. Very rarely, patients with refractory bleeding will require surgical intervention. This usually consists of creating a longitudinal esophagotomy and over-sewing the bleeding vessels. With the improvement of endoscopic therapies, surgery is the last line therapy and is required in a very small percentage of patients. After successful intervention, the patient should be observed for bleeding for at least 48 h.

Conclusion

Mallory–Weiss syndrome is characterized by bleeding esophageal lacerations most commonly caused by forceful retching. Although up to 70 % of patients receive blood transfusions, the majority of bleeding is self-limited and requires no

intervention. Early endoscopy is the diagnostic and therapeutic modality of choice. If no bleeding is visualized, the patient can be observed for 24–48 h. If the laceration is actively bleeding, endoscopic therapies, such as sclerotherapy, electrocautery, band ligation or clipping, are highly effective, with a rebleeding rate of approximately 5 %.

References

1. Mallory GK, Weiss S. Hemorrhages from lacerations of the cardiac orifice of the stomach due to vomiting. Am J Med Sci. 1929;178(4):506–14.
2. Quincke H. *Ulcus oesophagi ex digestone.* Deutsch Arch Klin Med. 1879;24(72).
3. Sugawa C, Benishek D, Walt AJ. Mallory-Weiss syndrome. A study of 224 patients. Am J Surg. 1983;145(1):30–3.
4. van Leerdam ME. Epidemiology of acute upper gastrointestinal bleeding. Best Pract Res Clin Gastroenterol. 2008;22(2):209–24.
5. Yin A, Li Y, Jiang Y, Liu J, Luo H. Mallory-Weiss syndrome: clinical and endoscopic characteristics. Eur J Intern Med. 2012;23(4):e92–6.
6. Marmo R et al. Mortality from nonulcer bleeding is similar to that of ulcer bleeding in high-risk patients with nonvariceal hemorrhage: a prospective database study in Italy. Gastrointest Endosc. 2012;75(2):263–72. 272.e1.
7. Kim JW et al. Mallory-Weiss Tear during Esophagogastroduodenoscopy. Case Rep Gastroenterol. 2015;9(1):62–7.
8. Penston JG, Boyd EJ, Wormsley KG. Mallory-Weiss tears occurring during endoscopy: a report of seven cases. Endoscopy. 1992;24(4):262–5.
9. Santoro MJ, Chen YK, Collen MJ. Polyethylene glycol electrolyte lavage solution-induced Mallory-Weiss tears. Am J Gastroenterol. 1993;88(8):1292–3.
10. Gilbert DA, Silverstein FE, Tedesco FJ. National ASGE survey on upper gastrointestinal bleeding: complications of endoscopy. Dig Dis Sci. 1981;26(7 Suppl):55S–9.
11. Knauer CM. Mallory-Weiss syndrome. Characterization of 75 Mallory-Weiss lacerations in 528 patients with upper gastrointestinal hemorrhage. Gastroenterology. 1976;71(1):5–8.
12. Harris JM, DiPalma JA. Clinical significance of Mallory-Weiss tears. Am J Gastroenterol. 1993;88(12):2056–8.
13. Younes Z, Johnson DA. The spectrum of spontaneous and iatrogenic esophageal injury: perforations, Mallory-Weiss tears, and hematomas. J Clin Gastroenterol. 1999;29(4):306–17.
14. Bharucha AE, Gostout CJ, Balm RK. Clinical and endoscopic risk factors in the Mallory-Weiss syndrome. Am J Gastroenterol. 1997;92(5):805–8.
15. Kortas DY et al. Mallory-Weiss tear: predisposing factors and predictors of a complicated course. Am J Gastroenterol. 2001;96(10):2863–5.
16. Kim JW et al. Predictive factors of recurrent bleeding in Mallory-Weiss syndrome. Korean J Gastroenterol. 2005;46(6):447–54.
17. Barkun AN et al. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med. 2010;152(2):101–13.
18. Laine L, Jensen DM. Management of patients with ulcer bleeding. Am J Gastroenterol. 2012;107(3):345–60. quiz 361.
19. Bataller R et al. Endoscopic sclerotherapy in upper gastrointestinal bleeding due to the Mallory-Weiss syndrome. Am J Gastroenterol. 1994;89(12):2147–50.
20. Llach J et al. Endoscopic injection therapy in bleeding Mallory-Weiss syndrome: a randomized controlled trial. Gastrointest Endosc. 2001;54(6):679–81.
21. Peng YC et al. Efficacy of endoscopic isotonic saline-epinephrine injection for the management of active Mallory-Weiss tears. J Clin Gastroenterol. 2001;32(2):119–22.

22. Laine L. Multipolar electrocoagulation in the treatment of active upper gastrointestinal tract hemorrhage. A prospective controlled trial. N Engl J Med. 1987;316(26):1613–7.
23. Cho YS et al. Endoscopic band ligation and endoscopic hemoclip placement for patients with Mallory-Weiss syndrome and active bleeding. World J Gastroenterol. 2008;14(13):2080–4.
24. Huang SP et al. Endoscopic hemoclip placement and epinephrine injection for Mallory-Weiss syndrome with active bleeding. Gastrointest Endosc. 2002;55(7):842–6.
25. Shimoda R et al. Endoscopic hemostasis with metallic hemoclips for iatrogenic Mallory-Weiss tear caused by endoscopic examination. Dig Endosc. 2009;21(1):20–3.
26. Yamaguchi Y et al. Endoscopic hemoclipping for upper GI bleeding due to Mallory-Weiss syndrome. Gastrointest Endosc. 2001;53(4):427–30.
27. Yuan Y, Wang C, Hunt RH. Endoscopic clipping for acute nonvariceal upper-GI bleeding: a meta-analysis and critical appraisal of randomized controlled trials. Gastrointest Endosc. 2008;68(2):339–51.
28. Lecleire S et al. Endoscopic band ligation could decrease recurrent bleeding in Mallory-Weiss syndrome as compared to haemostasis by hemoclips plus epinephrine. Aliment Pharmacol Ther. 2009;30(4):399–405.
29. Park CH et al. A prospective, randomized trial of endoscopic band ligation vs. epinephrine injection for actively bleeding Mallory-Weiss syndrome. Gastrointest Endosc. 2004;60(1): 22–7.
30. Ivekovic H, et al. The esophagus as a working channel: successful closure of a large Mallory-Weiss tear with clips and an endoloop. Endoscopy. 2011;43 Suppl 2 UCTN:E170.
31. Skinner M et al. Over-the-scope clip placement is effective rescue therapy for severe acute upper gastrointestinal bleeding. Endosc Int Open. 2014;2(1):E37–40.
32. Clark RA. Intraarterial vasopressin infusion for treatment of Mallory-Weiss tears of the esophagogastric junction. AJR Am J Roentgenol. 1979;133(3):449–51.
33. Walker TG. Acute gastrointestinal hemorrhage. Tech Vasc Interv Radiol. 2009;12(2):80–91.

Chapter 8
Diagnosis and Management of Bleeding Small Bowel Tumors

Maria S. Altieri and Aurora D. Pryor

Introduction

The small bowel, which is defined as the region between the ligament of Treitz and the ileocecal valve, is an uncommon source of gastrointestinal (GI) bleeding; however it is the most common cause of obscure GI bleeding, accounting for 75 % of these cases [1]. Although it accounts for only 5 % of all GI bleeding [2], understanding and diagnosis of bleeding originating in the small bowel is important. Such patients may require multiple blood transfusions, diagnostic procedures, and interventions until the diagnosis is made, thus leading to significantly greater financial burden to the health care system associated with this pathology [3]. Historically, due to the length of small bowel, bleeding originating from this location has represented a diagnostic challenge. Recently, the advent of new techniques, such as capsule endoscopy (CE), balloon-assisted enteroscopy (BAE), double-balloon enteroscopy (DBE), spiral-assisted enteroscopy, single-balloon enteroscopy (SBE), and computed tomography enterography, have improved our ability to evaluate obscure gastrointestinal bleeding from the small bowel.

A variety of lesions may result in small bowel bleeding (Table 8.1). The most common cause is vascular lesions, accounting for 70–80 % of all bleeding cases [4]. Bleeding from vascular sources is often managed nonoperatively. Small bowel

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Table 8.1 Sources of small bowel bleeding

Vascular lesions	Arteriovenous malformation (AVM)
	Venous ectasia
	Angiodysplasia
	Telangiectasia
	Varices
	Dieulafoy's lesion
	Arterial aneurysm
	Aortoenteric fistula
	Celiac sprue
Benign small bowel tumors	Adenoma
	Lipoma
	Neurofibroma
	Brunner's gland hamartoma
	Hemangioma
	Cowden disease
	Ganglioneuromas
	Schwannomas
	Nodular lymphoid hyperplasia
Malignant small bowel tumors	Adenocarcinoma
	Lymphoma
	Leiomyosarcoma (GIST)
	Carcinoid
Metastatic small bowel tumors	Melanoma
	Karposi's sarcoma
	Lung carcinoma
	Breast carcinoma
	Renal cell carcinoma

tumors, both benign and malignant, are the second most common cause of small bowel bleeding and the most common cause in younger patients. These often require a surgical approach. Other sources of small bowel bleeding are shown in Table 8.1.

The purpose of this chapter is to examine the etiology of bleeding small bowel tumors. In addition, the diagnostic approach and surgical management of the patient with small bowel bleeding are explored. We include an emphasis on the recommended therapeutic approach to each tumor type.

Epidemiology of Bleeding Small Bowel Tumors

Cancer of the small bowel is very uncommon. Tumors of the small intestine account for only 0.42 % of all total cancer cases and 2.3 % of cancers of digestive system in the USA [5]. Small bowel neoplasms have increased in incidence recently primarily due

to the increase in incidence of carcinoid tumors [6, 7]. Recent studies have showed that carcinoid now has the highest incidence of 37.4%, followed by adenocarcinoma (36.9%), lymphomas (16.3%), and stromal tumors (8.4%) [8]. Moreover, the USA has the highest age-adjusted incidence of these tumors in the world [9]. Four histologic types of cancer predominate: adenocarcinomas, neuroendocrine tumors, gastrointestinal stromal tumors, and lymphomas. The mean age of diagnosis is 65; however, the incidence rises after the age of 40 for all histologic subtypes [9].

In the USA, there is an unexplained higher incidence in the African-American population compared to the Caucasian population for both male and female gender [9]. In addition, mortality rate is higher in the African-American population [8]. This can be partially due to higher incidence of adenocarcinoma and carcinoid tumors in the US black population compared to Caucasian population [9]. Due to the rarity of this malignancy, the risk factors have not been well studied and it is believed that there is an association with a number of inflammatory bowel diseases and conditions [10]. A review of malignant small bowel tumors cites an association with Crohn's disease, celiac disease, presence of adenomas, Peutz Jeghers syndrome, familial adenomatous polyposis (FAP), other familial symptoms, sporadic colorectal cancer, diet and alcohol consumption, obesity, cigarette smoking, among others [11].

Although relatively infrequent, GI bleeding is the usual clinical onset. Bleeding is caused by the erosion of the tumor surface or by the rupture of aberrant vascular structures within the lesion [12]. Thus, small bowel tumors should be in the differential diagnosis for occult gastrointestinal bleeding.

Approach to Patients with Bleeding Small Bowel Neoplasms

Bleeding small bowel neoplasms are a common cause for occult GI bleed [1, 13]. Due to the difficulty of assessing the small bowel, diagnosis may be a challenge and is often delayed. The usual workup will often begin with esophagogastroduodenoscopy (EGD) and colonoscopy. In the case of bleeding small bowel neoplasms, these tests will often be non-diagnostic unless the source is in the proximal duodenum. However, these tests are still necessary and should be performed initially to rule out higher frequency sources. Other tests that can be performed can be categorized as low-yield and high-yield tests (discussed below). Low-yield tools include abdominal plain films, small bowel follow-through (SBFT), computed tomography (CT) scan, angiography, and technetium-labeled nuclear scans. These tests are relatively nonspecific for small bowel tumors, but can be used as a means of exclusion. Higher yield studies include enteroscopy, wireless capsule endoscopy, intraoperative endoscopy, and CT enterography. For this chapter, we examine the higher yield tools.

Higher Yield Diagnostic Tools

Enteroscopy

Push Enteroscopy

Push enteroscopy (PE), which was first described in 1973 by Ogoshi and colleagues [14], involves peroral insertion of a long, thin endoscope (220–250 cm). This allows visualization of the proximal bowel up to 100 cm distal to the ligament of Treitz [15]. It can be both diagnostic and therapeutic. The reported diagnostic yield is between 3 and 70 % [1, 16–18]. The main disadvantages are the inability to reach lesions beyond the middle jejunum, time-consuming nature of the procedure, and patient discomfort [19]. Thus, it has been largely replaced by capsule endoscopy and DBE.

Double-Balloon Enteroscopy

DBE is a relatively novel technique [20]. First described in 2001, it is now widely available. This procedure consists of 200 cm of working enteroscope length and a flexible overtube of 140 cm in length with a latex balloon at the tip of the enteroscope and the overtube. The alternative inflation and progression with the overtube and the balloon enteroscope allows for deeper progression, which allows for significant increase in the length of bowel that is explored [21, 22]. In addition, it allows for insertion through both antegrade and retrograde approaches. Thus, it has replaced push enteroscopy as the method of choice for endoscopic evaluation [23] and has become the gold standard for therapeutic intervention of many small bowel disorders in occult GI bleed [24]. A controlled prospective trial in 52 patients with suspected small bowel bleeding showed that antegrade DBE is significantly superior to push enteroscopy in terms of detection of lesions (73 % vs. 44 %, $p < 0.0001$) and the length of small bowel visualized (230 cm vs. 80 cm, $p < 0.0001$) [21]. Further, DBE detected additional lesions in the distal small bowel for patients who had positive findings on push enteroscopy. A recent study showed that the accuracy of DBE for locating small bowel neoplasms, such as adenocarcinoma, gastrointestinal stromal tumor, and lymphoma, was 94.4 %, 100 %, and 100 %, respectively. DBE is a useful diagnostic tool and should be considered the gold standard for localizing small bowel neoplasms [25].

Limitations of DBE include prolonged procedural times, sedation requirements, and availability [15]. Complications of DBE include bleeding, intestinal perforations, ileus, pancreatitis, or sedation-related issues (arrhythmia, hypotension, respiratory failure) [24].

DBE may have a critical role in the diagnosis and therapeutic management of small bowel tumors, as it can delay or help avoid emergency surgery. DBE can clarify the tumor location and characteristics.

Other Enteroscopic Techniques

Spiral Enteroscopy

Spiral enteroscopy (Endo-Ease Discovery SB, Spirus Medical Inc.) includes an overtube with a helical portion which grasps the bowel forms, reaching as far as 200 cm beyond the ligament of Treitz. The insertion method is based on "rotate to advance." It is a two-person procedure with the first person rotating the overtube, while the endoscopist keeps the lumen in view [26].

Sonde Enteroscopy

Sonde enteroscopy is another endoscopic technique, which is dependent on peristaltic propagation of a flexible enteroscope. The enteroscope has a working length of 250–400 cm. It is advanced into the duodenum with the help of another orally passed endoscope and propelled through the small bowel by peristalsis. Examination of the small bowel is then performed during withdrawal of the enteroscope. Due to its many disadvantages, such as lack of tip deflection, absence of biopsy channel, patient discomfort, and long procedure times (~4–6 h), sonde enteroscopy is no longer used [27].

Single-Balloon Enteroscopy

SBE (Olympus Inc.) has similar exploration times and depth of insertion to DBE. However, studies comparing SBE to DBE have shown that DBE is superior to SBE in terms of achieving higher number of complete enteroscopies and higher number of findings [28]. However, more recent studies have shown no differences between the two systems [29, 30].

Intraoperative Enteroscopy

This technique is reserved to facilitate intraoperative localization of presumed small bowel bleeding. One surgeon or gastroenterologist performs an upper GI endoscopy while a second surgeon telescopes the bowel over the endoscope. Alternatively, an endoscope may be inserted via a small enterotomy in the bowel through which the scope can be maneuvered proximally or distally. The endoscope is physically maneuvered though the bowel lumen by the surgeon, either laparoscopically or manually using an air-trapping technique. It has been considered the gold standard for a long time, as it has a diagnostic yield of 50–100 % with therapeutic abilities [31, 32]. However, it is an invasive procedure with 0–52 % of post-procedure complications, including avulsion of mesenteric vessels, prolonged ileus, serosal tears, and perforation [21, 22], and 8–11 % mortality [33–35]. Due to these reasons, intraoperative enteroscopy is reserved for cases, where other diagnostic methods are contraindicated or impossible.

Capsule Endoscopy

Wireless capsule endoscopy (WCE) is a safe and minimally invasive method for the diagnosis of occult GI bleeding. The capsule endoscope is a small 2.6 × 1.1 cm capsule, which is ingested by the patient. Subsequently, the capsule transmits images to a portable recorder via leads tapped to the patient's body. This method provides evaluation of the small bowel and identification of lesions with a diagnostic yield similar to, if not better than, DBE [36]. The disadvantages of this method, especially in the evaluation of small bowel tumors, are the inability to accurately localize lesions for later therapeutic intervention, increased rate of capsule retention at tumor sites (10–25 % compared to 0 % in healthy volunteers), and a false-negative rate of 1.5–18.9 % [37]. Regardless of its disadvantages, capsule endoscopy does allow reliable and relatively noninvasive imaging of the small bowel, and it is quickly becoming a first-line diagnostic tool for evaluation of obscure GI bleeding. Further advances are being made in this field with devices that will allow biopsy sampling and therapeutic interventions. The clinical utility of flexible spectral imaging color enhancement (FICE) remains controversial, although some studies have shown improvement in detection of bleeding lesions [38].

Management of Bleeding Small Bowel Tumors

Once a bleeding small bowel tumor has been identified, specific therapeutic intervention must be decided upon. Options are currently limited to endoscopic or surgical approaches. Initial management should be individualized based on clinical presentation, type of bleeding, duration, frequency, severity, acuity, and need for transfusion. In the case of hemodynamically stable patients, endoscopic resources can be used (either capsule endoscopy or balloon enteroscopy) to locate the bleeding source. In all cases, attempts to stabilize and resuscitate the patient with massive bleeding should be performed prior to proceeding to the definitive therapy. In cases of acute and severe blood loss, more rapid interventions may be necessary [15]. Surgery should be used for patients with transfusion dependency and massive recurrent bleeding, or when the lesion is not accessible via enteroscopy. It is also appropriate for lesions requiring resection.

In the stable patient, small bleeding intestinal polyps and adenomas may be successfully removed endoscopically. In addition, endoscopy may be used to stop bleeding originating from small bowel tumors, although rebleeding can occur. Endoscopic therapeutic options include photocoagulation, injection, mucosectomy, polypectomy, and enucleation [39]. However, endoscopic therapy is not a feasible therapeutic option for the majority of bleeding small bowel neoplasms, especially in the case of malignancy or when suspicions for malignancy exist. Thus, surgical intervention remains the mainstay of treatment.

The surgical approach to bleeding small bowel neoplasms depends primarily on the location of the lesion, as well as type and size. Resection of duodenal lesions

depends on the portion and extent of duodenal involvement, as well as the nature of the tumor. Small and benign lesions may be amenable to duodenotomy with local resection of the tumor. Lesions involving nonampullary portions of the duodenum may be amenable to segmental resection with primary anastomosis. Ampullary lesions, malignant lesions of the duodenum, or diffuse duodenal disease (such as in FAP) generally require a more extensive resection such as a pancreaticoduodenectomy [40–42]. In the case of benign disease, low-grade and early lesions, a less extensive pancreas-preserving duodenectomy or a pancreatic head resection with segmental duodenectomy may be an option. Alternatively, novel techniques that combine laparoscopy and endoluminal approaches have been described [43] although data regarding safety and outcomes have not been published.

Resection of small bowel neoplasms in the mesenteric small bowel may be preformed via laparoscopy or via laparotomy. Due to the length of the small bowel, localization of the tumor is often difficult. During laparoscopic exploration, three 5 mm port sites are generally sufficient for initial evaluation (Fig. 8.1). Following establishment of peritoneal insufflation, the entire peritoneum should be explored for evidence of metastatic disease. To localize the lesion, the entire mesenteric small bowel should be run proximally from the ligament of Treitz distally to the ileocecal valve. Two atraumatic graspers may be used to palpate the small bowel

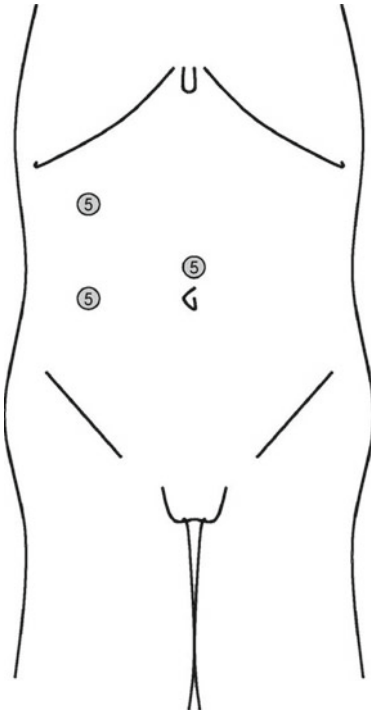

Fig. 8.1 Laparoscopic setup for exploration of bleeding small bowel tumor. During initial evaluation, three 5 mm ports are generally sufficient. One port is placed supra-umbilically, one to the right of midline, and the other in the right upper quadrant. The supra-umbilical port can later be expanded for placement of a 12 mm port if bowel resection is necessary

for intraluminal masses (Fig. 8.2), and visual inspection should be performed to evaluate for stigmata of bleeding and for extraluminal masses. Following identification of the bleeding small bowel tumor, segmental resection of the affected section of bowel can be performed with either intracorporeal or extracorporeal small bowel anastomosis (Fig. 8.3). The umbilical port may be enlarged to accommodate a larger trocar or wound protector, if necessary for specimen retrieval, and additional port sites may be needed for resection. If laparotomy is required due to adhesions, previous abdominal surgeries, or tumor size, exploration of the abdomen and palpation of the entire bowel should be similarly performed.

Benign versus malignant tumors are treated differently and treatment is diverse for the different types of tumors depending on the different locations, even among these two classifications.

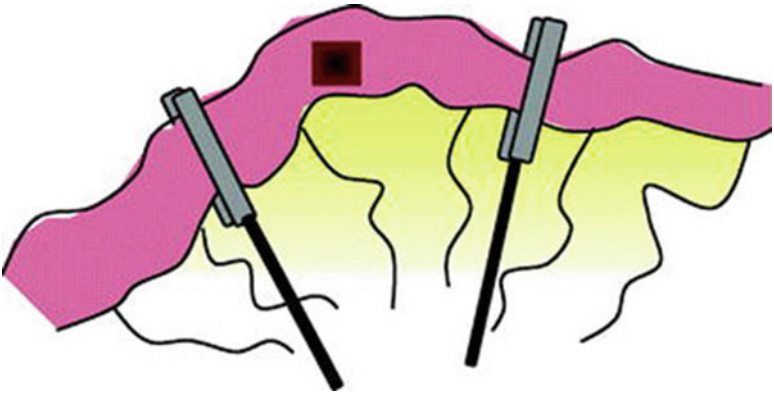

Fig. 8.2 Laparoscopic localization of bleeding small bowel tumors. To localize a bleeding small bowel lesion, two atraumatic bowel clamps are used to run the bowel and gently palpate for small bowel intraluminal masses. The bowel is visually examined for stigmata for bleeding

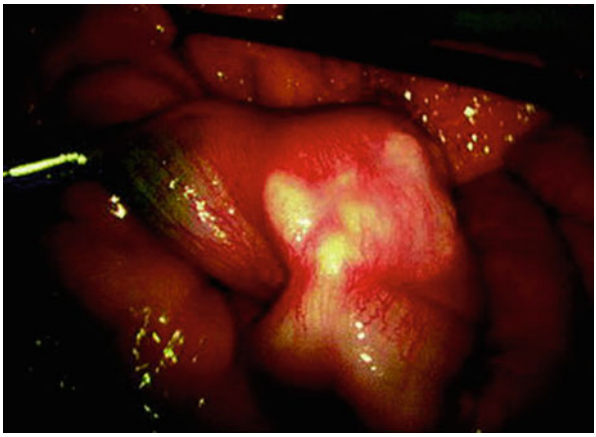

Fig. 8.3 Identification of a small bowel mass. This jejunal mass was previously tattooed on enteroscopy

Malignant Tumors

Carcinoid Tumors

Carcinoid tumors are not the most common tumor of the small intestine, accounting for 35–42 % of neoplasms. They occur mostly in the ileum and rarely in the duodenum [8, 10, 44]. Patients can present with abdominal pain, obstruction, or carcinoid syndrome. Carcinoid tumors rarely present with bleeding, due to the submucosal location of the tumor. If detected in the evaluation of a bleeding small bowel tumor, a careful evaluation of the entire small bowel is necessary to exclude the presence of multiple synchronous carcinoid nodules, in addition to evaluation of the liver [45]. As carcinoid tends to metastasize to regional lymph nodes, en bloc resection with extensive lymphadenectomy and wide resection of the mesentery are necessary.

Adenocarcinoma

Adenocarcinomas represent approximately 30–40 % of the cancers observed in the small intestine and are the second most common malignancy of the small intestine. Most of these tumors are located in the duodenum and the duodenal-jejunal junction, with a lower incidence in the jejunum and ileum [8, 44]. Massive GI bleeding is uncommon with adenocarcinoma; however, they commonly present with overt or occult bleeding.

As symptoms of small bowel adenocarcinomas are frequently nonspecific, diagnosis is often delayed and the majority of small bowel adenocarcinomas are metastatic at the time of detection. Depending on the location, lesions can be diagnosed by upper endoscopy, endoscopic ultrasound, and MRCP if in the periampullary location or video capsule endoscopy and double-balloon endoscopy if distal to the ligament of Treitz. As adenomas are typically metastatic at the time of diagnosis, if small bowel adenocarcinoma is suspected or detected, patient workup should include chest, abdomen, and pelvis CT scans to evaluate for metastatic disease. In addition, MRI, EUS, and angiography may also be useful for evaluation of metastases or tumor extent in some cases. Five-year disease-free survival is 30.5 % with median survival of 19.7 months for small bowel adenocarcinoma [46].

The primary treatment for small bowel adenocarcinomas is surgical resection. While endoscopy, polypectomy, or mucosectomy may be appropriate for small, especially polypoid, lesions confined to the mucosa or submucosa, the preferred treatment is small bowel resection. If in the proximal portions of the duodenum, pancreaticoduodenectomy is performed. In the distal portions of the duodenum, segmental resection can be performed. When located in the jejunum or ileum, segmental resection should be performed, as well as wide resection of lymph-node bearing mesentery.

Lymphomas

Lymphoma is the third most common malignancy located in the small intestine, accounting for 15–20 % of cases. It occurs most commonly in the ileum and jejunum [8]. Bleeding is less common with lymphoma than with other small bowel tumors, and lymphomas are more commonly associated with occult GI bleeding and with anemia rather than with overt bleeding. Treatment depends on the stage of the disease at diagnosis. Surgery is reserved for patients with intractable bleeding. Surgical resection of intestinal lymphomas remains the mainstay of treatment, and segmental resection with concurrent lymphadenectomy is important for local control.

Benign Tumors

Adenomas

Small bowel adenomas represent approximately 25 % of benign small bowel tumors. Similar to adenomas found in the large intestine, they may occasionally cause bleeding. The duodenum, especially the periampullary region, is the most frequent location for adenomas. However, they may occasionally be found throughout the small intestine [46]. Similar to their colonic counterparts, small bowel adenomas represent premalignant lesions and may lead to malignant transformation. Especially in the case of villous adenomas, a large proportion may progress to malignancy. In a retrospective analysis of duodenal villous adenomas, 42 % were found to posses malignant changes [47]. Due to the propensity for malignant transformation, surgical or endoscopic removal of these tumors is recommended.

Lipomas

Lipomas are the second most common benign tumor of the small bowel with very little malignant potential. They arise from submucosal adipose tissue and are most common in the ileum. Usually asymptomatic, they can present with bleeding. Small asymptomatic lipomas can be left untreated; however, when symptomatic or greater than 2 cm, resection should be performed.

Summary

Although an uncommon cause of gastrointestinal bleeding, bleeding small bowel tumors represent an important source of obscure GI blood loss. Timely identification and therapeutic intervention of these tumors are of utmost importance, as delay in diagnosis may affect patient outcomes. Concurrent symptoms such as weight

loss, intermittent obstruction, and fever may give clues to diagnosis. In addition, specific attention must be paid to patients presenting with small bowel bleeding who have conditions that may predispose them to the development of small bowel neoplasms. A variety of diagnostic tools facilitate diagnosis of bleeding tumors of the small bowel. These tools, including DBE and capsule endoscopy, should be employed after ruling out more common causes of GI bleeding through EGD and colonoscopy. Once identified, the bleeding small bowel tumors should be resected surgically or endoscopically, as appropriate.

References

1. Raju GS, Gerson L, Das A, Lewis B, American Gastroenterological Association. American Gastroenterological Association (AGA) Institute technical review on obscure gastrointestinal bleeding. Gastroenterology. 2007;133(5):1697–717.
2. Katz LB. The role of surgery in occult gastrointestinal bleeding. Semin Gastrointest Dis. 1999;10(2):78–81.
3. Prakash C, Zuckerman GR. Acute small bowel bleeding: a distinct entity with significantly different economic implications compared with GI bleeding from other locations. Gastrointest Endosc. 2003;58(3):330–5.
4. Lewis BS. Small intestinal bleeding. Gastroenterol Clin North Am. 2000;29(1):67–95.
5. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics. Cancer J Clin. 2009;59(4):225–49.
6. Severson RK, Schenk M, Gurney JG, Weiss LK, Demers RY. Increasing incidence of adenocarcinoma and carcinoid tumors of the small intestine in adults. Cancer Edidemiol Biomarkers Prev. 1996;5(2):81–4.
7. Hatzaras I, Palesty JA, Abir F, Sullivan P, Kozol RA, Dudrick SJ, et al. Small-bowel tumors: epidemiologic and clinical characteristics of 1260 cases from the connecticut tumor registry. Arch Surg. 2007;142(3):229–35.
8. Billimoria KY, Bentrem DJ, Wayne JD, Ko CY, Bennett CL, Talamonti MS. Small bowel cancer in the United States: changes in epidemiology, treatment, and survival over the last 20 years. Ann Surg. 2009;249(1):63–71.
9. Haselkorn T, Qhittemore AS, Lilienfeld DE. Incidence of small bowel cancer in the United States and worldwide: geographic, temporal, and racial differences. Cancer Causes Control. 2005;16(7):781–7.
10. Pan SY, Morrison H. Epidemiology of cancer of small intestine. World J Gastrointest Oncol. 2011;3(3):33–43.
11. Reynolds I, Healy P, Mcnamara DA. Malignant tumours of the small intestine. Surgeon. 2014;12(5):263–70.
12. Sanchez-Capilla AD, De La Torre-Rubio P, Redondo-Cerezo E. New insignts to occult gastrointestinal bleeding: from pathophysiology to therapeutics. World J Gastrointest Pathophysiol. 2014;5(3):271–83.
13. Keum B, Chun HJ. Capsule endoscopy and double balloon enteroscopy for obscure gastrointestinal bleeding: which is better? Gastroenterol Hepatol. 2011;26(5):794–5.
14. Ogoshi K, Hara Y, Ashizawa S. New technique for small intestinal fiberoscopy. Gastrointest Endosc. 1973;20(2):64–5.
15. Pasha SF, Hara AK, Leighton JA. Diagnostic evaluation and management of obscure gastrointestinal bleeding: a changing paradigm. Gastroenterol Hepatol. 2009;5(12):839–50.
16. Chak A, Koehler MK, Sundaram SN, Cooper GS, Canto MI, Sivak Jr MV. Diagnostic and therapeutic impact of push enteroscopy: analysis of factors associated with positive findings. Gastrointest Endosc. 1998;47(1):18–22.

17. Lin S, Branch MS, Shetzline M. The importance of indication in the diagnostic value of push enteroscopy. Endoscopy. 2003;35(4):315–21.
18. Chak A, Cooper GS, Canto MI, Pollack BJ, Sivak Jr MV. Enteroscopy for the initial evaluation of iron deficiency. Gastrointest Endosc. 1998;47(2):144–8.
19. Santhakumar C, Liu K. Evaluation and outcomes of patients with obscure gastrointestinal bleeding. World J of Gastrointest Pathophysiol. 2014;15(4):479–86.
20. Carey EJ, Fleischer DE. Investigation of the small bowel in gastrointestinal bleeding—enteroscopy and capsule endoscopy. Gastroenterol Clin North Am. 2005;34(4):719–34.
21. May A, Nachbar L, Schneider M, Ell C. Prospective comparison of push enteroscopy and push and pull enteroscopy in patients with suspected small-bowel bleeding. Am J Gastroenterol. 2006;101(9):2016–24.
22. Matsumoto T, Moriyama T, Esaki M, Nakamura S, Iida M. Performance of antegrade double-balloon enteroscopy: a comparison with push enteroscopy. Gastrointest Endosc. 2005;62(3): 392–8.
23. Saygili F, Saygili SM, Oztas E. Examining the whole bowel, double balloon enteroscopy: inducations, diagnostic yield and complication. World J Gastrointest Endosc. 2014;7(3): 247–52.
24. Fry LC, Bellutti M, Neumann H, Malfertheiner P, Monkemuller K. Incidence of bleeding lesions within reach of conventional upper and lower endoscopes in patients undergoing double-balloon enteroscopy for obscure gastrointestinal bleeding. Alim Pharmacol Ther. 2009;29(3):342–9.
25. Chen WG, Shan GD, Zhang H, Li L, Yue M, Xiang Z, et al. Double-balloon enteroscopy in small bowel tumors: a Chinese single-center study. World J Gastroenterol. 2013;19(23): 3665–71.
26. Akerman PA, Cantero D. Spiral enteroscopy and push enteroscopy. Gastrointest Endosc Clin N Am. 2009;19(3):357–69.
27. Gostout CJ. Sonde enteroscopy. Technique, depth of insertion, and yield of lesions. Gastrointest Endosc Clin N Am. 1996;6(4):777–92.
28. May A, Farber M, Aschmoneit I, Pohl J, Manner H, et al. Prospective multicenter trial comparing push-and-pull enteroscopy with single- and double-ballon techniques in patients with small-bowel disorders. Am J Gastroenterol. 2010;105(3):575–81.
29. Domagk D, Mensink P, Aktas H, Lenz P, Meister T, et al. Single- vs. double-balloon enteroscopy in small-bowel diagnostics: a randomized multicenter trial. Endoscopy. 2011;43(6):472–6.
30. Efthymiou M, Desmond PV, Brown G, La Nauze R, Kaffles A, Chua TJ, et al. SINGLE-01: a randomized, controlled trial comparing the efficacy and depth of insertion of single-and double-balloon enterosopy by using a novel method to determine insertion depth. Gastrointest Endosc. 2012;76(5):972–80.
31. Gralnek IM. Obscure-overt gastrointestinal bleeding. Gastroenterology. 2005;128(5): 1424–30.
32. Schulz HJ, Schmidt H. Intraoperative enteroscopy. Gastrointest Endosc Clin N Am. 2009;19(3):371–9.
33. Douard R, Wind P, Berger A, Maniere T, Landi B, Cellier C, et al. Role of intraoperative enteroscopy in the management of obscure gastrointestinal bleeding at the time of video-capsule endoscopy. Am J Surg. 2009;198(1):6–11.
34. Zaman A, Sheppard B, Katom RM. Total peroral intraoperative enteroscopy for obscure GI bleeding using a dedicated push enteroscope: diagnostic yield and patient outcome. Gastrointest Endosc. 1999;50(4):506–10.
35. Desa LA, Ohri SK, Hutton KA, Lee H, Spencer J. Role of intraoperative enteroscopy in obscure gastrointestinal bleeding of small bowel origin. Br J Surg. 1991;78(2):92–5.
36. Kameda N, Higuchi K, Shiba M, Machida H, Okazaki H, Yamagami H, et al. A prospective, single-blind trial comparing wireless capsule endoscopy and double-balloon enteroscopy in patients with obscure gastrointestinal bleeding. J Gastroenterol. 2008;43(6):434–40.

37. Pennazio M, Rondonotti E, de Franchis R. Capsule endoscopy in neoplastic diseases. World J Gastroenterol. 2008;14(34):5245–53.
38. Sato Y, Sagawa T, Hirakawa M, Ohnuma H, Osuga T, Okagawa Y, et al. Clinical utility of capsule endoscopy with flexible spectral imaging color enhancement for diagnosis of small bowel lesions. Endosc Int Open. 2014;2(2):E80–7.
39. Ponsaing LG, Hansen MB. Therapeutic procedures for submucosal tumors in the gastrointestinal tract. World J Gastroenterol. 2007;13(24):3316–22.
40. Kemp CD, Russell RT, Sharp KW. Resection of benign duodenal neoplasms. Am Surg. 2007;73(11):1086–91.
41. Chong KC, Cheah WK, Lenzi JE, Goh PM. Benign duodenal tumors. Hepatogastroenterology. 2000;47(35):1298–300.
42. Perez A, Saltzman JR, Carr-Locke DL, Brooks DC, Osteen RT, Zinner MJ, et al. Benign non-ampullary duodenal neoplasms. J Gastrointest Surg. 2003;7(4):536–41.
43. Franklin Jr ME, Portillo G, Trevino JM, Gonzalez JJ, Glass JL. Laparoscopic intraluminal surgery for gastrointestinal malignancies. World J Surg. 2008;32(8):1709–13.
44. Schottenfeld D, Beebe-Dimmer DL, Vigneau FD. The epidemiology and pathogenesis of neoplasia in the small intestine. Ann Epidemiol. 2009;19(1):58–69.
45. Yantiss RK, Odze RD, Farraye FA, Rosenberg AE. Solitary versus multiple carcinoid tumors of the ileum: a clinical and pathologic review of 68 cases. Am J Surg Pathol. 2003;27(6):811–7.
46. Gill SS, Heuman DM, Mihas AA. Small intestinal neoplasms. J Clin Gastroenterol. 2001;33(4):267–82.
47. Witteman BJ, Janssens AR, Griffioen G, Lamers CB. Villous tumours of the duodenum. An analysis of the literature with emphasis on malignant transformation. Neth J Med. 1993;42(1–2):5–11.

Chapter 9
Management of Bleeding from the Bile Duct

Cecilia T. Ong and Kevin N. Shah

Overview

Hemobilia, bleeding originating from the biliary tract or gallbladder, is an uncommonly encountered clinical entity that is most frequently the result of accidental or iatrogenic trauma. While accidental trauma was historically the most common etiology of hemobilia, iatrogenic trauma has supplanted it as use of invasive diagnostic and therapeutic biliary procedures has increased. Other causes include gallstones, inflammation, vascular disorders, and neoplasms. Timely identification and treatment of hemobilia is important, but the presentation and diversity of sources can create diagnostic challenges that make this difficult.

Historical Context

Francis Glisson is credited with first describing biliary tract bleeding in 1654 [1]. The case report chronicled a young nobleman who was stabbed in the right upper quadrant who eventually died of massive upper gastrointestinal hemorrhage. Autopsy demonstrated a deep laceration in the liver, after which Glisson posited that "the biliary tract takes unto itself […] some of the blood issuing into the liver and leads it down to the intestines," potentiating gastrointestinal blood loss should the biliary tract be disrupted.

Morgagni's Epistles, published in 1765, described hepatic abscesses and large gallstones as a source of biliary tract bleeding [2]. In 1871, Quincke described the cardinal signs of hemobilia, namely right upper quadrant pain, jaundice, and upper

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gastrointestinal tract bleeding, now referred to as Quincke's triad [3]. In his extensive review of hemobilia published in 1972, Sandblom chronicled these and other scattered case reports. He concluded that, though historically biliary tract bleeding was viewed as rare, improved awareness and diagnostic means were contributing to increasing frequency of diagnosis [4].

The first successful operation for hemobilia was performed in 1903 by Kehr. The patient presented with cholelithiasis but at the time of operation, a pulsating mass was felt at the gallbladder neck. A ruptured right hepatic artery aneurysm was identified and successfully managed by direct arterial ligation [5]. The first successful hepatic resection was reported in 1956, and this was the preferred management of hepatic sources of hemobilia until the first angiographic embolization was described in 1976 [6, 7].

Pathophysiology and Etiology

The segmental anatomy of the liver is defined by the portal triads, which are comprised of branches of the hepatic artery, portal vein, and bile duct [8]. Injury to the biliary system, therefore, can be associated with concomitant injury to the adjacent vascular structures. Thrombus formation related to hemobilia can lead to biliary obstruction and present with right upper quadrant abdominal pain, jaundice, and upper gastrointestinal bleeding. This complete constellation of symptoms, however, is seen in only 30–40 % of patients [9, 10]. Clot formation due to mild bleeds may present with symptoms of biliary obstruction such as biliary colic, jaundice, or cholecystitis [11]. Clinically significant bleeding may signify an abnormal fistulous communication between a hepatic arterial or portovenous branch and the biliary tree. These brisk bleeds, if drained through the ampulla of Vater, can present with melena, hematemesis, or in severe cases shock.

Accidental trauma has historically been the most common cause of hemobilia; however, with the growing utilization of invasive biliary procedures, iatrogenic trauma is increasing in frequency. Figure 9.1 demonstrates this shift in the etiology of hemobilia. Increased awareness of hemobilia as a cause of gastrointestinal hemorrhage and more refined diagnostics have increased the overall detection of biliary tract bleeding.

Accidental Trauma

Hemobilia is a complication following 3 % of all liver injuries, though there is a higher incidence following blunt injury [14, 15]. Most penetrating trauma to the abdomen is explored and repaired primarily at the time of injury. In contrast, nonoperative management has become increasingly common for blunt abdominal trauma, with liver injuries being discovered on imaging rather than intraoperatively [16, 17]. The presentation of

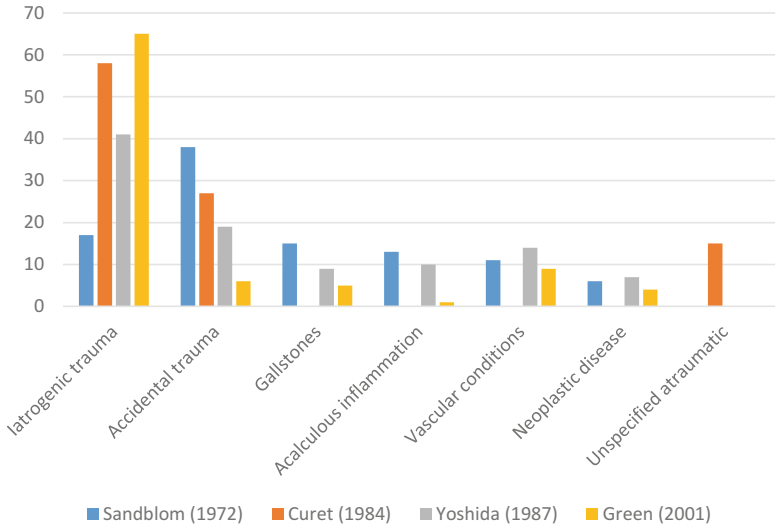

Fig. 9.1 Etiology of hemobilia. From Sandblom [4], Curet [12], Yoshida [13], and Green [10]

hemobilia following trauma may occur early in the course, but may occur as late as months following the event [18]. Delayed hemobilia after penetrating trauma can also be observed secondary to pseudoaneurysms and biliary-vascular fistula formation. It is during the interval of nonoperative management that factors which predispose to hemobilia such as post-traumatic bile stasis, hematomas, and abscesses can develop [19].

Iatrogenic Trauma

Hemobilia can be caused by endoscopic, percutaneous, or operative liver and biliary procedures. Percutaneous liver biopsy [20], percutaneous cholangiography [21], and endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy [22] are being used with increased frequency, but the rate of bleeding complications is still relatively small. Hemobilia has also been reported following radiofrequency ablation of primary hepatic malignancies [23]. Bleeding after percutaneous biliary drainage (PBD) occurs at a somewhat higher rate than the previously mentioned procedures but is often mild and the result of mucosal irritation. About 2 % of patients undergoing PBD will have bleeding significant enough that it requires intervention [24]. Transjugular intrahepatic portosystemic shunts also have a relatively increased (5 %) risk of hemobilia [25]. The risk of hemobilia is higher in patients with chronic liver disease due to the presence of ascites, coagulopathy, and platelet dysfunction, and coagulopathy is a relative contraindication to most biliary procedures [25, 26].

Neoplasms

Although rare, liver and biliary tract tumors can also be associated with hemobilia. Hepatocellular tumors are probably the most common neoplastic cause, but other tumors such as intrahepatic cholangiocarcinoma, gallbladder cancer, and pancreatic cancer are also potential sources [27, 28]. Bleeding may be the result of direct tumor invasion into the biliary tract or creation of a fistula between the biliary tract and adjacent vascular structures [13, 29, 30].

Vascular

As was evidenced in Kehr's first successful operation for hemobilia, vascular anomalies can be rare sources of hemobilia [5]. Hepatic artery aneurysms, which comprise approximately 20 % of all visceral aneurysms and carry a 21 % mortality rate following rupture, are linked to atherosclerosis, polyarteritis nodosa, fibromuscular dysplasia, and portal hypertension [31, 32]. Hepatic artery pseudoaneurysms, on the other hand, are uncommonly seen following procedures such as laparoscopic cholecystectomies [33, 34], presumably due to thermal injury during the procedure, or from other penetrating trauma, either iatrogenic or accidental [15, 31]. Recent hepatobiliary surgical intervention paired with the classic Quincke's triad should increase the suspicion for pseudoaneurysm rupture.

Gallstones

Morgagni posited that large gallstones can cause hemobilia, and it has since been demonstrated that large gallstones can erode through the gallbladder neck, creating a fistulous tract between the cystic artery and the biliary system [2, 35]. Even in cases of severe inflammation and erosion of large gallstones through the gallbladder wall, clinically significant hemobilia is rare because the subsequent inflammatory reaction leads to early thrombosis of the cystic artery.

Diagnostic Workup

As hemobilia is a rare, sometimes delayed, but clinically significant entity, a high degree of clinical suspicion is needed to avert morbidity and mortality. Laboratory evaluations demonstrate biliary obstruction with increased direct bilirubin and/or anemia secondary to gastrointestinal losses. If patients present with symptoms of upper gastrointestinal bleed, esophagogastroduodenoscopy is the initial diagnostic

test of choice. Blood or clot at the ampulla of Vater confirms the diagnosis. However, approximately, 10 % of upper endoscopies are nondiagnostic and necessitate further diagnostic evaluation [13]. Endoscopic retrograde cholangiopancreatography (ERCP) can also reveal clots in the bile ducts.

In patients who present following trauma with a concern for hepatic injury, ultrasound is being supplanted by CT scan as the preferred imaging and diagnostic modality [16]. Such imaging can demonstrate hepatic hematomas or lacerations, but do not readily demonstrate arterio-biliary fistulae. This latter entity is best demonstrated by selective arteriogram. Hemobilia may manifest as active extravasation and displacement of vessels around a liver mass, or by filling of a true aneurysm. In addition to the diagnostic utility, arteriogram offers the opportunity for therapeutic embolization [36]. However, similar to bleeding elsewhere in the GI tract, arteriography can miss slow or inactive bleeding.

Therapeutic Interventions

As the manifestations of hemobilia range from minor morbidity to life-threatening hemorrhage, there is a similarly broad range of therapeutic approaches to this problem. Conservative or expectant management is often appropriate for hemodynamically stable patients. As with all types of gastrointestinal bleeds, any underlying coagulopathy should be corrected as needed. Red blood cells and platelets should be transfused when indicated. In many cases, such interventions will be sufficient to stop bleeding. When bleeding persists, a number of interventions should be considered and tailored according to the setting.

Accidental Trauma

In cases of penetrating trauma, surgical exploration at the time of presentation remains a mainstay of treatment. Surgery in this setting, however, is pursued so that the abdomen can be explored for all injuries and is not typically undertaken to address hemobilia specifically. Nevertheless, potential sources of hemobilia may be encountered and controlled at the time of exploration. Bleeding pseudoaneurysms of hepatic artery branches are usually best managed by ligation of the bleeding vessel, as complex vascular reconstruction in the context of emergent trauma laparotomy is time consuming and challenging. Deep intrahepatic sources of hemobilia and large hepatic defects may not be easily accessible for direct ligation. While hemi-hepatectomy can be utilized for bleeding that is clearly localized to either the right or left hemi-liver, major liver resection in an emergent setting can be difficult and poorly tolerated. If wedge resection incorporating the defect is possible, this is usually preferable to hemi-hepatectomy. Alternatively, ligation of the feeding hepatic artery can be employed in emergent cases.

In general, however, angiographic approaches have become preferred, particularly in cases of delayed or intrahepatic hemobilia following penetrating trauma. Angiography can provide both accurate diagnostic identification of bleeding and effective intervention in a single procedure. Utilizing steel coils, gelfoam, and other materials, selective arterial embolization has a success rate of 80–97 % in controlling intrahepatic bleeding [12, 13]. As such, angio-embolization should be considered the standard of care for treatment of intrahepatic hemobilia and surgical interventions should be reserved for angiographic failures.

Iatrogenic Hemobilia

As noted previously, iatrogenic causes have replaced accidental trauma as the most common source of hemobilia. In many cases hemobilia will cease with correction of coagulopathy and supportive measures. When bleeding persists, nonoperative interventions are the first-line measures. Hemobilia secondary to percutaneous liver biopsy is best managed by angiography to identify the source of bleeding and embolization to control it. Depending on the level and location of the bleeding, post-embolization cholecystitis can be observed if the cystic artery is occluded by the embolization. In such cases, cholecystectomy is effective management [37].

Post-ERCP bleeding is typically a consequence of sphincterotomy and most cases are mild in severity. When more significant bleeding is present, endoscopic evaluation should be carried out. Control of the bleeding can be achieved with any combination of epinephrine injection, thermal therapy, or placement of clips. In the rare event that endoscopic measures fail to control ampullary bleeding, surgery can be considered. This is best carried out through a longitudinal duodenotomy to expose the ampulla. Bleeding can then be controlled with electrocautery or suture ligation of the bleeding vessel, taking care not to stricture the pancreatic or common bile duct.

Similarly, bleeding after PBD placement is generally mild and does not require intervention other than supportive measures. Slower venous bleeding can be managed by exchanging the PBD catheter for one of a larger caliber. This allows tamponade of the bleeding and the larger size also makes it less likely to obstruct from clot in conjunction with frequent flushing of the drains. If increasing the catheter size does not adequately control the bleeding, angiography should be attempted next to identify and embolize any vascular-biliary fistula.

Neoplasms

In hemobilia related to hepatobiliary tumors, surgery can play an important role. For slower, more chronic bleeds, resection of the mass is the definitive treatment. If there is brisk bleeding and hemodynamic instability, however, major liver, biliary,

or pancreactic surgery can be highly morbid. Angio-embolization can be used in this setting to gain hemostasis acutely. After the acute hemorrhage is stopped angiographically, surgery can be planned in a semi-elective setting.

Hemobilia from advanced, locally unresectable tumors can present a challenge, as surgical resection may not be safe. If amenable, angiography remains the preferred option. Tumors with bleeding related to mucosal erosion, particularly extrahepatic tumors, may not be well suited to angiographic intervention. For extrahepatic biliary bleeding, the use of fully covered, self-expanding metal stents has been described to tamponade biliary bleeding [38, 39].

Radiation therapy can also help palliate bleeding symptoms for tumors not resectable because of local invasion into adjacent structures. It is also important to keep in mind that patients with liver tumors often have underlying liver disease and corresponding coagulopathy. Aggressive medical correction of coagulopathy including consideration of adjuncts like recombinant factor VII is essential to achieving hemostasis and avoiding potentially morbid operations in the palliative setting.

Conclusion

Hemobilia is due increasingly to iatrogenic trauma; however accidental trauma, gallstones, inflammation, vascular disorders, and neoplasms still contribute to the incidence of this problem. Prompt identification of hemobilia as the source of gastrointestinal bleeding is key and diagnosis is confirmed with a combination of EGD, ERCP, and CT imaging. Transcatheter arterial embolization has largely supplanted operative interventions as the management strategy of choice for clinically significant hemobilia. This technique achieves a high success rate and has low peri-procedural morbidity and mortality when compared with open procedures [40]. Selective embolization of segmental hepatic artery branches rarely leads to hepatic necrosis, especially if the portal vein is patent. Though re-bleeding can occur after angiographic intervention, re-embolization is possible and highly successful [41, 42]. Surgical intervention, therefore, is generally reserved for instances in which nonoperative measures fail, in the presence of concomitant injuries, or when the etiology of the bleeding necessitates surgical resection or direct arterial ligation.

References

1. Glisson F. *Anatomia hepatis*. 1665: ap. Jo. Janss. a Waefberge.
2. Morgagni G, Valsalva AM. Jo Baptistae Morgagni Epistolae anatomicae duodeviginti. Bassani: Sumptibus Remondinianis; 1764. xii, 427 i.e. 327, 1 p.
3. Quincke H. Ein fall von aneurysma der leberarterie. Klin Wochenschr. 1871;8:349–51.
4. Sandblom P. Hemobilia (biliary tract hemorrhage): history, pathology, diagnosis, treatment. Springfield, IL: Charles C. Thomas Publisher; 1972.

5. Gould GM. American year-book of medicine and surgery. Philadelphia: W.B. Saunders; 1905.
6. Thomeret G, Dubost C, Dubray-Vautrin J, Cabrol A. Rupture traumatique du foie. Hémorragies digestives secondaires graves dues à une fistule artério-biliaire. Hépatectomie droite réglée. Guérison Mém Acad Chir. 1956;83:38.
7. Walter JF, Paaso BT, Cannon WB. Successful transcatheter embolic control of massive hematobilia secondary to liver biopsy. Am J Roentgenol. 1976;127(5):847–9.
8. Couinaud C. Liver anatomy: portal (and suprahepatic) or biliary segmentation. Dig Surg. 1999;16(6):459–67.
9. Petrou A et al. Hemobilia due to cystic artery stump pseudoaneurysm following laparoscopic cholecystectomy: case presentation and literature review. Int Surg. 2012;97(2):140–4.
10. Green MH, Duell RM, Johnson CD, Jamieson NV. Haemobilia. Br J Surg. 2001;88(6): 773–86.
11. Mosenkis BN, Brandt LJ. Bleeding causing biliary obstruction after endoscopic sphincterotomy. Am J Gastroenterol. 1997;92(4):708–9.
12. Curet P, Baumer R, Roche A, Grellet J, Mercadier M. Hepatic hemobilia of traumatic or iatrogenic origin: recent advances in diagnosis and therapy, review of the literature from 1976 to 1981. World J Surg. 1984;8(1):2–8.
13. Yoshida J, Donahue PE, Nyhus LM. Hemobilia: review of recent experience with a worldwide problem. Am J Gastroenterol. 1987;82(5):448–53.
14. Krige JE, Bornman PC, Terblanche J. Liver trauma in 446 patients. S Afr J Surg. 1997;35(1):10–5.
15. Schouten van der Velden AP, de Ruijter WM, Janssen CM, Kool LJ, Tan EC. Hemobilia as a late complication after blunt abdominal trauma: a case report and review of the literature. J Emerg Med. 2010;39(5):592–5.
16. Petrowsky H, Raeder S, Zuercher L, Platz A, Simmen HP, Puhan MA, et al. A quarter century experience in liver trauma: a plea for early computed tomography and conservative management for all hemodynamically stable patients. World J Surg. 2012;36(2):247–54.
17. Matthes G, Stengel D, Seifert J, Rademacher G, Mutze S, Ekkernkamp A. Blunt liver injuries in polytrauma: results from a cohort study with the regular use of whole-body helical computed tomography. World J Surg. 2003;27(10):1124–30.
18. Murugesan SD, Sathyanesan J, Lakshmanan A, Ramaswami S, Perumal S, Perumal SU, et al. Massive hemobilia: a diagnostic and therapeutic challenge. World J Surg. 2014;38(7): 1755–62.
19. Merrell SW, Schneider PD. Hemobilia—evolution of current diagnosis and treatment. Western J Med. 1991;155(6):621.
20. Lichtenstein DR, Kim D, Chopra S. Delayed massive hemobilia following percutaneous liver biopsy: treatment by embolotherapy. Am J Gastroenterol. 1992;87(12):1833–8.
21. Cahow CE, Burrell M, Greco R. Hemobilia following percutaneous transhepatic cholangiography. Ann Surg. 1977;185(2):235–41.
22. Freeman ML, Nelson DB, Sherman S, Haber GB, Herman ME, Dorsher PJ, et al. Complications of endoscopic biliary sphincterotomy. N Engl J Med. 1996;335(13):909–18.
23. Akahane M, Koga H, Kato N, Yamada H, Uozumi K, Tateishi R, et al. Complications of percutaneous radiofrequency ablation for hepato-cellular carcinoma: imaging spectrum and management. Radiographics. 2005;25 Suppl 1:S57–68.
24. Rivera-Sanfeliz GM, Assar OS, LaBerge JM, Wilson MW, Gordon RL, Ring EJ, et al. Incidence of important hemobilia following transhepatic biliary drainage: left-sided versus right-sided approaches. Cardiovasc Intervent Radiol. 2004;27(2):137–9.
25. Boyer TD, Haskal ZJ, American Association for the Study of Liver Diseases. The role of transjugular intrahepatic portosystemic shunt in the management of portal hypertension. Hepatology. 2005;41(2):386–400.
26. Gurakuqi GC, Stadlbauer V, Portugaller HR, Högenauer C, Trauner M, Stauber RE. Fatal hemobilia resulting from an iatrogenic arteriobiliary fistula as a rare complication of transjugular liver biopsy. Eur J Gastroenterol Hepatol. 2008;20(1):83–6.

27. Coulier B, Maldague P, Ramboux A, Gielen I. Mass-forming intrahepatic cholangiocarcinoma presenting with painful obstructive hemobilia. JBR-BTR. 2014;97(6):366–9.
28. Verset G, Maréchal R, Bali MA, Devière J, Van Laethem JL. Fatal hemobilia in advanced hepatocellular carcinoma invading biliary tract after treatment with sorafenib and biliary stenting. Ann Oncol. 2010;21(6):1381–2.
29. Wright RC, Roberts JW. Fibrolamellar carcinoma of the liver presenting with hemobilia. Contemp Surg. 1988;33:29–35.
30. Hasan S, Quintana J, Siddiqui Y, Maldonado V. Carcinoma of the pancreas presenting with hemobilia (Letter). Gastrointest Endosc. 1986;32:305–30.
31. Pasha SF, Gloviczki P, Stanson AW, Kamath PS. Splanchnic artery aneurysms. Mayo Clin Proc. 2007;82(4):472–9.
32. Shanley CJ, Shah NL, Messina LM. Common splanchnic artery aneurysms: splenic, hepatic, and celiac. Ann Vasc Surg. 1996;10(3):315–22.
33. Yao CA, Arnell TD. Hepatic artery pseudoaneurysm following laparoscopic cholecystectomy. Am J Surg. 2010;199(1):e10–1.
34. Deziel DJ, Millikan KW, Economou SG, Doolas A, Ko ST, Airan MC. Complications of laparoscopic cholecystectomy: a national survey of 4,292 hospitals and an analysis of 77,604 cases. Am J Surg. 1993;165(1):9–14.
35. Strickland SK, Khoury MB, Kiproff PM, Raves JJ. Cystic artery pseudoaneurysm: a rare cause of hemobilia. Cardiovasc Intervent Radiol. 1991;14(3):183–4.
36. Marynissen T, Maleux G, Heye S, Vaninbroukx J, Laleman W, Cassiman D, et al. Transcatheter arterial embolization for iatrogenic hemobilia is a safe and effective procedure: case series and review of the literature. Eur J Gastroenterol Hepatol. 2012;24(8):905–9.
37. Dousset B, Sauvanet A, Bardou M, Legmann P, Vilgrain V, Belghiti J. Selective surgical indications for iatrogenic hemobilia. Surgery. 1997;121(1):37–41.
38. Barresi L, Tarantino I, Ligresti D, Curcio G, Granata A, Traina M. Fully covered self-expandable metal stent treatment of spurting bleeding into the biliary tract after endoscopic ultrasound-guided fine-needle aspiration of a solid lesion of the pancreatic head. Endoscopy. 2015;47 Suppl 1.
39. Goenka MK, Harwani Y, Rai V, Goenka U. Fully covered self-expandable metal biliary stent for hemobilia caused by portal biliopathy. Gastrointest Endosc. 2014;80(6):1175.
40. Srivastava DN, Sharma S, Pal S, Thulkar S, Seith A, Bandhu S, et al. Transcatheter arterial embolization in the management of hemobilia. Abdom Imaging. 2006;31(4):439–48.
41. Melissano G, Chiesa R. Successful surgical treatment of visceral artery aneurysms. After failure of percutaneous treatment. Tex Heart Inst J. 1998;25(1):75–8.
42. Tulsyan N, Kashyap VS, Greenberg RK, Sarac TP, Clair DG, Pierce G, et al. The endovascular management of visceral artery aneurysms and pseudoaneurysms. J Vasc Surg. 2007;45(2):276–83. discussion 283.

Chapter 10
Management of Bleeding from the Pancreas

Scott Dolejs and Eugene P. Ceppa

Introduction

Acute hemorrhage originating from the pancreas is the least common form of upper gastrointestinal bleed [1, 2]. Specifically, hemorrhage from the pancreatic duct through the papilla of Vater is rare with approximately 200 cases having been reported in the literature. The first report by Lower and Farrell in 1931 identified a splenic artery aneurysm as the cause [3]. This phenomenon has been described in various terms including *wirsungorrhagia* and *hemowirsungia*, highlighting the identification of hemorrhage from the pancreatic duct into the duodenum [4–7]. *Hemosuccus pancreaticus* was first proposed by Sandblom in 1970 signifying emission of blood from the pancreatic duct through the ampulla of Vater [8]. Longmire proposed *hemoductal pancreatitis* as another synonymous term [9].

Surgical Anatomy

Eristratos first described the pancreas in 300 BC. The origin of the word pancreas is Greek for *pan* meaning all and *kreas* defined as meat/flesh. The pancreas is a retroperitoneal organ situated at the level of the L2 vertebrae. The pancreas is commonly divided into segments consisting of the head, uncinate process, neck, body, and tail. The head of the pancreas lies nestled in the c-loop of the duodenum and the uncinate process is the portion of the head that extends posterior to the superior mesenteric vessels. The neck overlies the superior mesenteric vessels. The body begins at the level of the superior mesenteric vessels and the tail extends into the splenic hilum.

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The duct of Wirsung (main pancreatic duct) was first described in 1642 and the duct of Santorini (accessory duct) in 1734. These are the two main ducts that drain exocrine secretions into the duodenum. The duct of Wirsung drains most of the head, body, and tail of the pancreas, while the duct of Santorini drains the superior portion of the head. Most possess branching that connects these two major ducts. Vater described the common bile duct and ampulla in 1720. However, it was not until 1919 that a pathologist from Johns Hopkins by the name of Oddi described the common duct theory where the common bile duct and main pancreatic duct joined together to drain via the ampulla of Vater into the duodenum. Of note, the accessory duct empties directly into the duodenum (minor papilla) several centimeters proximal to the ampulla of Vater.

The arterial blood supply of the pancreas is both redundant and profound. The celiac axis provides the common hepatic artery which in turn supplies the gastroduodenal artery as the origin of the superior branches of the pancreaticoduodenal artery. The pancreaticoduodenal branches supply the head of the pancreas. In addition the splenic artery provides the dorsal pancreatic, the great pancreatic, and the caudal pancreatic arteries as it travels toward the splenic hilum. These branches supply the body and tail of the pancreas. The superior mesenteric artery supplies the inferior branches of the pancreaticoduodenal artery as well as the inferior pancreatic artery. The venous anatomy parallels the arterial supply. Specifically, the superior pancreaticoduodenal veins drain into the portal vein; meanwhile the inferior pancreaticoduodenal veins unite to form the Henle trunk just proximal to the superior mesenteric vein. The veins from the body and tail drain directly into the splenic vein.

Clinical Presentation

Hemosuccus pancreaticus (HP) is a rare cause of upper gastrointestinal hemorrhage seen predominantly in men (sex ratio 7:1) [4, 7, 10]. Frayssinet et al. reported the mean age of onset as 50 or 60 years when the site of pathology was either the pancreatic parenchyma or the pancreatic arterial supply [11]. Patients with HP typically present with a triad of abrupt epigastric pain and hyperamylasemia followed later by acute gastrointestinal hemorrhage [4, 7, 12]. The epigastric pain begins and radiates posteriorly due to increased intraductal pressure by the presence of blood in the main pancreatic duct [12, 13]. Within 48 h, gastrointestinal hemorrhage ensues as either hematemesis or melena. The onset of hemorrhage is usually associated with improvement of the abdominal pain. The amelioration of the abdominal pain is considered pathognomonic for HP. In addition, the intermittent nature of hemorrhage is specific for HP as a result of the cyclic balance between clot formation and dissolution within the pancreatic duct [1, 4, 6, 7, 12]. Patients are usually hemodynamically normal possibly secondary to clot formation when blood enters the pancreatic duct combined with the pressure buildup in this duct [4, 8, 12]. Other possible associated symptoms include jaundice, anemia, weight loss, and a palpable pulsatile, epigastric mass with a systolic thrill.

Diagnostic Studies

The diagnosis of HP is a clinical dilemma due to the nature of intermittent hemorrhage from a source that is difficult to detect by common diagnostic studies. A literature-based algorithm for diagnosis of HP can be found in Fig. 10.1. Upper gastrointestinal endoscopy can visualize active hemorrhage from the papilla in 30% of patients (Figs. 10.2 and 10.3) [1]. This confirms either HP or hemobilia, while blood seen in the second portion of the duodenum without obvious source provides evidence suggestive of these diagnoses. Endoscopy is also useful to exclude other causes of upper gastrointestinal hemorrhage. Endoscopic retrograde cholangiopancreatography (ERCP) can also help sort through HP as a cause of hemorrhage via visualizing pancreatic duct-filling defects that can represent the presence of blood clot or via opacification of pseudocysts and/or communicating arterial aneurysms that can identify the etiology of HP. Papilla sphincterotomy with ERCP can also facilitate clot retrieval and help ameliorate symptoms. Endoscopic ultrasound (EUS) is a growing technique to diagnose HP as it can help guide diagnosis, localize the lesion, and even allow for intervention [4, 14]. Abdominal CT angiography rarely provides direct evidence of HP. However, pseudocysts and aneurysms are sometimes visible which can lead to a diagnosis with correlating symptoms. It can also reveal findings of pancreatitis and on occasion a sentinel clot inside the pancreatic duct itself [4]. Technetium 99m-labeled red cell scintigraphy can identify a zone of upper GI hemorrhage when active hemorrhage is present; yet the intermittent nature of HP makes this test unlikely to yield any helpful data [12].

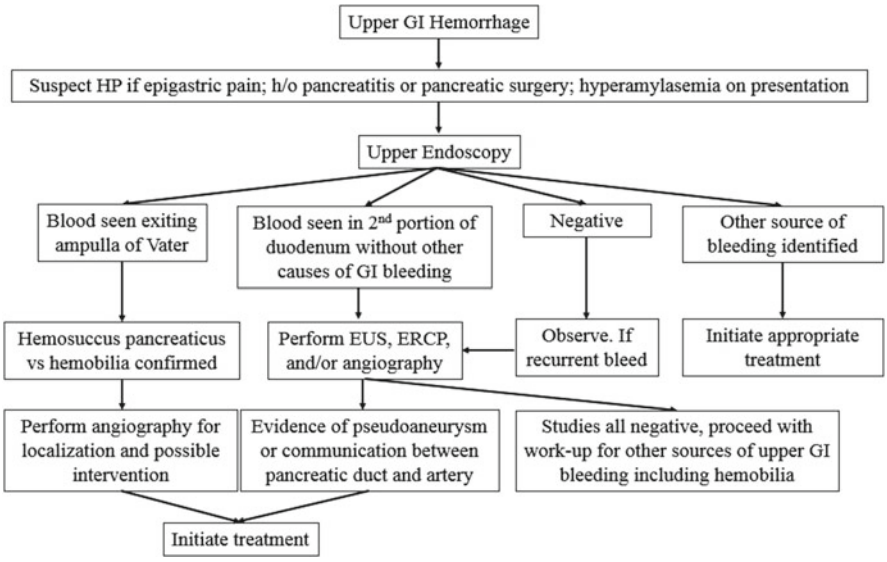

Fig. 10.1 Diagnostic algorithm for hemosuccus pancreaticus

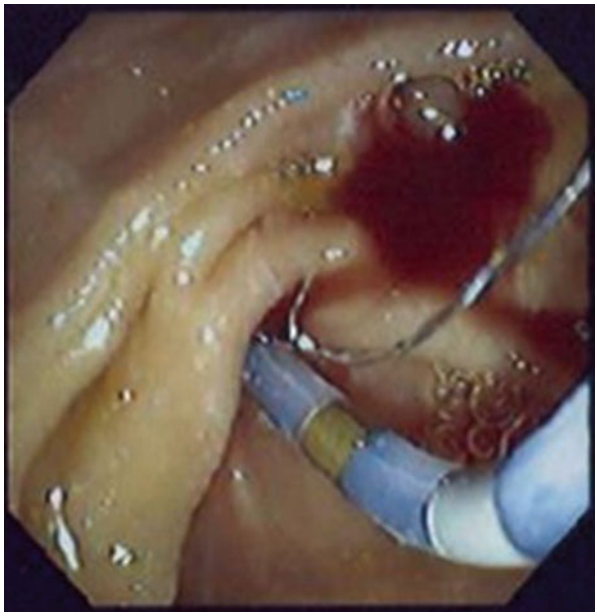

Fig. 10.2 Hemobilia visualized at the ampulla of Vater on endoscopic exam

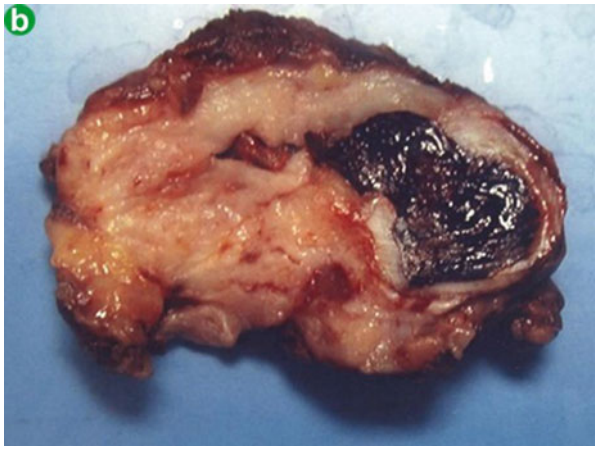

Fig. 10.3 Substantial hemobilia is more difficult to localize

Selective mesenteric arteriography provides the best opportunity for diagnosis of HP. Arteriography has a 93–96 % sensitivity in diagnosis of pseudoaneurysms of the common hepatic, gastroduodenal, or splenic arteries which is suggestive of HP in the setting of gastrointestinal hemorrhage [15, 16]. This modality is capable of providing definitive proof of HP by opacification of the main pancreatic duct [5]. However, identifying this direct vascular communication with the pancreatic duct is rare and given the intermittent nature of hemorrhage there can be difficulties localizing the exact source of the bleeding [17, 18]. There have been case reports of using provocative maneuvers such as locally instilling heparin and tissue plasminogen activator to stimulate bleeding to better localize the source of bleeding for eventual endovascular intervention but as of yet this is not a well-described technique [19].

Pathophysiology

There are various etiologies to HP. Pseudoaneurysms or primary aneurysms of the common hepatic, gastroduodenal, pancreaticoduodenal, splenic, left gastric, and superior mesenteric arteries or thrombosis of the splenic vein have been found to be causative of HP [4, 7, 20–23]. Acute or chronic pancreatitis is the most common cause of pseudoaneurysm formation [24]. Pseudoaneurysms occur due to exocrine enzyme autodigestion and erosion into peripancreatic vessels [20, 24]. The most common cause of hemorrhage is due to a rupture of the splenic artery (60–65 %) followed by gastroduodenal (20–25 %), pancreaticoduodenal (10–15 %), and hepatic artery (5–10 %) [7, 23, 25–27]. Ruptured pseudoaneurysms portend a poor prognosis with a reported mortality of 12–57 % [23]. Tumors including pancreatic adenocarcinoma, serous cystic neoplasms, microcystic adenoma, neuroendocrine tumor, and metastatic cancers have been reported to cause HP [4, 7, 28]. Other uncommon causes include pancreatic pancreaticolithiasis, trauma, iatrogenic causes (e.g., pancreatic surgery, ERCP, EUS), congenital abnormalities, infection (e.g., Brucellosis, syphilis), and thrombasthenia.

Management

Upon confirmation of HP, intervention generally consists of two treatment options: endovascular control of arterial hemorrhage versus operative intervention. An evidence-based treatment algorithm for HP can be found in Fig. 10.4. Hemodynamically stable patients should be treated with endovascular techniques for control of hemorrhage. Transcatheter balloon occlusion, coil embolization, and vascular stent deployment are several distinct methods for treatment. Balloon occlusion obstructs the artery prior to a planned surgery, limiting blood loss and shortening operative times, which has been found to be particularly useful in cases of massive hemorrhage or splenic vein thrombosis causing portal hypertension [1, 4]. Coil embolization induces thrombus formation within the diseased vessel inducing complete obliteration of the artery [29, 30]. Embolization of the celiac axis, common hepatic artery, and superior mesenteric artery is contraindicated. Stent deployment allows for exclusion of a pathologic segment of an artery with continued distal perfusion of vital organs. Overall success of endovascular techniques for treatment of HP is 79–100 % [7, 10, 15, 31]. There is a reported 17–37 % recurrence rate associated following endovascular therapy [15]. Given the excellent success rates with relatively low recurrence rates, many reports now highlight endovascular therapy as definitive therapy and an alternative to operative intervention [19, 32, 33].

Surgery is considered as first-line therapy for persistent shock despite initial resuscitation, uncontrolled hemorrhage, and rebleeding after embolization, or when endovascular techniques are not feasible or successful [4, 7]. Surgical management can include management of pancreatic parenchymal disease by drainage of pseudo-

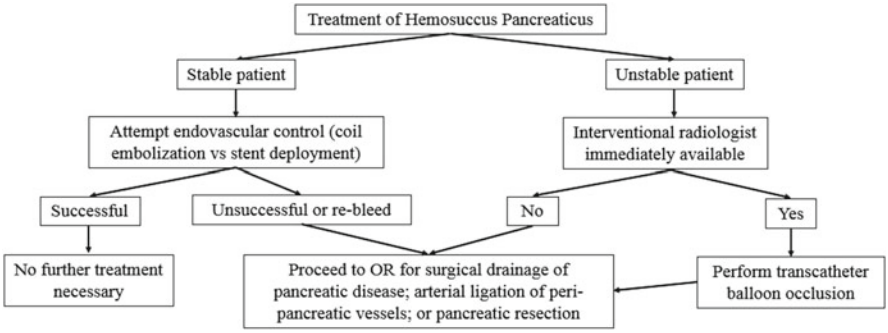

Fig. 10.4 Management algorithm for hemosuccus pancreaticus

cysts, arterial disease by ligation of bleeding arterial disease, or a combination of drainage procedure and arterial ligation. The risk of recurrent bleeding, infection, and necrosis is possible after these procedures [34, 35]. A more aggressive and preferable approach is pancreatic resection which would address both problems [36]. Disease involving the pancreaticoduodenal arteries requires ligation of arterial bleeding, resection of the head, and drainage of the distal pancreas. Splenic artery etiologies require distal pancreatectomy and splenectomy. Nevertheless, surgical management of HP is technically difficult with a 70–85 % success rate and associated with a 20–25 % mortality [23, 25, 27, 32].

Endoscopic ultrasound-guided sclerotherapy is another new investigational modality that can be useful for both diagnosis and treatment [14, 37]. This technique is rarely reported and thus it is difficult to extrapolate its overall efficacy at this time.

Conclusion

HP is a rare cause of upper gastrointestinal hemorrhage. Diagnosis is often delayed due to intermittent hemorrhage and the limitations of diagnostic studies to identify active hemorrhage. Most patients have previously suffered from acute or chronic pancreatitis; thus these patients should have a higher index of suspicion for HP as the cause of gastrointestinal hemorrhage. Endovascular techniques have increased the available therapeutic options with less invasive alternatives; these serve well as first-line therapies in hemodynamically stable patients. Endovascular techniques can also be used as a bridge to surgical treatment. Surgical drainage of pancreatic disease, arterial ligation of peripancreatic vessels, and pancreatic resection are all valid options should the need for surgery arise. Anatomic pancreatic resections have the most durable outcomes but are still associated with a significant mortality.

References

1. Peroux JL, Arput JP, Saint-Paul MC, Dumas R, Hastier P, Caroli FX, et al. Wirsungorrhagia complicating chronic pancreatitis associated with a neuroendocrine tumor of the pancreas. Gastroenterol Clin Biol. 1994;18(12):1142–5.
2. Suter M, Doenz F, Chapuis G, Gillet M, Sandblom P. Haemorrhage into the pancreatic duct (Hemosuccus pancreaticus): recognition and management. Eur J Surg. 1995;161(12):887–92.
3. Lower W, Farrell J. Aneurysm of the splenic artery: report of a case and review of the literature. Arch Surg. 1931;23:182–90.
4. Han B, Song ZF, Sun B. Hemosuccus pancreaticus: a rare cause of gastrointestinal bleeding. Hepatobiliary Pancreat Dis Int. 2012;11(5):479–88.
5. van Kemmel M. Massive digestive hemorrhage due to erosion of the gastroduodenal artery into a pseudocyst of the pancreas. Sem Hop. 1969;45(41):2564–6.
6. Kim SS, Roberts RR, Nagy KK, Joseph K, Bokhari F, An G, et al. Hemosuccus pancreaticus after penetrating trauma to the abdomen. J Trauma. 2000;49(5):948–50.
7. Koren M, Kinova S, Bedeova J, Javorka V, Kovacova E, Kekenak L. Hemosuccus pancreaticus. Bratisl Lek Listy. 2008;109(1):37–41.
8. Sandblom P. Gastrointestinal hemorrhage through the pancreatic duct. Ann Surg. 1970;171(1):61–6.
9. Longmire Jr WP, Rose III AS. *Hemoductal pancreatitis*. Surg Gynecol Obstet. 1973;136(2):246–50.
10. Etienne S, Pessaux P, Tuech JJ, Lada P, Lermite E, Brehant O, et al. Hemosuccus pancreaticus: a rare cause of gastrointestinal bleeding. Gastroenterol Clin Biol. 2005;29(3):237–42.
11. Frayssinet R, Sahel J, Sarles H. Wirsungorrhagia. Report of a case and review of the literature (author's transl). Gastroenterol Clin Biol. 1978;2(12):993–1000.
12. Sakorafas GH, Sarr MG, Farley DR, Que FG, Andrews JC, Farnell MB. Hemosuccus pancreaticus complicating chronic pancreatitis: an obscure cause of upper gastrointestinal bleeding. Langenbecks Arch Surg. 2000;385(2):124–8.
13. Rohner A. Severe digestive hemorrhage caused by rupture of an aneurysm of the splenic artery into the pancreatic ducts. Gastroenterologia. 1967;108(1):31–43.
14. Seicean A. Endoscopic ultrasound in the diagnosis and treatment of upper digestive bleeding: a useful tool. J Gastrointestin Liver Dis. 2013;22(4):465–9.
15. Boudghene F, L'Hermine C, Bigot JM. Arterial complications of pancreatitis: diagnostic and therapeutic aspects in 104 cases. J Vasc Interv Radiol. 1993;4(4):551–8.
16. Gambiez LP, Ernst OJ, Merlier OA, Porte HL, Chambon JP, Quandalle PA. Arterial embolization for bleeding pseudocysts complicating chronic pancreatitis. Arch Surg. 1997;132(9):1016–21.
17. Arnaud JP, Bergamaschi R, Serra-Maudet V, Casa C. Pancreatoduodenectomy for hemosuccus pancreaticus in silent chronic pancreatitis. Arch Surg. 1994;129(3):333–4.
18. El Hamel A, Parc R, Adda G, Bouteloup PY, Huguet C, Malafosse M. Bleeding pseudocysts and pseudoaneurysms in chronic pancreatitis. Br J Surg. 1991;78(9):1059–63.
19. Smith JC, Smith DC. Hemosuccus pancreaticus. J Vasc Interv Radiol. 2014;25(4):533.
20. Stanley JC, Frey CF, Miller TA, Sm L, Child CG. Major arterial hemorrhage: a complication of pancreatic pseudocysts and chronic pancreatitis. Arch Surg. 1976;111(4):435–40.
21. Rao RC, Kumar A, Berry M. Pseudoaneurysm of anomalous right hepatic artery as a cause for hemosuccus pancreatitis. Gastrointest Radiol. 1987;12(4):313–4.
22. Fernandez-Cruz L, Pera M, Vilella A, Llovera JM, Navasa M, Teres J. Hemosuccus pancreaticus from a pseudoaneurysm of the hepatic artery proper in a patient with a pancreatic pseudocyst. Hepatogastroenterology. 1992;39(2):149–51.
23. Bender JS, Bouwman DL, Levison MA, Weaver DW. Pseudocysts and pseudoaneurysms: surgical strategy. Pancreas. 1995;10(2):143–7.
24. Maus TP. Pseudoaneurysm hemorrhage as a complication of pancreatitis. Mayo Clin Proc. 1993;68(9):895–6.

25. Heath DI, Reid AW, Murray WR. Bleeding pseudocysts and pseudoaneurysms in chronic pancreatitis. Br J Surg. 1992;79(3):281.
26. Smith RE, Fontanez-Garcia D, Plavsic BM. Gastrointestinal case of the day. Pseudoaneurysm of the left gastric artery as a complication of acute pancreatitis. Radiographics. 1999;19(5):1390–2.
27. Negi SS, Sachdev AK, Bhojwani R, Singh S, Kumar N. Experience of surgical management of pseudo-aneurysms of branches of the coeliac axis in a North Indian Hospital. Trop Gastroenterol. 2002;23(2):97–100.
28. Ashindoitiang JA, Anunobi CC, Atoyebi OA. Haemosuccus pancreaticus as a rare initial manifestation of pancreatic carcinoma. Nig Q J Hosp Med. 2008;18(4):191–3.
29. Quandalle P, Gambiez L, Brami F, Ghisbain H, Andre JM, Zahredine A, et al. Gastrointestinal hemorrhage caused by rupture of an aneurysm of visceral arteries. Presentation of 4 cases. Chirurgie. 1998;123(2):139–47.
30. Akpinar H, Dicle O, Ellidokuz E, Okan A, Goktay Y, Tankurt E, et al. Hemosuccus pancreaticus treated by transvascular selective arterial embolization. Endoscopy. 1999;31(2):213–4.
31. Salam TA, Lumsden AB, Martin LG, Smith RB. Nonoperative management of visceral aneurysms and pseudoaneurysms. Am J Surg. 1992;164(3):215–9.
32. Waltman AC, Luers PR, Athanasoulis CA, Warshaw AL. Massive arterial hemorrhage in patients with pancreatitis. Complementary roles of surgery and transcatheter occlusive techniques. Arch Surg. 1986;121(4):439–43.
33. Adams DB, Zellner JL, Anderson MC. Arterial hemorrhage complicating pancreatic pseudocysts: role of angiography. J Surg Res. 1993;54(2):150–6.
34. Knight RW, Kadir S, White Jr RI. Embolization of bleeding transverse pancreatic artery aneurysms. Cardiovasc Intervent Radiol. 1982;5(1):37–9.
35. Morse JM, Reddy KR, Thomas E. Hemosuccus pancreaticus: a cause for obscure gastrointestinal bleeding—diagnosis by endoscopy and successful management by total parenteral nutrition. Am J Gastroenterol. 1983;78(9):572–4.
36. Clay RP, Farnell MB, Lancaster JR, Weiland LH, Gostout CJ. Hemosuccus pancreaticus. An unusual cause of upper gastrointestinal bleeding. Ann Surg. 1985;202(1):75–9.
37. Levy MJ, Wong Kee Song LM, Farnell MB, Misra S, Sarr MG, Gostout CJ. Endoscopic ultrasound (EUS)-guided angiotherapy of refractory gastrointestinal bleeding. Am J Gastroenterol. 2008;103(2):352–9.

Part II
Lower GI Bleeding

Chapter 11
Urgent Workup of Lower Gastrointestinal Bleeding

Megan Turner and Leila Mureebe

Introduction

Melena and bright red blood per rectum (hematochezia) are common presentations of gastrointestinal bleeding. Upper gastrointestinal bleeding (UGIB) is the most common etiology of a lower gastrointestinal bleed (LGIB), ultimately encompassing 80 % of blood per rectum (BPR). The remaining 20 % originate distal to the ligament of Treitz [1]. The vast majority of these situations arise in the colon; a smaller proportion from the anus and rectum; a significant minority originate in the small bowel [1, 2]. As blood moves through the bowel, hematin becomes oxidized and darkens, mixing with intestinal contents, and emerging as melena. The appearance of bright red blood per rectum can be attributable either to fast transit time as seen brisk bleeding, or a distal source. The annual incidence of LGIB is approximately 20 cases per 100,000 per year in Western countries [3] with the overall mortality rate reported as 3 %, similar to UGIB [1, 3]. Prognosis is favorable given the fact that most LGIB spontaneously cease [2], however negative prognostic factors include advanced age, high transfusion requirements, comorbid factors, and hospitalization at the onset of the bleeding episode [1, 4–6]. Velayos et al. described an initial hematocrit of less than 35 %, abnormal vital signs, and gross blood on rectal exam as three independent risk factors for poor outcome [1]. As in UGIB, approximately 80 % of LGIB spontaneously cease. this chapter addresses the urgent management of patients who require inpatient evaluation and intervention.

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Table 11.1 Common etiologies of LGIB by age (Edelman and Sugawa [1]; Elta [9]; Leung and Wong [2]; Zuckerman and Prakash [3])

Infants/toddlers	Children/teenagers	Adults	Older adults
Milk allergy	Anal fissures	Diverticulosis	Angiodysplasia
Necrotizing enterocolitis	Polyps	Upper GI source	Diverticulosis
Volvulus	Inflammatory bowel disease	Neoplasm/polyps	Neoplasm/polyps
Anal fissure	Intussusception	Inflammatory bowel disease	Upper GI source
Intussusception	Infectious colitis	Anorectal disease	Anorectal disease
Hirschsprung disease	Meckel diverticulum	Iatrogenic (radiation proctitis, post-polypectomy)	Iatrogenic (radiation proctitis, post-polypectomy)
Meckel diverticulum	Angiodysplasia	Angiodysplasia	Mesenteric ischemia
	Henoch–Schoenlein purpura		Inflammatory bowel disease
	Hemolytic uremic syndrome		

Etiology

The etiology of LGIB varies widely by age, and the epidemiology of the disease must be considered in arriving at the correct diagnosis (Table 11.1). The most common causes of LGIB in adults are colonic diverticulosis [2, 3, 5], benign anorectal disease, inflammatory bowel disease, malignancy, and angiodysplasia [5]. Rarer causes include infection, ischemia, iatrogenic, and aortoenteric fistulous disease. In as many as 10–35 % of cases a source of bleeding is never identified [2, 5, 6].

Diverticular Disease

Diverticular disease of the colon is the most common cause of LGIB in adults [1, 2]. Diverticula are outpouchings of colonic mucosa through the muscularis and serosa, most commonly found on the mesenteric side of the colon at the site of penetrating blood vessels, vasa recta, where the colonic wall is weakest. A propensity towards developing diverticular disease include advancing age, with estimates of greater than 50 % of adults over the age of 60 in the United States having diverticular disease, with up to 17 % of those affected experience bleeding [6]. A Western diet, low in fiber and high in saturated fats, is associated with development of diverticula. Thirty percent of LGIB are attributed to diverticula with bleeding requiring urgent evaluation and intervention as described later in the chapter [2, 7].

Benign Anorectal Disease

Hemorrhoids are a common problem with greater than 30 % of people over the age of 50 having hemorrhoids on exam, regardless of symptoms. Bleeding can range in severity from a minor inconvenience to a source of massive hemorrhage. 20 % of instances of BPR requiring intervention are attributable to hemorrhoidal bleeding [2, 8]. Internal hemorrhoids are painless and intermittent bleeding is often the only symptom. Bleeding can also be a symptom of external hemorrhoids; however pain and itching are predominant symptoms. In the evaluation of blood per rectum the identification of hemorrhoids should not provide diagnostic satisfaction as hemorrhoids remain common in the presence of additional pathology, and a thorough evaluation of the remainder of the colon should be undertaken. Anal fissures can also present with blood per rectum; however this is predominantly scant bleeding associated with pain on defecation.

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD), inclusive of ulcerative colitis and Crohn's disease, is associated with LGIB, although bleeding is a rare complication of these diseases. Ulcerative colitis is isolated to the colon and can present with profuse bleeding. Crohn's disease affects the mucosa along the entire gastrointestinal tract, and while bleeding is less common overall, it presents more severely than bleeding from ulcerative colitis. Patients with LGIB from inflammatory bowel disease is rare, with approximately 2 % with bleeding requiring intervention [9].

Malignancy

Neoplasm must always be part of the differential diagnosis when considering a source of blood loss per rectum, as cancers may bleed from surface erosions or ulcerations. This bleeding is usually characterized as scant and low volume located predominantly within the colon or rectum. However of all patients requiring intervention for LGIB, 12 % percent are associated with a neoplastic lesion [2].

Arteriovenous Malformation

With aging, the presence of angiodysplasia, or arteriovenous malformations (AVM), increases, specifically within the colon [6]. AVM are vascular anomalies of the gastrointestinal tract characterized by dilated and tortuous submucosal vessels. AVM can be congenital, but more often angiodysplasias develop over time from chronic venous obstruction, chronic mucosal ischemia, or as a complication of cardiopulmonary or vascular comorbidities [10].

Rarer Causes

A broad differential for LGIB includes infectious causes, ischemia, and iatrogenic causes. Infectious colitis can present as blood per rectum, most commonly seen with *Escherichia coli 0157H7*, *salmonella*, *shigella* and *Clostridium difficile* bacterial infections and occasionally cytomegalovirus. These patients require urgent intervention.

Iatrogenic LGIB are most common after procedures or clinical irradiation. Significant bleeding following an endoscopic polypectomy can occur at a median of five days, with overall rates of post-polypectomy bleeding varying from 0.3 to 6% [11]. Although LGIB due to radiation may also present as LGIB, this incidence is decreasing due to improved radiation precision in the management of pelvic cancers. Radiation proctitis affects approximately 6% of patients treated with brachytherapy for prostate cancer [12]. These patients are typically treated with topical therapies and do not require endoscopic therapies, although a small subset ultimately require operative intervention [13].

Mesenteric ischemia and ischemic colitis are infrequent causes of LGIB. In mesenteric ischemia, blood per rectum is a late and ominous finding. With ischemic colitis, bleeding is typically scant and hemodynamically insignificant. These events can be chronic, acute, or iatrogenic as determined by the history and physical exam. In critically ill patients, acute mesenteric ischemia can be a result of shock and a low-flow state to the intestine. Evaluation and management of mesenteric ischemia follows algorithms for management of the acute abdomen, and for nontoxic ischemic colitis includes nonurgent colonoscopy, rarely requiring urgent endoscopic intervention, with treatment directed at the underlying cause.

Resuscitation and Stabilization for Massive LGIB

A massive, acute LGIB is a life-threatening emergency defined by a transfusion requirement of more than four units of blood in a 24-h period with hemodynamic instability. Patients with massive hemorrhage present with shock, hemodynamic instability, precipitously dropping hemoglobin levels, and immediate transfusion requirements [1]. Hemorrhage that does not spontaneously resolve in less than 3 days or that recurs after initial stabilization are also considered significant LGIB. Fortunately, most cases of are mild to moderate.

The critical care principles for patients in hemorrhagic shock provide an evaluation and treatment foundation for patients with massive LGIB. Assessment and securing of the airway, confirmation of breathing and circulation are paramount, followed by establishing large-bore peripheral intravenous access, monitoring of hemodynamics, and release of emergency blood products. A nasogastric tube is placed and the stomach lavaged [14]. If bloody or coffee ground material is aspirated, the evaluation and intervention algorithm for UGIB is initiated. The aspira-

tion of bilious material confirms bleeding distal to the ligament of Treitz (LGIB); aspiration of clear fluid favors a distal source, but does not definitively rule out UGIB and a combination of approaches may be more appropriate in these patients.

As resuscitation is initiated, important information to discern with a detailed history and physical examination includes a history of prior GI bleeds, the use of anticoagulants or nonsteroidal anti-inflammatory drugs, a history of thrombotic or thrombophilic disorders, and prior interventions and operations. Essential laboratory investigations include a complete blood count, arterial blood gas, electrolytes, coagulation screening, and type and cross-match in anticipation of blood product transfusion. Physical exam should include cardiovascular pulmonary exam, abdominal exam, digital rectal exam, and anoscopy or rigid proctoscopy.

Diagnostic Modalities

Once the diagnosis of LGIB is suspected, three urgent diagnostic modalities are available for further evaluation, although controversy still exists regarding the ideal testing algorithm (Fig. 11.1). The algorithm for colonoscopy, arteriography, and radionucleotide scintigraphy is largely contingent on the rate of bleeding, but other considerations include local resources and availability. For exsanguinating hemorrhage, arteriography is most appropriate, for profuse but less severe hemorrhage urgent colonoscopy, and for slow or intermittent hemorrhage radionucleotide scintigraphy followed by colonoscopy. Operative interventions are outlined based on the details obtained with each evaluation.

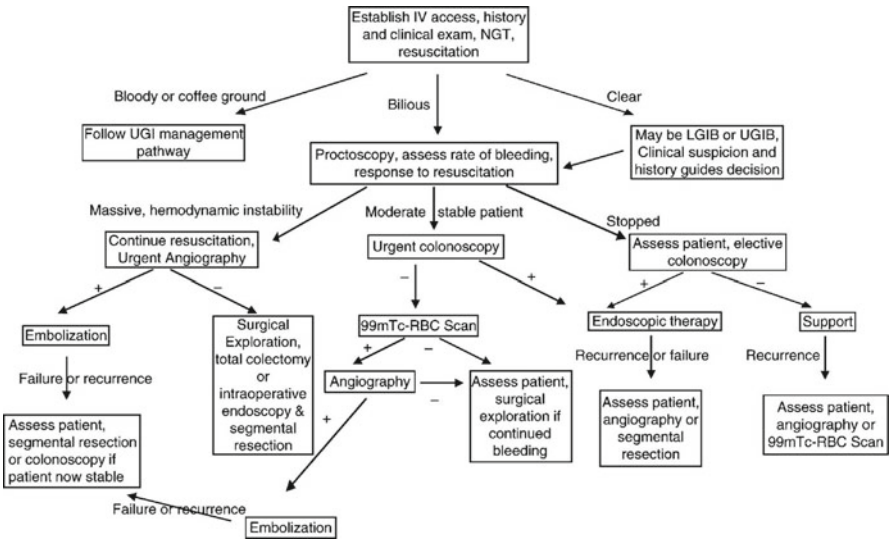

Fig. 11.1 Suggested workup and treatment algorithm for lower gastrointestinal bleeding

Urgent Colonoscopy

In patients where profuse bleeding does not cease, or in patients where rebleeding recurs early, urgent colonoscopy after a rapid bowel preparation is the appropriate diagnostic modality. Endoscopic stigmata of bleeding include visualization of active bleeding, visible vessels, and adherent clot [7]. Early colonoscopy, within 12–48 h of admission, has a higher diagnostic yield and lower complication rate than arteriography, results in shorter length of stay, and avoids further surgical intervention in those patients who respond appropriately to initial resuscitation efforts [6, 7, 15]. This is contrasted to the historical opinion that colonoscopy is of little yield in a briskly bleeding patient with an unprepared colon because of inadequate visualization.

Colonoscopy is both a diagnostic and a therapeutic tool. Bowel preparation should be given via nasogastric tube prior to endoscopy for improved visualization of the lesion. Colonoscopy provides direct visualization of the colonic mucosa and the capability for simultaneous treatment of bleeding via endoscopic clipping, epinephrine injection, thermal therapy, and other hemostatic techniques are in development. However, it is uncommon to identify a bleeding vessel or stigmata of recent bleeding, such as adherent clot. More often, there is a presumed area of concern that can be intervened upon (Fig. 11.2). In cases where endoscopic intervention is not effective in stopping the hemorrhage, the area of bleeding can be marked or tattooed in planning for surgical intervention and this should be performed at the area of concern in the rare event of recurrent hemorrhage. The American Society for Gastrointestinal Endoscopy guidelines for LGIB includes early colonoscopy [16].

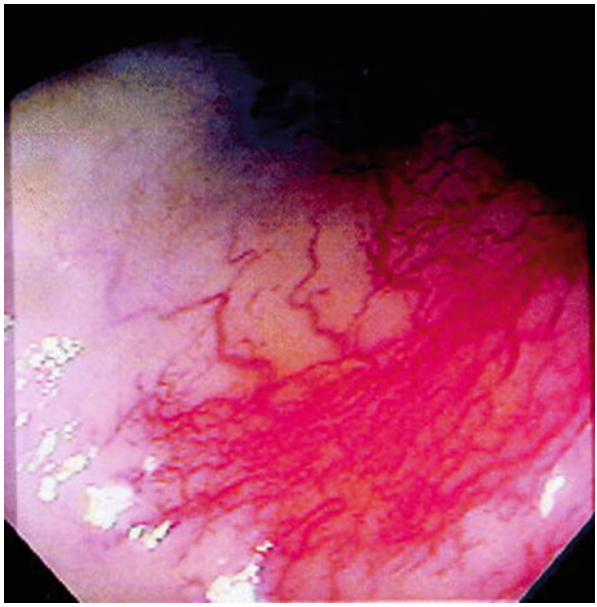

Fig. 11.2 Arteriovenous malformation, no signs of active or recent stigmata of bleeding (courtesy of John Migaly, M.D., Duke University Medical Center, Durham, NC)

While commonly performed, colonoscopy is an invasive study that is not without risk. Perforation occurs in 1 in 1000 colonoscopies and can require hospital admission and surgical resection. The utility of colonoscopy is operator dependent, and urgently recruiting a skilled endoscopist may be difficult. If colonoscopy reveals a bleeding mass, biopsies should be taken of the mass for pathologic diagnosis, and a full oncologic workup is indicated. Further disadvantages to colonoscopy include poor diagnostic yield in brisk bleeds due to poor visualization and inability to detect small bowel sources. All patients with LGIB that have resolved spontaneously should have a semi-elective colonoscopy after thorough preparation of the bowel to identify potential diverticula, AVMs, and neoplasm. In massive ongoing bleeding that obscures diagnostics with colonoscopy, arteriography, and prompt surgical consultation are appropriate.

Urgent Arteriography

Arteriography for rapid LGIB is both diagnostic and potentially therapeutic; it is useful in the urgent setting and in brisk to hemorrhagic bleeding. In hemodynamically unstable patients who have high transfusion requirements of greater than four units of blood, urgent arteriography is preferred over colonoscopy [16]. For a bleeding vessel to be detectible during a normal, non-provocative angiography, it must bleed at a rate of at least 0.5 mL/min [14]. Arteriography must not impede resuscitation efforts.

Once a bleeding vessel or AVM is identified through angiography, there are several options for treatment (Fig. 11.3). Traditionally, embolization was used in UGIB sources, but avoided in LGIB due to of the risk of bowel infarction. However, improved technology has decreased this risk, embolization has proven to be a safe and effective mechanism for management of LGIB. It currently is the preferred therapy compared to the historic vasopressin infusion [17] (Fig. 11.4) which is effective in stopping a LGIB, but requires several days of femoral artery catheter placement and the potential complications that arise from this. A second appropriate use of arteriography is in a patient whom has undergone colonoscopy localizing the area of hemorrhage, but experiences recurrent bleeding despite endoscopic treatment. A second colonoscopy with repeat endoscopic treatment is within the standard of care, as is arteriography prior to proceeding to surgical intervention for these difficult cases [16].

Arteriography is an invasive procedure with risks including contrast-induced nephropathy and injury during arterial access. As in colonoscopy, the success of both diagnosis and therapy can be operator dependent. In cases where endoscopic therapy is not effective in controlling the bleeding, angiography provides a more detailed location of the hemorrhage for surgical intervention. Additionally, angiography can detect rare bleeding sources in the small bowel. However, angiography is not as effective as direct visualization in differentiating the cause of bleeding (Fig. 11.5).

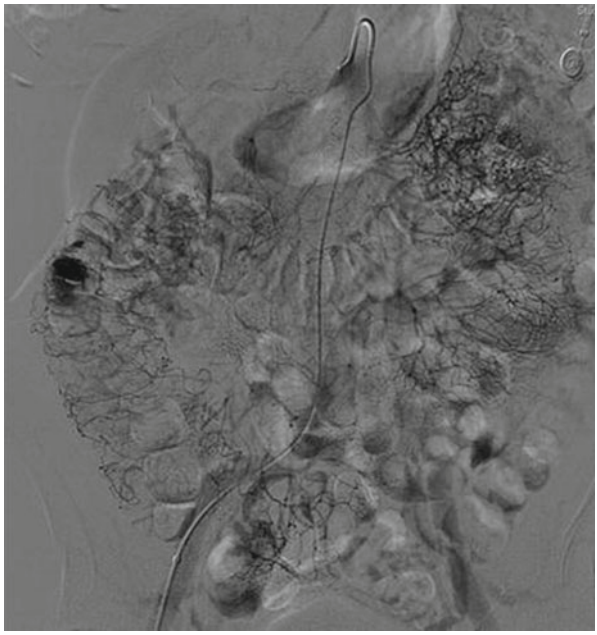

Fig. 11.3 Superior mesenteric angiography positive for right colonic bleeding

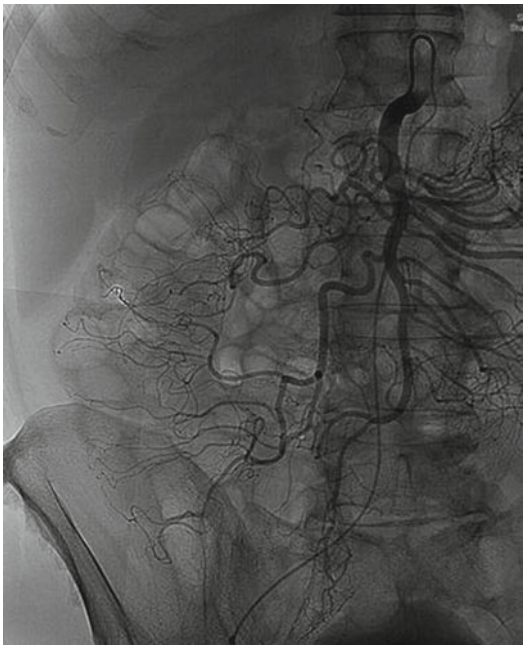

Fig. 11.4 Superior mesenteric angiography for the same patient in Fig. 11.3 after embolization with coils

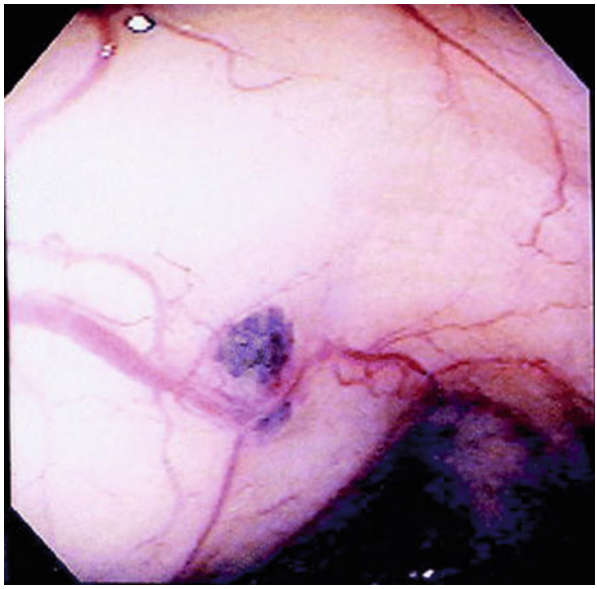

Fig. 11.5 Venous ectasia (courtesy of John Migaly, M.D., Duke University Medical Center, Durham, NC)

Slower bleeds or bleeds that have stopped, even temporarily, will not be visualized on an angiogram. There are provocative maneuvers that can be performed during the examination to identify occult bleeding, but a tagged red blood cell scan can be of utility in these scenarios.

Urgent Tagged Red Blood Cell Scan

Radionucleotide scintigraphy is an appropriate diagnostic modality for localizing slow or intermittent hemorrhage [14, 16]. Technetium 99m-labeled red blood cell scintigraphy is the most widely available method. This test requires radiolabeling the patients own blood ex vivo and infusing it, or using an in vivo labeling kit. The labeled red blood cells are resident for roughly 24 h, and repeat scanning during intermittent bleeding is possible. Injection does not have to occur during a period of active hemorrhage. Delayed images are taken at 1-h intervals and can detect blood pooling from occult locations not initially detected. Radionucleotide scintigraphy is relatively non-invasive. It can localize lower volume and intermittent bleeding as has a limited risk profile compared to angiography and colonoscopy There are several limitations to these studies as well. it is rarely sufficient for definitive diagnosis, and has no capacity for intervention requiring adjunctive subsequent colonoscopy or angiography

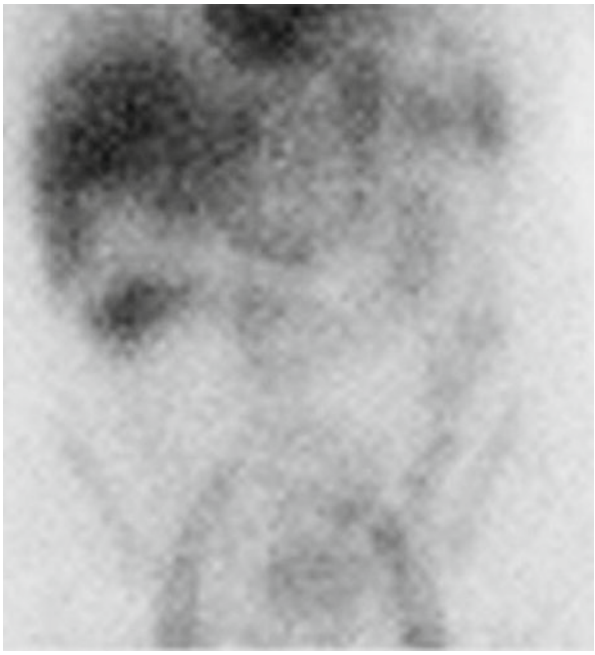

Fig. 11.6 Technetium 99m-labeled erythrocyte scintigraphy positive for bleeding in the area of the hepatic flexure

Technetium 99m-labeled erythrocyte scintigraphy can detect hemorrhage at rates as low as 0.1 mL/min, thus can be more sensitive than angiography in slower bleeds. False-positive studies may lead to inappropriate surgery, and false negatives lead to diagnostic delays [5, 18] (Fig. 11.6). For most surgeons, an operation is rarely planned solely on the results of 99mTc-labeled erythrocyte scintigraphy [14]. In light of low resolution, it is generally not recommended that segmental resection be performed solely on the basis of scintigraphy results. Its use is limited in the urgent setting and should be implemented based on clinical judgment for an individual patient who may not be a suitable candidate for either colonoscopy or angiography.

Summary

Blood per rectum is a common patient presentation with a diverse etiology and broad spectrum of urgency. While most bleeding ceases spontaneously and does not recur, an understanding of critical care principles for stabilization of the hemorrhaging patient, diagnostic algorithms, and potential interventions are important concepts for all providers. Ensuring follow-up is paramount for the medical and surgical management of underlying pathology leading to the bleeding episode.

References

1. Velayos FS, Williamson A, Sousa KH, Lung E, Bostrom A, Weber EJ, Ostroff JW, Terdiman JP. Early predictors of severe lower gastrointestinal bleeding and adverse outcomes: a prospective study. Clin Gastroenterol Hepatol. 2004;2(6):485–90.
2. Gayer C, Chino A, Lucas C, Tokioka S, Yamasaki T, Edelman DA, Sugawa C. Acute lower gastrointestinal bleeding in 1,112 patients admitted to an urban emergency medical center. Surgery. 2009;146(4):600–6. discussion 606–7.
3. Longstreth GF. Epidemiology and outcome of patients hospitalized with acute lower gastrointestinal hemorrhage: a population-based study. Am J Gastroenterol. 1997;92(3):419–24.
4. Kollef MH, O'Brien JD, Zuckerman GR, Shannon W. BLEED: a classification tool to predict outcomes in patients with acute and lower gastrointestinal hemorrhage. Crit Care Med. 1997;25(7):1125–32.
5. Al Qahtani AR, Satin R, Stern J, Gordon PH. Investigative modalities for massive lower gastrointestinal bleeding. World J Surg. 2002;26(5):620–5.
6. Edelman DA, Sugawa C. Lower gastrointestinal bleeding: a review. Surg Endosc. 2007;21(4):514–20.
7. Pilichos C, Bobotis E. Role of endoscopy in the management of acute diverticular bleeding. World J Gastroenterol. 2008;14(13):1981–3.
8. Riss S, Weiser FA, Schwameis K, Riss T, Mittlböck M, Steiner G, Sift A. The prevalence of hemorrhoids in adults. Int J Colorectal Dis. 2012;27(2):215–20.
9. Pardi DS, Loftus Jr EV, Tremaine WJ, Sandborn WJ, Alexander GL, Balm RK, Gostout CJ. Acute major gastrointestinal hemorrhage in inflammatory bowel disease. Gastrointest Endosc. 1999;49(2):153–7.
10. Feinman M, Haut ER. Lower gastrointestinal bleeding. Surg Clin North Am. 2014;94(1):55–63.
11. Sorbi D, Norton I, Conio M, Balm R, Zinsmeister A, Gostout CJ. Postpolypectomy lower GI bleeding: descriptive analysis. Gastrointest Endosc. 2000;51(6):690–6.
12. Price JG, Stone NN, Stock RG. Predictive factors and management of rectal bleeding side effects following prostate cancer brachytherapy. Int J Radiat Oncol Biol Phys. 2013;86(5):842–7.
13. Sarin A, Safar B. Management of radiation proctitis. Gastroenterol Clin North Am. 2013;42(4):913–25.
14. Strate LL. Lower GI bleeding: epidemiology and diagnosis. Gastroenterol Clin North Am. 2005;34(4):643–64.
15. Rockey DC. Lower gastrointestinal bleeding. Gastroenterology. 2006;130(1):165–71.
16. National Guideline Clearinghouse. ACR Appropriateness Criteria® radiologic management of lower gastrointestinal tract bleeding. http://www.guideline.gov/content.aspx?id=49074&search=lower+gi+bleeding. Accessed 19 Dec 2015.
17. Darcy M. Treatment of lower gastrointestinal bleeding: vasopressin infusion versus embolization. J Vasc Interv Radiol. 2003;14(5):535–43.
18. Howarth DM. The role of nuclear medicine in the detection of acute gastrointestinal bleeding. Semin Nucl Med. 2006;36(2):133–46.

Chapter 12
Bleeding Hemorrhoids

Zhifei Sun, Mohamed A. Adam, and Julie K.M. Thacker

Introduction

Hemorrhoid disease is a prevalent outpatient diagnosis with self-reported incidence of 4.4%, and accounts for more than three million ambulatory care visits in the USA each year [1]. Both sexes report peak incidence from age 45–65, with Caucasians being affected more frequently than African Americans [2]. While overall morbidity of symptomatic hemorrhoid disease is low, it has significant impact on a patient's quality of life. Furthermore, due to overlapping symptoms with neoplastic disease, recognition and understanding of hemorrhoid disease is important for primary care physicians, gastroenterologists, general surgeons, and colorectal surgeons.

Anatomically, hemorrhoids are clusters of vascular, fibromuscular tissues that lie along the anal canal in three columns—left lateral, right anterior, and right posterior positions [3]. Hemorrhoids are present universally in healthy individuals as vascular anastomoses between the superior rectal artery and the superior,

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middle, and inferior rectal veins. Nevertheless, the term “hemorrhoid” commonly refers to the pathologic process of symptomatic hemorrhoid disease, characterized by pain, pruritus, or bleeding.

Classification of a symptomatic hemorrhoid corresponds to its position relative to the dentate line. External hemorrhoids are located below the dentate line and derived from ectoderm. They are covered with squamous epithelium and innervated by pain-sensitive somatic nerves. In contrast, internal hemorrhoids lie above the dentate line and develop from endoderm. They are covered by columnar epithelium, innervated by visceral nerve fibers and therefore cannot cause pain. Vascular outflows of internal hemorrhoids include the middle and superior rectal veins, which subsequently drain into the internal iliac vessels. While external hemorrhoids tend cause pain, internal hemorrhoids are associated with intermittent rectal bleeding, and can be accompanied by significant patient anxiety. This review focuses on diagnosis and management of bleeding internal hemorrhoids.

Presentation and Diagnosis

For internal hemorrhoids, anorectal bleeding is the most commonly reported symptom. Bleeding from internal hemorrhoids is usually associated with defecation, and is almost always painless. Blood loss is typically bright red and coats the stool at the end of defection. Prolapsed internal hemorrhoids may be associated with mild fecal incontinence, mucus discharge, sensation of fullness, and irritation of perianal skin. Pain is considerably less frequent with internal hemorrhoids than with external hemorrhoids, but can occur in the setting of strangulated internal hemorrhoids that acquire gangrenous changes due to tissue ischemia.

Because of the more sinister etiologies of rectal bleeding and pain, a thorough history and physical exam, and possible colonoscopy are necessary before settling on the diagnosis of hemorrhoids. If anorectal bleeding is a presenting symptom of presumed or examined hemorrhoids, it should not be confidently attributed to hemorrhoids until the entire colon has been meticulously surveyed for neoplastic or inflammatory disease. A patient’s perineum should be inspected in a prone-jackknife or left lateral position that allows for adequate exposure and provider comfort. External inspection will reveal any thrombosed or prolapsing hemorrhoid. Skin tags may be signs of previous hemorrhoids as well as fissure disease. Digital exam can exclude distal rectal mass and anorectal abscess or fistula. Importantly, evaluation of sphincter integrity during the digital exam to establish baseline function is essential, especially in patients who report preoperative incontinence due to the risk of exacerbating function as a result of surgical intervention. Lastly, anoscopy and rigid or flexible proctosigmoidoscopy can be performed in the clinic setting to identify to rule out distal rectal masses.

Based on the degree of prolapse, internal hemorrhoids are clinically stratified into four levels of severity. First-degree (grade I) internal hemorrhoids are characterized by bulging vasculature but do not prolapse out of the anal canal, and respond

to conservative measures in most cases. Second-degree (grade II) hemorrhoids prolapse outside of the anal canal during defecation, but reduce spontaneously; they also can be mostly controlled with conservative methods. While third-degree (grade III) hemorrhoids require manual reduction to reduced prolapsed tissue, fourth-degree (grade IV) hemorrhoids are irreducible even with manipulation. Both third- and fourth-degree internal hemorrhoids typically will require active intervention for resolution of symptoms [4].

Management of Bleeding Hemorrhoids

In cases of acute hemorrhoidal hemorrhage, several options are available. First, application of direct pressure using Gelfoam packing may be attempted. Alternatively, a large-bore Foley catheter can be inserted into the rectum, inflating the balloon with at least 25 mL of fluid and retracting the balloon tight against the anal ring. Epinephrine can also be injected at the bleeding site. Finally, suture ligation or operative intervention under anesthesia may be necessary if less-invasive methods fail.

Once acute bleeding has been stabilized locally, laboratory studies, including hemoglobin, platelet count, and coagulation studies, should be ordered. Adjunctive management should be aimed to maintain patient stability with volume resuscitation and correcting any coagulopathies, if exists.

For a patient whose acute hemorrhoidal bleeding has resolved or has presented with intermittent bleeding, management includes therapy choices to minimize or to eliminate the risk of recurrent symptoms. Specific choices of treatments are guided by patients' age, severity of symptoms, and comorbidities. A summary of management strategies is shown in Table 12.1.

Table 12.1 Summary of management options for bleeding internal hemorrhoids

Treatment	Grade I	Grade II	Grade III	Grade IV
Dietary and lifestyle modification	X	X	X	X
Office procedures				
Rubber band ligation	X	X	X	
Sclerotherapy	X	X		
Infrared coagulation	X	X		
Operating room procedures				
Hemorrhoidectomy			X	X
Stapled hemorrhoidopexy			X	X
Doppler-guided hemorrhoid artery ligation		X	X	

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Conservative Medical Treatments

Lifestyle and dietary modifications are the basis of conservative medical treatment of hemorrhoid disease. Specifically, lifestyle modifications including increasing oral fluid intake, reducing fat consumptions, avoiding straining, and regular exercise are beneficial to all patients with hemorrhoid disease, regardless of severity. The major diet modification recommendation is an increase in fiber intake, which decreases the shearing action of passing hard stool. In a 2006 meta-analysis of 7 randomized trials comparing fiber to non-fiber interventions for hemorrhoids, fiber supplementation (7–20 g per day) reduced risk of persisting symptoms and bleeding by 50 %. Follow-up demonstrated persistent improvement at 6 weeks and 3 months. However, fiber intake did not significant ameliorate symptoms of prolapse, pain, and itching [5].

For non-bleeding symptom management, topical treatments containing various local anesthetic, corticosteroid, or anti-inflammatory drugs are available, but may be associated with side effects. For example, 0.2 % glyceryl trinitrate is effective in relieving first- and second-degree hemorrhoids with high resting anal canal pressures, but can cause headaches in 43 % of patients [6]. Patients also commonly self-medicate with Preparation-H (Pfizer Incorporated, Kings Mountain, USA), a formulation of phenylephrine, petroleum, mineral oil, and shark liver oil, which has vasoconstriction and barrier protectant properties. Preparation-H provides temporary relief from acute symptoms of hemorrhoids such as bleeding and pain on defecation, but long-term effects are not well studied [7]. Topic corticosteroids in cream or ointment forms are often prescribed, but their efficacy remains unproven.

Overall, 80 % of first- and second-degree hemorrhoids respond to conservative measures alone [8]. However, when medical interventions fail or if the extent of disease is severe, more invasive procedures should be considered to prevent symptom recurrence. Although there is no consensus on its optimal treatment, rubber band ligation, sclerotherapy, and infrared coagulation are the most frequently used procedures for internal hemorrhoids. In general, the goals of each procedure are to decrease vascularity, reduce redundant tissue, and increase hemorrhoidal rectal wall fixation in order to minimize recurrent prolapse.

Rubber Band Ligation

Rubber band ligation is the most often performed procedure in the office and is indicated for grade II–III internal hemorrhoids [9]. Contraindications of utilizing this approach include large external tags or external hemorrhoids and patients with coagulopathies or on chronic anticoagulation, as there is a risk of delayed hemorrhage. Additionally, in immunocompromised patients, banding carries an increased risk of pelvic sepsis [10]. Performing rubber band ligation is quick and does not

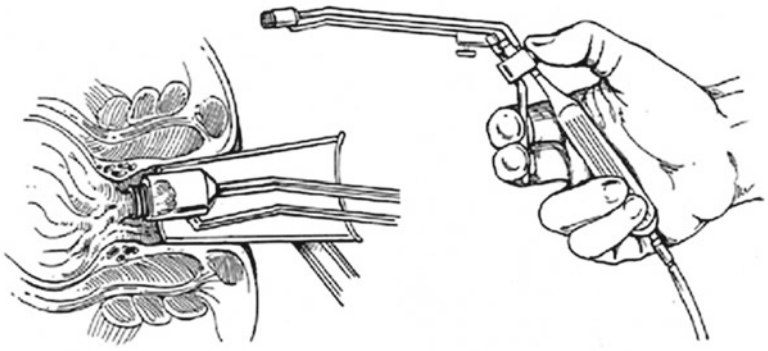

Fig. 12.1 Banding of an internal hemorrhoid through an anoscope using a McGown suction-ligator (Adapted with permission from Cintron J, Abcarian H. Benign anorectal: hemorrhoids. In: The ASCRS textbook of colon and rectal surgery. New York: Springer-Verlag, Inc; 2007. p. 156–77; with kind reprint permission of Springer Science+Business Media)

require any local anesthetic, which is responsible for its popularity for use in the office setting. Using an anoscope, small rubber band rings are placed onto or just proximal to the internal hemorrhoids with a suction apparatus. Importantly, each band should be placed at least half of a centimeter above the dentate line to avoid placement onto somatically innervated tissue, which can be associated with severe pain (Fig. 12.1). Multiple columns can be banded at one time, but limited intervention is recommended during a single session due to increased risk of infection and post-procedural discomfort from multiple bands [11, 12]. Application of rubber bands causes hemorrhoid tissue necrosis and subsequent scarring-fixation to the surrounding rectal mucosa. As the tissue become ischemic, necrotic changes develop in the following 3–5 days, resulting in an ulcer bed. Complete healing occurs several weeks later. Complications include anal pain (2–5 %), urinary retention (2–5 %), band slippage (1–2 %), post-banding ulcer (1 %), hemorrhage (1 %), or severe pelvic infection (<0.5 %) [13]. Higher bleeding rates were encountered with the use of aspirin, nonsteroidal anti-inflammatory drugs, and warfarin [14].

Outcomes of hemorrhoid banding are excellent for the primary complaint of blood with defecation from Grade II–III internal hemorrhoids. Overall initial success rates of 86–95 % [15, 16]. In a large review of 805 patients from a single practice that performed 2,114 rubber band ligations, placement of four or more bands was associated with a trend towards higher failure rates and higher need for subsequent excisional hemorrhoidectomy. Time to symptomatic recurrence was less with more subsequent treatment courses, with success rates of 73 %, 61 %, and 65 % for first, second, and third recurrences, respectively [9]. Overall, rubber banding is a safe, quick, and effective procedure, and banding ligation is often the first-line therapy for patients with second- and third-degree prolapsing hemorrhoids (Fig. 12.2).

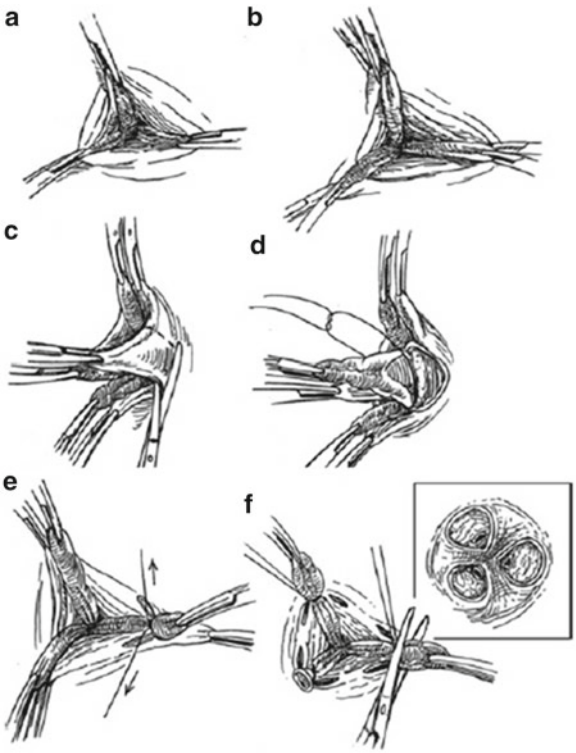

Fig. 12.2 Open (Milligan–Morgan) hemorrhoidectomy. Panel **a**: External hemorrhoid is grasped. Panel **b**: Internal hemorrhoid is grasped. Panel **c**: External skin and hemorrhoids excised. Panel **d**: Tie placed around the hemorrhoid vascular bundle. Panel **e**: Ligation of the vascular bundle. Panel **f**: Excision of the hemorrhoid tissue distal to the tie (Reprinted with permission from Cintron J, Abcarian H. Benign anorectal: hemorrhoids. In: The ASCRS textbook of colon and rectal surgery. New York: Springer-Verlag, Inc; 2007. p. 156–77; with kind reprint permission of Springer Science+Business Media)

Sclerotherapy

For patients with grade I–II internal hemorrhoids but taking anticoagulants, sclerotherapy is an alternative to rubber band ligation. Like band ligation, sclerotherapy does not require local anesthesia and can be performed in the office. Using an anoscope, internal hemorrhoids are located and injected with a sclerosant substance—typically a phenol in vegetable oil—into rectal submucosa. The sclerosant then causes fibrosis, fixation to the anal canal, and eventual obliteration of the redundant hemorrhoidal tissue. Minor discomfort or bleeding are the most common side effects of sclerotherapy, but fistulas or perforation can occur due to misplaced injections [17].

Infrared Coagulation

Infrared coagulation therapy is another alternative for patients with grade I–II hemorrhoids, where infrared light waves are directly applied to the hemorrhoidal tissues. The tip of the infrared coagulation applicator is applied to the base of the internal

hemorrhoid for 1–2 s, which converts infrared light into heat. This effectively causes necrosis and leads to scarring retraction of the prolapsed hemorrhoid mucosa. Overall, infrared therapy is very safe with only minor pain and bleeding reported [18].

In comparing rubber band ligation, sclerotherapy, and infrared coagulation, MacRae et al. performed a meta-analysis of 18 trials and concluded that rubber band ligation resulted in the best initial response for treatments of bleeding from internal, grade I–III hemorrhoids, with no difference in the complication rates [15]. Patients treated with sclerotherapy or infrared coagulation are more likely to develop recurrent symptoms.

HET Bipolar System

The HET Bipolar System (HET Systems, LLC, Oxford, CT, USA) is a relatively new device for patients with grade I–II bleeding hemorrhoids. The HET system, a combination of a tissue ligator and temperature monitor, allows compression and ligation of the target tissue with a constant force and predictable energy delivery [19]. When applied to a bleeding hemorrhoid, HET occludes and ligates the superior hemorrhoidal blood supply, thus controlling bleeding symptoms.

Evidence supporting its use is limited but promising. In a single-center experience, 23 patients with bleeding internal hemorrhoids were treated with the HET system, including five without sedation [20]. At average follow up of 11 months, there were no recurrences of bleeding or prolapse. Despite limited data, HET has been reported to be safe, effective, and essentially painless.

Hemorrhoidectomy

Persistent or recurrent hemorrhoid bleeding, despite conservative or minimally invasive measures, usually requires surgical intervention to resect the involved tissue. Additionally, surgery is the initial treatment of choice in patients with large, symptomatic grade IV hemorrhoids.

Open hemorrhoidectomy, or the Milligan–Morgan approach, involves resection of hemorrhoids and leaving the wound open to heal by secondary intention and has been the mainstay of surgical therapy since its introduction in 1937 [21]. Closed Hemorrhoidectomy, or the Ferguson technique, was developed in 1959 and involves closure of the resected mucosa primarily after resection of hemorrhoids [22]. In a randomized trial of elective hemorrhoidectomies, there were no differences in open vs. closed hemorrhoidectomy [23] (Fig. 12.3).

Hemorrhoidectomies are performed with the patient placed in the jackknife position. Preoperatively, full mechanical bowel prep is not necessary and administration of preoperative antibiotics such as metronidazole has not shown any benefit [24].

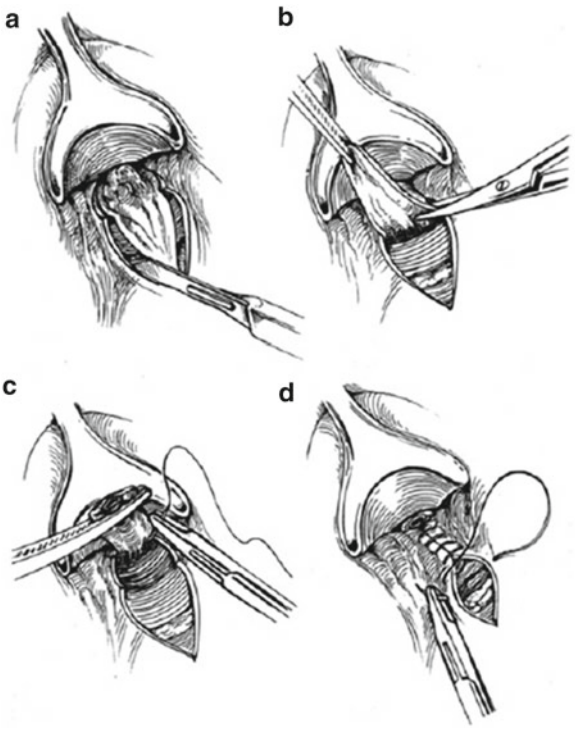

Fig. 12.3 Closed (Ferguson) hemorrhoidectomy. Panel **a**: Incision made in the mucosa and anoderm around the hemorrhoid bundle. Panel **b**: Dissecting the sphincter away from the hemorrhoid. Panel **c**: Pedicle of the hemorrhoid is clamped and excised. The pedicle is suture ligated. Panel **d**: The wound is closed with a running stitch (Reprinted with permission from Cintron J, Abcarian H. Benign anorectal: hemorrhoids. In: The ASCRS textbook of colon and rectal surgery. New York: Springer-Verlag, Inc; 2007. p. 156–77; with kind reprint permission of Springer Science+Business Media)

Anesthesia can be achieved with either a local perianal block or spinal block. In a small randomized trial of comparing local vs. spinal block, local perianal block for hemorrhoidectomy had lower requirements for parenteral analgesics postoperatively, as well as a lower incidence of urinary retention [25]. After exposing the anal canal using a Hill-Ferguson retractor, the junction between the internal and external component of the hemorrhoid is grasped and serves as a handle to retract the hemorrhoid away from the sphincter muscles. An elliptical incision is then made, and the hemorrhoid tissue is dissected away from the superficial internal and external sphincter muscles to the main vascular pedicle in the anal canal, carefully avoiding any injury to the sphincter muscles.

Morbidity of surgical hemorrhoidectomy is more significant compared to nonoperative approaches. Postoperatively, pain is the most common complaint and may delay return to normal activities. Intentional pain management strategies can be successfully managed with adequate oral analgesics, avoidance of constipation, and sitz baths. Self-limited bleeding may occur in 1–2 % of patients as result of eschar separation [26]. Infection, in the form of submucosal abscesses, occurs in less than 1 % of cases after hemorrhoid surgery, but severe fasciitis or necrotizing infections may rarely occur [26]. Urinary retention, attributed to pelvic floor spasm, narcotic use, and excess intravenous fluids, has been reported to

be as high as 34 % of cases [27]. However, temporary Foley catheter insertion results in self-resolution in majority of cases. Sphincter injury resulting in fecal or gas incontinence occurs in 2–10 % of cases and can have significant adverse impact on quality of life, emphasizing the importance of avoiding intraoperative injury [28]. Finally, anal stenosis may occur as a result of excessive resection and suturing of multiple quadrants, and can be difficult to manage. Avoiding extensive resection and leaving muscosal bridges between resected hemorrhoids is the best option to avoid anal stenosis.

Despite its relative higher morbidity, surgical hemorrhoidectomy is more effective than band ligation for preventing recurrent symptoms [15]. Patients with grade III and IV hemorrhoids, or those on anticoagulation (contraindication to rubber banding), benefit the most from surgical hemorrhoidectomy.

Stapled Hemorrhoidopexy

Stapled hemorrhoidopexy (also known as the procedure for prolapsing hemorrhoids, or PPH), in which a stapling device is used to resect and fixate the internal hemorrhoid tissues to the rectal wall, has been gaining popularity since its introduction in 1998 by Longo [29]. As its name suggests, stapled hemorrhoidopexy is most beneficial for patients with significant prolapse. In this procedure, a circular stapler is introduced into the anus and prolapsing tissue is conveyed into the stapler, and a circumferential purse-string suture is placed in the submucosa far enough away to avoid sphincter injury. Before engaging the stapler, an exam of the posterior vaginal wall should be conducted due to the risk of inadvertently incorporating the vagina into the staple line. Finally, the staple line should be evaluated for any bleeding that would require additional suture ligation (Fig. 12.4).

Complications from stapled hemorrhoidopexy include bleeding from the staple line, incontinence from injury of the sphincter muscles, and stenosis from incorporation of excess rectal tissue. Additionally, there is a risk of recto-vaginal fistula in women due to incorporation of vaginal tissue into the purse-string suture.

In a 2010 European multicenter randomized trial of stapled hemorrhoidopexy versus open hemorrhoidectomy, both options were equally effective in preventing recurrence after 1 year [30]. However, three systematic reviews concluded that compared to conventional hemorrhoidectomy, stapled hemorrhoidopexy was associated with a higher long-term risk of recurrence [31–33]. Additionally, due to the need for subsequent operations, incidence of prolapse and tenesmus was also more often observed after stapled hemorrhoidopexy as compared to conventional hemorrhoidectomy. Despite these issues, patients after the stapled hemorrhoidopexy reported less pain and shorter delay to resumption of normal activity, which accounts for its popularity.

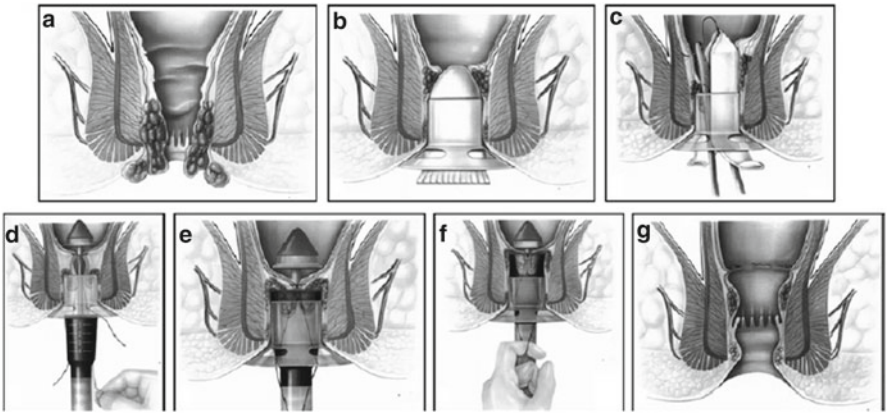

Fig. 12.4 Stapled hemorrhoidopexy. Panel **a**: Prolapsing hemorrhoid. Panel **b**, **c**: Circular anoscope is inserted and circumferential purse string suture is placed proximal to hemorrhoids. Panel **d**, **e**: The purse strings are drawn through the stapler, and traction draws the redundant mucosa into the head of the stapler. Panel **f**, **g**: The stapler is closed onto the mucosa and fired, and the final staple line draws the hemorrhoids into the anatomic positions (Reprinted with permission from Cintron J, Abcarian H. Benign anorectal: hemorrhoids. In: The ASCRS textbook of colon and rectal surgery. New York: Springer-Verlag, Inc; 2007. p. 156–77; with kind reprint permission of Springer Science+Business Media)

Doppler-Guided Hemorrhoidal Artery Ligation (DGHAL)

Introduced in 1995, DGHAL involves insertion of a Doppler-equipped anoscope into the anal canal for identification of each hemorrhoidal arterial blood supply, which is subsequently suture ligated [34]. Recurrence rate after DGHAL is 3–60 % with the highest risk in patients with grade IV hemorrhoids. Moreover, although traditional DGHAL does not remove any tissue, postoperative analgesia was required in 0–38 % of the patients [35].

More recently, some surgeons have coupled DGHAL with recto-anal repair (RAR), a technique that reduces and fixates the prolapsed rectal mucosa. Instead of excision of the hemorrhoids, the goal of this modification is to restore near-normal anatomical position of the prolapsed mucosa. In 1-year follow-up of 20 patients who underwent DGHAL-RAR, there were no major complications. However, residual mucosal prolapse occurred in 40 % of patients, with 5 % reporting occasional soiling [36].

Conclusions

Hemorrhoid disease is a common but complex disease with a variety of management options. Patients who present with bleeding hemorrhoids should be carefully evaluated to exclude hidden neoplastic disease. Specific management choice should be individualized, based on patient factors and disease severity.

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References

1. Everhart JE, Ruhl CE. Burden of digestive diseases in the United States part I: overall and upper gastrointestinal diseases. Gastroenterology. 2009;136(2):376–86.
2. Johanson JF, Sonnenberg A. The prevalence of hemorrhoids and chronic constipation. An epidemiologic study. Gastroenterology. 1990;98(2):380–6.
3. Shafik A. Surgical anatomy of hemorrhoids. Surgical treatment of hemorrhoids. New York: Springer; 2009. p. 7–13.
4. Banov Jr L, Knoepp Jr LF, Erdman LH, Alia RT. Management of hemorrhoidal disease. J S C Med Assoc. 1985;81(7):398–401.
5. Alonso-Coello P, Mills E, Heels-Ansdell D, Lopez-Yarto M, Zhou Q, Johanson JF, et al. Fiber for the treatment of hemorrhoids complications: a systematic review and meta-analysis. Am J Gastroenterol. 2006;101(1):181–8.
6. Tjandra JJ, Tan JJ, Lim JF, Murray-Green C, Kennedy ML, Lubowski DZ. Rectogesic (glyceryl trinitrate 0.2%) ointment relieves symptoms of haemorrhoids associated with high resting anal canal pressures. Colorectal Dis. 2007;9(5):457–63.
7. Sneider EB, Maykel JA. Diagnosis and management of symptomatic hemorrhoids. Surg Clin North Am. 2010;90(1):17–32. Table of Contents.
8. Moesgaard F, Nielsen ML, Hansen JB, Knudsen JT. High-fiber diet reduces bleeding and pain in patients with hemorrhoids: a double-blind trial of Vi-Siblin. Dis Colon Rectum. 1982;25(5):454–6.
9. Iyer VS, Shrier I, Gordon PH. Long-term outcome of rubber band ligation for symptomatic primary and recurrent internal hemorrhoids. Dis Colon Rectum. 2004;47(8):1364–70.
10. Buchmann P, Seefeld U. Rubber band ligation for piles can be disastrous in HIV-positive patients. Int J Colorectal Dis. 1989;4(1):57–8.
11. Law WL, Chu KW. Triple rubber band ligation for hemorrhoids: prospective, randomized trial of use of local anesthetic injection. Dis Colon Rectum. 1999;42(3):363–6.
12. Liu J, Petersen BT, Tierney WM, Chuttani R, DiSario JA, Coffie JM, et al. Endoscopic banding devices. Gastrointest Endosc. 2008;68(2):217–21.
13. Jacobs D. Clinical practice. Hemorrhoids N Engl J Med. 2014;371(10):944–51.
14. Nelson RS, Ewing BM, Ternent C, Shashidharan M, Blatchford GJ, Thorson AG. Risk of late bleeding following hemorrhoidal banding in patients on antithrombotic prophylaxis. Am J Surg. 2008;196(6):994–9.
15. MacRae HM, McLeod RS. Comparison of hemorrhoidal treatment modalities. A meta-analysis. Dis Colon Rectum. 1995;38(7):687–94.
16. Su MY, Chiu CT, Wu CS, Ho YP, Lien JM, Tung SY, et al. Endoscopic hemorrhoidal ligation of symptomatic internal hemorrhoids. Gastrointest Endosc. 2003;58(6):871–4.
17. Barwell J, Watkins RM, Lloyd-Davies E, Wilkins DC. Life-threatening retroperitoneal sepsis after hemorrhoid injection sclerotherapy: report of a case. Dis Colon Rectum. 1999; 42(3):421–3.
18. Johanson JF, Rimm A. Optimal nonsurgical treatment of hemorrhoids: a comparative analysis of infrared coagulation, rubber band ligation, and injection sclerotherapy. Am J Gastroenterol. 1992;87(11):1600–6.

19. Piskun G, Tucker R. New bipolar tissue ligator combines constant tissue compression and temperature guidance: histologic study and implications for treatment of hemorrhoids. Med Devices (Auckl). 2012;5:89–96.
20. Kantsevoy SV, Bitner M. Nonsurgical treatment of actively bleeding internal hemorrhoids with a novel endoscopic device (with video). Gastrointest Endosc. 2013;78(4):649–53.
21. Milligan E, Morgan CN, Jones L, Officer R. Surgical anatomy of the anal canal, and the operative treatment of haemorrhoids. Lancet. 1937;230(5959):1119–24.
22. Ferguson JA, Heaton JR. Closed hemorrhoidectomy. Dis Colon Rectum. 1959;2(2):176–9.
23. Reis Neto JA, Quilici FA, Cordeiro F, Reis Junior JA. Open versus semi-open hemorrhoidectomy: a random trial. Int Surg. 1992;77(2):84–90.
24. Wesarachawit W, Pattana-arun J. Antibiotics and early post operative complications of closed hemorrhoidectomy: a retrospective matched pair study. J Med Assoc Thai. 2007;90(9):1828–32.
25. Anannamcharoen S, Cheeranont P, Boonya-usadon C. Local perianal nerve block versus spinal block for closed hemorrhoidectomy: a ramdomized controlled trial. J Med Assoc Thai. 2008;91(12):1862–6.
26. Bleday R, Pena JP, Rothenberger DA, Goldberg SM, Buls JG. Symptomatic hemorrhoids: current incidence and complications of operative therapy. Dis Colon Rectum. 1992;35(5): 477–81.
27. Hoff SD, Bailey HR, Butts DR, Max E, Smith KW, Zamora LF, et al. Ambulatory surgical hemorrhoidectomy--a solution to postoperative urinary retention? Dis Colon Rectum. 1994;37(12):1242–4.
28. Gravie JF, Lehur PA, Huten N, Papillon M, Fantoli M, Descottes B, et al. Stapled hemorrhoidopexy versus Milligan-Morgan hemorrhoidectomy: a prospective, randomized, multicenter trial with 2-year postoperative follow up. Ann Surg. 2005;242(1):29–35.
29. Longo A, editor Treatment of hemorrhoids disease by reduction of mucosa and hemorrhoidal prolapse with a circular stapler suturing device: a new procedure. Proceeding of the 6th world Congress of Endoscopic Surgery; 1998.
30. Nystrom PO, Qvist N, Raahave D, Lindsey I, Mortensen N. Randomized clinical trial of symptom control after stapled anopexy or diathermy excision for haemorrhoid prolapse. Br J Surg. 2010;97(2):167–76.
31. Giordano P, Gravante G, Sorge R, Ovens L, Nastro P. Long-term outcomes of stapled hemorrhoidopexy vs conventional hemorrhoidectomy: a meta-analysis of randomized controlled trials. Arch Surg. 2009;144(3):266–72.
32. Jayaraman S, Colquhoun PH, Malthaner RA. Stapled versus conventional surgery for hemorrhoids. Cochrane Database Syst Rev. 2006;4:Cd005393.
33. Nisar PJ, Acheson AG, Neal KR, Scholefield JH. Stapled hemorrhoidopexy compared with conventional hemorrhoidectomy: systematic review of randomized, controlled trials. Dis Colon Rectum. 2004;47(11):1837–45.
34. Morinaga K, Hasuda K, Ikeda T. A novel therapy for internal hemorrhoids: ligation of the hemorrhoidal artery with a newly devised instrument (Moricorn) in conjunction with a Doppler flowmeter. Am J Gastroenterol. 1995;90(4):610–3.
35. Pucher PH, Sodergren MH, Lord AC, Darzi A, Ziprin P. Clinical outcome following Doppler-guided haemorrhoidal artery ligation: a systematic review. Colorectal Dis. 2013;15(6): e284–94.
36. Walega P, Romaniszyn M, Kenig J, Herman R, Nowak W. Doppler-guided hemorrhoid artery ligation with recto-anal-repair modification: functional evaluation and safety assessment of a new minimally invasive method of treatment of advanced hemorrhoidal disease. Scientific World Journal. 2012;2012:324040.

Chapter 13
Management of Colonic Diverticular Bleeding and Bleeding Colitis

Mohamed A. Adam, Zhifei Sun, and John Migaly

Colonic Diverticular Bleeding

Colonic diverticular bleeding is the most common cause of overt lower gastrointestinal bleeding, accounting for over 40 % of cases [1]. Colonic diverticula are outpouchings of the colonic mucosa and submucosa through areas of weakness at the site of vascular perforation in the wall of the colon [2]. The prevalence of diverticulosis increases significantly with advancing age, reaching a rate of up to 66 % of the elderly population 80 years or older [3]. Although not fully understood, the etiology of colonic diverticular disease has been attributed to a variety of factors, such as colonic aging, dysmotility, transient increases in colonic intraluminal pressures, and environmental conditions such as a highly refined, low-residue diet [4–6]. While most diverticuli are located in the sigmoid, diverticulosis can also involve the ascending, transverse, and descending colon.

Even though diverticular disease may remain asymptomatic for decades, approximately 10–20 % of patients with colonic diverticula will have a complication during their lifetime [7]. The two major complications of diverticulosis include diverticulitis and gastrointestinal bleeding. Typically, diverticular bleeding occurs in the absence of diverticulitis. As a diverticulum herniates, the penetrating vasa recta associated with the weakness become separated from the lumen only by the mucosa. This exposes the vasa recta to repeated luminal trauma, predisposing to

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rupture of the vessel and resultant intraluminal bleeding [2]. In contrast to diverticulitis that mainly occurs in the left colon, colonic diverticular bleeding most commonly originates in the ascending colon in 50–90 % of cases [2, 8–10].

Diagnosis

Establishing the diagnosis of colonic diverticular bleeding starts with a complete history and physical examination. Colonic diverticular bleeding is often sudden and brisk, and may result in hemodynamic instability. Patients usually present with lower abdominal discomfort and rectal urgency, followed by passage of bloody stool. The presence of any associated comorbidity, family history of bleeding disorders, cancer, medications, and date of last colonoscopic examination should be investigated. Physical examination can demonstrate tachycardia, hypotension, and postural changes based on the amount of blood loss. Stool is guaiac positive, but negative guaiac stool specimens can be found since bleeding may be intermittent. Basic laboratory data should be obtained including a complete blood count, coagulation parameters, and serum iron levels. While the diagnosis of diverticulosis can be established with imaging studies, such as barium enema or computer tomography, colonoscopy remains the most effective method establishing the diagnosis of diverticular bleeding.

Colonoscopy

Considerable controversy exists with regard to the role of urgent colonoscopy in the evaluation and management of patients with lower gastrointestinal bleeding. Many endoscopists argue that stigmata of recent bleeding such as active bleeding from a diverticulum, a non-bleeding visible vessel, or an adherent clot may not be identified by colonoscopy in the urgent setting (Fig. 13.1); therefore, performing elective colonoscopy, where aggressive bowel preparation can be obtained, is more appropriate. In a recent clinical trial of 72 patients with significant lower gastrointestinal bleeding, patients were randomized to urgent (≤12 h) or elective (36–60 h) colonoscopy. Use of urgent colonoscopy demonstrated no evidence of improving clinical outcomes or lowering costs as compared with routine elective colonoscopy [11]. Conversely, there are some data demonstrating the superiority of urgent colonoscopy in identifying sites of diverticular bleeding. Green et al. randomized 100 patients with lower gastrointestinal bleeding into two groups: (1) cathartic preparation followed by urgent colonoscopy, and (2) the standard care algorithm (elective colonoscopy if no active bleeding suspected; if active bleeding suspected, then tagged red blood scan). A definitive source of bleeding was found more often in the urgent colonoscopy group compared with the “standard care” group (42 % vs. 22 %, respectively). However, patient outcomes were not different between the two groups [12]. Other studies utilizing urgent colonoscopy have found this approach to yield a

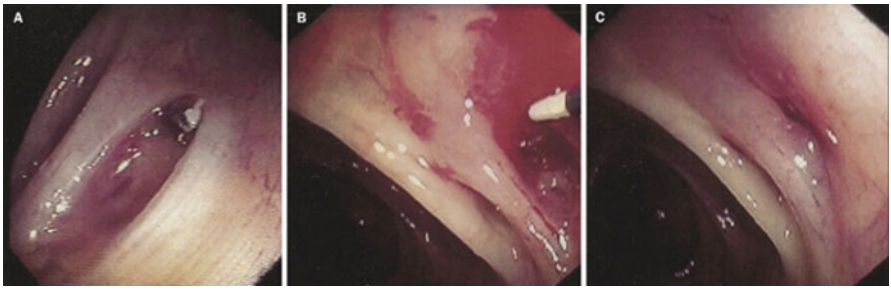

Fig. 13.1 Colonoscopic images of a diverticulum with (**a**) visible blood vessels, (**b**) active oozing of blood during epinephrine injection, and (**c**) post-injection (From Stollman, N. and J.B. Raskin, Diverticular disease of the colon. Lancet, 2004. 363(9409): p. 631–9)

definitive bleeding site in 7–100 % of patients [13–15]. The wide discrepancy reported in the literature is likely reflective of a number of factors such as differences in equipment used between studies, timing, quality of the bowel preparation among studies, and experience of the endoscopist.

While previous clinical trials data have failed to demonstrate a difference in patient outcomes between urgent vs. delayed colonoscopy, these trials were criticized by lack of adequate statistical power to detect a difference in outcomes between these two strategies. Therefore, others have attempted to answer this question from large population-based data. In a recent study from the Nationwide Inpatient Sample dataset of 58,296 discharges of lower gastrointestinal bleeding (including 12,746 diverticular bleeding), patient outcomes were compared between those who underwent early (≤24 h) vs. late (>24 h) colonoscopy. Early colonoscopy was associated with a shorter hospital length of stay, decreased blood transfusion requirement, and lower costs for all patients as well as for those with diverticular bleeding [16]. As such, we believe that urgent colonoscopy is advantageous in the evaluation of patients with diverticular bleeding and may provide therapeutic options for bleeding source.

Visceral Angiography

Angiography is an alternative diagnostic and therapeutic method that should be employed in patients with lower gastrointestinal bleeding who cannot undergo colonoscopy or in those who underwent unsuccessful colonoscopic localization or intervention (Fig. 13.2). A tagged red blood cell scan is typically performed before angiography to facilitate localization. If the patient underwent colonoscopy first, a hemoclip should be placed to mark the bleeding site. The sensitivity of visceral angiography in identifying the source of bleeding is variable (27–86 %), as the accuracy of this method is predicated on the presence of active arterial bleeding at the time of the study and a bleeding rate greater than 0.5–1 cc/min [17].

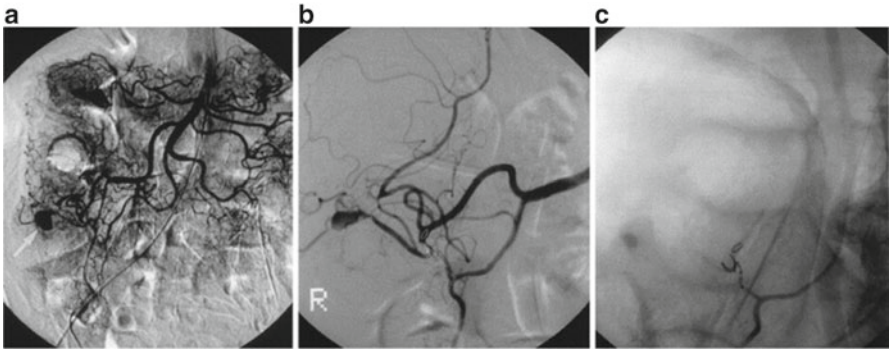

Fig. 13.2 A patient with acute lower gastrointestinal bleeding who underwent visceral angiography. (**a**) Pooling of contrast material (*white arrow*) is seen within the cecum. (**b**) A magnified view of the cecum after initial coil placement within the vasa recta demonstrates persistent hemorrhage. (**c**) A total of five coils were placed through a 3-F microcatheter. Complete cessation of bleeding was achieved (From Evangelista, P.T. and M.J. Hallisey, Transcatheter embolization for acute lower gastrointestinal hemorrhage. J Vasc Interv Radiol, 2000. 11(5): p. 601–6)

Red Blood Cell Scan

Red blood cells labeled with technetium-99 (^{99m}Tc) are helpful in the work-up of patients with lower gastrointestinal bleeding. A small amount of the patient's blood is obtained, and the red blood cells are then labeled with ^{99m}Tc and returned to the patient. This technology is advantageous in its ability to detect bleeding at a slower rate, as low as 0.05 cc/min [18]. The tracer persists in the bloodstream long after injection, which is particularly useful in evaluating intermittent bleeding, without the need for repeat injections. Nevertheless, red blood cell scans are limited by the potential of significant migration of contrast back and forth in the colon particularly towards dependent areas, such as the flexures, which can sometimes make localization of the bleeding sites difficult. Thus, the false localization rate of red blood cell scans is relatively high, reaching 25 %. Segmental resections should therefore be avoided if they are based purely on red blood cell scanning; in these cases, supplemental information should be sought if possible.

Management

The first step in the management of patients with diverticular bleeding is adequate resuscitation. Diverticular bleeding can be sudden and massive, compromising the hemodynamic state of the patient. In this situation, the patient must be transferred to the intensive care unit, with the immediate goal of aggressive resuscitation, blood transfusion, and correction of coagulopathic derangement. In patients in whom bleeding is not too significant, hemorrhage will cease in about 90 % of the time. The

recurrence rate over time after the first episode of bleeding is 9 % at 1 year, 10 % at 2 years, and 90 % at 3 years [1]. Once resuscitation is underway, efforts should be focused on localizing the source of bleeding. An upper gastrointestinal source of bleeding should be excluded first, followed by colonoscopic evaluation.

Endoscopic Treatment

Identified diverticular bleeding sites in the colon should be approached endoscopically if possible. Endoscopic treatment can be accomplished by a variety of methods including heater probe or argon plasma coagulation, injection of vasoactive substances, or application of clips. Although there have been widespread practical experience to support the efficacy of these approaches in upper gastrointestinal bleeding, limited data exist with regard to its role in lower gastroinestinal bleeding. In a study by Jensen et al., urgent colonoscopic treatment reduced the number of patients requiring surgery and reduced rebleeding rates [19]. This statement, however, has not been proven true in large randomized trials. The difficulties in controlling bleeding endoscopically reside not only in the need for large-dual channel endoscopes, but also in the endoscopic characteristics of the diverticulum (i.e., the bleeding vessel may originate from deep inside the diverticulum as well as from the rim) making endoscopic therapy especially difficult. Most experts agree that severe or ongoing recurrent bleeding mandates management by radiologic embolization or urgent surgery.

Selective Visceral Angiography

Selective mesenteric angiography should be reserved for patients in whom colonoscopy is not appropriate [20] or in patients who are actively bleeding. Selected infusions of vasopressin via angiography have proven effective in 36–90 % of cases with ongoing bleeding [21, 22]. The recurrent bleeding rate after infusion of vasopressin is in the 22–71 % range. Vasopressin infusion during angiography can control bleeding, but potential complications including bowel infarction and perforation, arterial vasospasm, and lower extremity ischemia can occur. Selective embolization, on the other hand, has a success rate of 71–90 %, with a rebleeding rate of 15–20 %. Even with highly selective transcatheter embolization, the rate of significant intestinal ischemia can be as high as 20 %.

Surgical Intervention

Surgical resection is indicated for ongoing or recurrent diverticular bleeding that is resistant to endoscopic and angiographic attempts. Specific indications for surgery include patients that require more than four units of blood in a 24-h period to remain hemodynamically stable, those in whom bleeding has not stopped after 72 h, or those who experience rebleeding within 1 week after an initial episode.

Surgical options include segmental resections or more extended operations depending upon the location of the disease and the overall state of the patient. Patients who cannot tolerate a prolonged operation might be much better off with limited control of the bleeding with the understanding that leaving disease behind can be associated with recurrent bleeding. In general, control of bleeding can be obtained in most patients and the need for transfusions decreases significantly after surgery.

Blind segmental resection is discouraged if preoperative imaging has failed to identify localization of the bleeding source. Partial colectomy with unidentified bleeding source has been linked with a rebleeding rate of approximately 75 % and higher mortality [23]. In these cases, intraoperative localization options should be pursued, such as upper endoscopy, colonoscopy, or small bowel endoscopy assisted by hand manipulation of the small bowel by the operating surgeon.

In patients where localization of chronic, ongoing bleeding has proven difficult, such as in situations where arteriogram and red blood cell scans have both been non-diagnostic, the choice of procedure is sometimes difficult. If pandiverticulosis has been documented and upper gastrointestinal/obscure sources of bleeding have been ruled out via upper endoscopy and/or capsule endoscopy, total abdominal colectomy with or without ileoproctostomy is an acceptable option in the face of ongoing bleeding.

Bleeding Colitis

Colitis refers to inflammation of the mucosa of the colon and can be associated with inflammation of other segments of the gastrointestinal tract (e.g., ileitis), while proctitis refers to inflammation limited to the rectal mucosa. Overall, colitis contributes to approximately 20 % of all causes of lower gastrointestinal bleeding [20]. Bleeding from colitis is usually intermittent, self-limited, and is commonly associated with other symptoms such as diarrhea, fevers, and/or abdominal pain.

Classification of colitis (Table 13.1) depends on the etiology of the offending factor, but in general, the clinical presentation and endoscopic appearance are similar in different types of colitis. Inflammatory bowel disease, infectious, or ischemic colitis can all present with lower gastrointestinal bleeding. Endoscopic examination usually reveals a friable mucosa with edema, erythema, and a tendency to bleed upon manipulation.

The diagnosis of colitis is established with a complete history and physical examination, evaluation of stool in cases where infection is suspected. Findings of mucosal inflammation can also be detected by computer tomography and barium enema in some cases. In patients that remain hemodynamically stable, treatment is aimed at the source of the inflammation. If hemodynamic stability is compromised or if bleeding is severe enough to require multiple transfusions or angiography, emergent surgery is indicated.

Table 13.1 Causes of colitis

• Inflammatory bowel disease
• Ischemic colitis
• Infectious colitis
• Radiation-induced colitis
• Medication-related colitis

Ulcerative Colitis

Ulcerative colitis is a chronic mucosal inflammatory process of the colon and rectum. The mildest form of this disease, ulcerative proctitis, only affects the rectum, but this may progress and involve the more proximal colon. Diarrhea and lower gastrointestinal bleeding are the hallmark of the disease. History and stool examination usually permit a presumptive diagnosis, which must be confirmed with colonoscopic evaluation and biopsy. The diagnosis of severe disease is based on the criteria of Truelove and Witts [24] and is defined as colitis with more than six bloody bowel movements per day, fever (temperature >35.5 °C), tachycardia (heart rate >90 beats per minutes), anemia (hemoglobin <75 % of normal), and elevated sedimentation rate (>30 mm/h) [25]. Toxic or fulminant colitis is characterized by more than 10 bloody bowel movements per day, fever (temperature >35.5 °C), tachycardia (heart rate >90 beast per minutes), anemia (hemoglobin <75 % of normal), elevated sedimentation rate (>30 mm/h), colonic dilation on radiography, and abdominal distention with tenderness [25]; toxic megacolon is diagnosed when the colonic distention of the transverse colon exceeds 6 cm [26, 27].

Medical therapy represents the mainstay of treatment for ulcerative colitis-related gastrointestinal bleeding. Most patients respond to medical treatment, while few patients require surgical intervention. Bleeding from mild disease confined to the rectum and sigmoid colon can be treated topically, thus systemic treatment is not always necessary. All patients with severe colitis should be hospitalized and treated with intravenous corticosteroids [27]. Hydrocortisone or 5-ASA enemas can be quite effective in the treatment of left-sided disease. Patients receiving oral corticosteroid treatment ≥30 days prior to admission, hydrocortisone 300 mg/day should be given as a continuous IV infusion. In patients who have not received recent corticosteroids then ACTH 75–120 U/day by continuous drip should be initiated. Treatment is given for 7–10 days and response is monitored by noting the nature and frequency of the bowel movements. An initial radiographic imaging should be obtained to assess colonic involvement and the patient must be followed closely for the development of toxic megacolon. Oral prednisone 60 mg/day may be substituted after remission has been achieved and after a course of parenteral treatment. Stability on an oral regimen can be followed by hospital discharge with close home monitoring.

Cyclosporine has been used as a final therapeutic measure prior to colectomy in patients with bleeding refractory to high-dose intravenous steroids; however, it may

take up to a week for patients to have a significant improvement in symptoms. Cyclosporine is nephrotoxic, and its overall benefit is questioned given that most patients receiving cyclosporine will eventually require surgery within a year. Risks and benefits of cyclosporine therapy should factor in the treatment plan.

Surgery is rarely required for ulcerative colitis bleeding; it is indicated for cases of massive hemorrhage, fulminant toxic colitis, or perforation. Subtotal colectomy with ileostomy and rectosigmoid closure is usually the procedure of choice [28, 29]. Subsequent rectal stump bleeding can be controlled with steroids, and in severe cases of bleeding, intrarectal tamponade may be necessary. The rectosigmoid stump may be removed at another setting since it may represent a site for disease reactivation.

Ischemic Colitis

Ischemic colitis is a common etiology of lower gastrointestinal bleeding, accounting for 11 % of cases [30]. Intestinal ischemia occurs most commonly in the colon and results from a low-flow state, and less frequently from small vessel occlusion. Usually, signs and symptoms of ischemic colitis reflect the extent of bowel involvement and may begin suddenly with severe left lower abdominal pain followed by bloody diarrhea; however, absence of abdominal pain does not preclude the diagnosis. Diagnosis can be made by colonoscopy and treatment depends on clinical severity. Endoscopically, mild ischemic colitis can appear as a long segment strip of ischemic mucosa on the anti-mesenteric surface of the colonic lumen, where the blood flow is most tenuous.

Roughly 80 % of patients with ischemic colitis will recover from the disease with conservative management, including bowel rest, hydration, and broad-spectrum antibiotics [30]. Hemodynamic parameters must be optimized especially in the setting of hypotension and suspected low-flow states. This process may progress to bowel necrosis, perforation, and peritonitis. Colonoscopy should be performed after recovery to evaluate for strictures and to rule out other pathology. Failure to improve with continued bloody bowel movements after 2–3 days of therapy is an indication for surgery.

Antibiotic-Associated Colitis

Various antibiotics may alter the balance of normal colonic flora allowing the overgrowth of Clostridium species. *Clostridium difficile* is a gram-positive, anaerobic, spore-forming bacillus that is responsible for the development of antibiotic-associated diarrhea and colitis. *Clostridium difficile* produces two toxins: Toxin A

and B. Toxin A is a cytotoxin that creates the colonic inflammation, which in turn allows Toxin B to enter the colonic mucosal cells. Diarrhea and colitis are caused by toxins produced by pathogenic strains of this bacteria. Clinical manifestations may range from simply loose stools to active colitis with bloody diarrhea, pain, fever, leukocytosis, and protein-losing enteropathy. Diagnosis is suspected when there is a history of diarrhea after antibiotic use. Most cases involve the distal colon and flexible sigmoidoscopy usually detects the disease. Endoscopically, pseudomembranes appear as multiple raised, white/yellow adherent plaques. Diagnosis can also be confirmed by detection of *Clostridium difficile* toxin in the stool. Most cases will resolve with metronidazole or oral vancomycin therapy. Intractable or fulminant disease may require hospitalization for supportive measures including blood transfusion according to the same principles for the management of ulcerative colitis.

Surgery is reserved for cases that continue to deteriorate despite medical management. In these cases, the operation of choice for severe colitis is subtotal abdominal colectomy with end-ileostomy [31]; other operations such as loop ileostomy, segmental resection, or "blowhole" stoma carry a significantly higher mortality in comparison to total colectomy with end-ileostomy [32–34]

Infectious Colitis

The most common pathogens of infectious colitis in immunocompetent patients in the USA are Salmonella, Campylobacter, Shigella, enterohemorrhagic *Escherichia coli*, enteroinvasive *Escherichia coli*, and Yersinia. Immunocompromised patients can experience colitis from Cytomegalovirus, Campylobacter, or Cryptosporidium.

Radiation Colitis

Radiation therapy is a major form of treatment for many malignancies, such as cervical, uterine, bladder, anal, and prostate cancer. Radiation to the pelvic area can lead to lower gastrointestinal bleeding. The underlying mechanism is through direct damage to DNA and free radicals formation. Acute changes occur during 6 weeks of radiation therapy, which constitute crypt atrophy, diarrhea, tenesmus, and bleeding. Chronic radiation changes occur 6–12 months after the exposure, and it can manifest as non-healing ulcers, telangiectasia, fistulas, obstruction, or sepsis (Fig. 13.3).

Patients with hemorrhagic proctitis may benefit from endoscopic electrocautery and/or mesalamine, steroid, and carafate enemas. Surgery should be reserved for those with refractory bleeding [35–37] (Fig. 13.4).

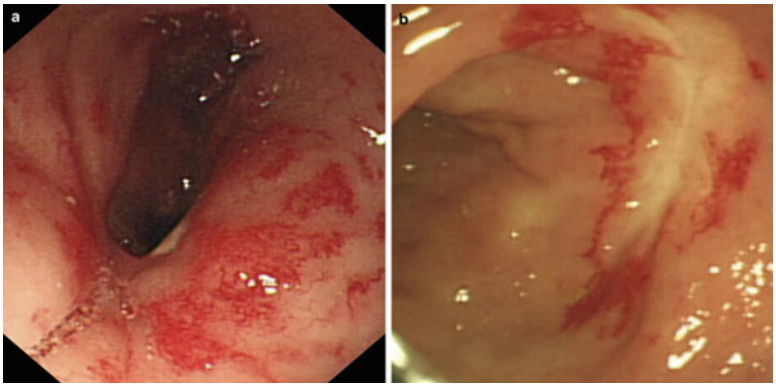

Fig. 13.3 Findings of mild radiation proctitis with erythema, telangiectasia, and mild rectal stenosis (**a**). Scarred area in the lower rectum with surrounding radiation proctitis (**b**) (From Leiper, K. and A.I. Morris, Treatment of radiation proctitis. Clin Oncol (R Coll Radiol), 2007. 19(9): p. 724–9)

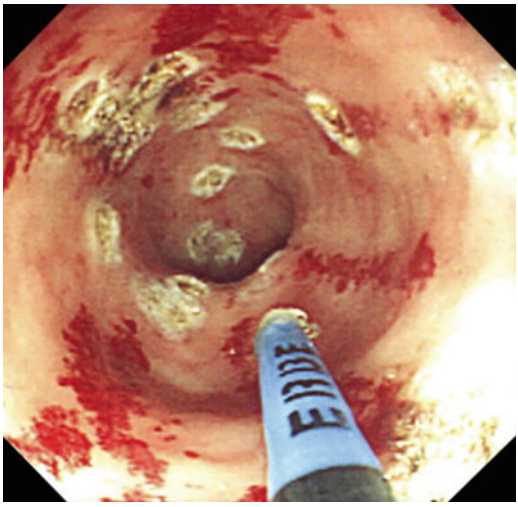

Fig. 13.4 Argon plasma coagulation treatment of radiation proctitis (From Leiper, K. and A.I. Morris, Treatment of radiation proctitis. Clin Oncol (R Coll Radiol), 2007. 19(9): p. 724–9)

References

1. Longstreth GF. Epidemiology and outcome of patients hospitalized with acute lower gastrointestinal hemorrhage: a population-based study. Am J Gastroenterol. 1997;92(3):419–24.
2. Meyers MA, Alonso DR, Gray GF, Baer JW. Pathogenesis of bleeding colonic diverticulosis. Gastroenterology. 1976;71(4):577–83.
3. Stollman N, Raskin JB. Diverticular disease of the colon. Lancet. 2004;363(9409):631–9.
4. Painter NS. Diverticular disease of the colon. The first of the Western diseases shown to be due to a deficiency of dietary fibre. S Afr Med J. 1982;61(26):1016–20.
5. Golder M et al. Smooth muscle cholinergic denervation hypersensitivity in diverticular disease. Lancet. 2003;361(9373):1945–51.

6. Wess L, Eastwood MA, Wess TJ, Busuttil A, Miller A. Cross linking of collagen is increased in colonic diverticulosis. Gut. 1995;37(1):91–4.
7. McGuire Jr HH, Haynes Jr BW. Massive hemorrhage for diverticulosis of the colon: guidelines for therapy based on bleeding patterns observed in fifty cases. Ann Surg. 1972;175(6): 847–55.
8. Casarella WJ, Kanter IE, Seaman WB. Right-sided colonic diverticula as a cause of acute rectal hemorrhage. N Engl J Med. 1972;286(9):450–3.
9. Wong SK, Ho YH, Leong AP, Seow-Choen F. Clinical behavior of complicated right-sided and leftsided diverticulosis. Dis Colon Rectum. 1997;40(3):344–8.
10. Gostout CJ et al. Acute gastrointestinal bleeding. Experience of a specialized management team. J Clin Gastroenterol. 1992;14(3):260–7.
11. Laine L, Shah A. Randomized trial of urgent vs. elective colonoscopy in patients hospitalized with lower GI bleeding. Am J Gastroenterol. 2010;105(12):2636–41. quiz 2642.
22. Green BT et al. Urgent colonoscopy for evaluation and management of acute lower gastrointestinal hemorrhage: a randomized controlled trial. Am J Gastroenterol. 2005;100(11): 2395–402.
13. Wilcox CM, Clark WS. Causes and outcome of upper and lower gastrointestinal bleeding: the Grady Hospital experience. South Med J. 1999;92(1):44–50.
14. Angtuaco TL, Reddy SK, Drapkin S, Harrell LE, Howden CW. The utility of urgent colonoscopy in the evaluation of acute lower gastrointestinal tract bleeding: a 2-year experience from a single center. Am J Gastroenterol. 2001;96(6):1782–5.
15. Zuckerman GR, Prakash C. Acute lower intestinal bleeding. Part II: etiology, therapy, and outcomes. Gastrointest Endosc. 1999;49(2):228–38.
16. Navaneethan U, Njei B, Venkatesh PG, Sanaka MR. Timing of colonoscopy and outcomes in patients with lower GI bleeding: a nationwide population-based study. Gastrointest Endosc. 2014;79(2):297–306. e12.
17. Nusbaum M, Baum S. Radiographic demonstration of unknown sites of gastrointestinal bleeding. Surg Forum. 1963;14:374–5.
18. Zuckerman DA, Bocchini TP, Birnbaum EH. Massive hemorrhage in the lower gastrointestinal tract in adults: diagnostic imaging and intervention. AJR Am J Roentgenol. 1993;161(4): 703–11.
19. Jensen DM, Machicado GA, Jutabha R, Kovacs TO. Urgent colonoscopy for the diagnosis and treatment of severe diverticular hemorrhage. N Engl J Med. 2000;342(2):78–82.
20. Vernava 3rd AM, Moore BA, Longo WE, Johnson FE. Lower gastrointestinal bleeding. Dis Colon Rectum. 1997;40(7):846–58.
21. Leitman IM, Paull DE, Shires 3rd GT. Evaluation and management of massive lower gastrointestinal hemorrhage. Ann Surg. 1989;209(2):175–80.
22. Baum S et al. Selective mesenteric arterial infusions in the management of massive diverticular hemorrhage. N Engl J Med. 1973;288(24):1269–72.
23. Eaton AC. Emergency surgery for acute colonic haemorrhage-a retrospective study. Br J Surg. 1981;68(2):109–12.
24. Truelove SC, Witts LJ. Cortisone in ulcerative colitis; final report on a therapeutic trial. Br Med J. 1955;2(4947):1041–8.
25. Hanauer SB. Inflammatory bowel disease. N Engl J Med. 1996;334(13):841–8.
26. Jones JH, Chapman M. Definition of megacolon in colitis. Gut. 1969;10(7):562–4.
27. Katz JA. Medical and surgical management of severe colitis. Semin Gastrointest Dis. 2000; 11(1):18–32.
28. Present DH. Toxic megacolon. Med Clin North Am. 1993;77(5):1129–48.
29. Hyman NH, Cataldo P, Osler T. Urgent subtotal colectomy for severe inflammatory bowel disease. Dis Colon Rectum. 2005;48(1):70–3.
30. Chavalitdhamrong D et al. Ischemic colitis as a cause of severe hematochezia: risk factors and outcomes compared with other colon diagnoses. Gastrointest Endosc. 2011;74(4):852–7.
31. Steele SR et al. Practice parameters for the management of Clostridium difficile infection. Dis Colon Rectum. 2015;58(1):10–24.

32. Jobe BA, Grasley A, Deveney KE, Deveney CW, Sheppard BC. Clostridium difficile colitis: an increasing hospital-acquired illness. Am J Surg. 1995;169(5):480–3.
33. Grundfest-Broniatowski S et al. Clostridium difficile colitis in the critically ill. Dis Colon Rectum. 1996;39(6):619–23.
34. Morris JB, Zollinger Jr RM, Stellato TA. Role of surgery in antibiotic-induced pseudomembranous enterocolitis. Am J Surg. 1990;160(5):535–9.
35. Kochhar R et al. Radiation-induced proctosigmoiditis. Prospective, randomized, double-blind controlled trial of oral sulfasalazine plus rectal steroids versus rectal sucralfate. Dig Dis Sci. 1991;36(1):103–7.
36. Kochhar R, Sriram PV, Sharma SC, Goel RC, Patel F. Natural history of late radiation proctosigmoiditis treated with topical sucralfate suspension. Dig Dis Sci. 1999;44(5):973–8.
37. Chun M et al. Rectal bleeding and its management after irradiation for uterine cervical cancer. Int J Radiat Oncol Biol Phys. 2004;58(1):98–105.

Chapter 14
Colonic Arteriovenous Malformations

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Introduction

First described by Margolis et al. arteriovenous malformations (AVMs)—also known as angiodysplasias, angiectasias, or vascular ectasias—are aberrant, thin-walled arteriovenous communications located within the submucosa and mucosa of the gastrointestinal wall [1].

The exact etiology of AVM is not well understood. In congenital cases, McAllister et al. demonstrated that genetic errors may alter formation of TGF-**β**, which is in part responsible for the integrity of the vascular endothelial cells [2]. In acquired cases, the current hypothesis is that repeated episodes of colonic distention associated with increases in luminal pressure result in transient increases in wall tension and obstruction of submucosal venous outflow, particularly at the level of the muscularis propria [3]. These initially insignificant insults, accumulated over years, can lead to loss of pre-capillary sphincters and subsequent transmission of increased pressure through capillary beds into venules. Degenerative changes in the post-capillary venules occur as a result of increased pressure and lead to increasing vascular dilation and tortuosity. Ultimately, the vessels entangle in a tuft of disorganized vascular tissue within the submucosa and eventually erode into the mucosa (Fig. 14.1).

AVMs can occur anywhere along the gastrointestinal tract. Although they are most frequently detected in patients older than 60 years, the overall prevalence of AVMs is unknown. In a pooled analysis of three prospective studies of colonoscopic

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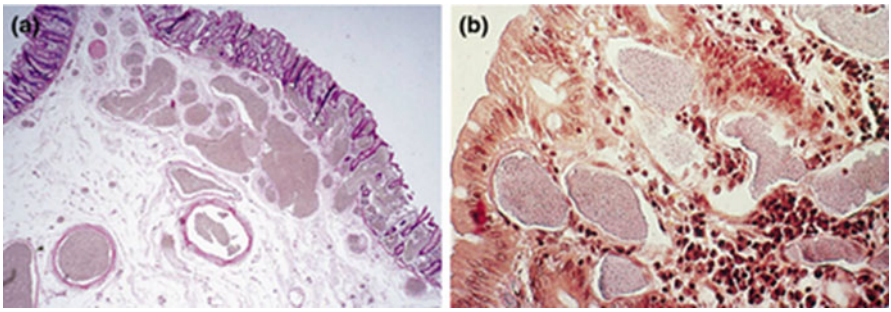

Fig. 14.1 Histological appearance of arteriovenous malformations. Panel (**a**): Histological appearance of a arteriovenous malformation with dilated thick-walled arteries and thin-walled veins. Panel (**b**): Histological appearances of arteriovenous malformation in the cecum showing dilated vessels within the mucosa adjacent to the epithelial cells (Reproduced with permission from Gordon FH, et al. Copyright Elsevier [30])

screening in healthy asymptomatic adults, colonic AVMs were detected in only 0.8 % of patients [4] but noted in 25 % of patients over 60 years of age in another report [5]. Conditions associated with increased prevalence of AVMs include end-stage renal disease [6], von Willebrand disease [7, 8], aortic stenosis [9–11], and in patients with left ventricular assist devices [12–14].

Colonic AVM is an important and common cause of lower gastrointestinal bleeding, especially in the elderly. This review will discuss the clinical presentation, diagnosis, and management of colonic arteriovenous malformations.

Clinical Presentation

Within the lower GI tract, AVMs are most common in the cecum (37 %) and sigmoid colon (18 %), followed by the ascending colon (17 %) and rectum (14 %) [15]. Overall, right-sided lesions are more common than left-sided lesions, accounting for 54–89 % of AVMs found [16]. Approximately 40–60 % of patients have more than one AVM at presentation, usually in the same portion of the GI tract [17, 18]. Synchronous lesions found elsewhere account for approximately 20 % of cases [19, 20]. In a series published by Steger et al. of 40 patients who underwent laparotomy for colonic AVM bleeding, 23 % of patients were found to have synchronous AVM in the small bowel either during the operation or at a later date [19]. Therefore, due to the multiplicity of AVMs occurrences, attributing one particular AVM as the bleeding source can only be confirmed by direct visualization either by colonoscopy or angiography.

Classically, symptomatic colonic AVMs present as sub-acute, low-grade, intermittent bleeding associated with defecation. This may manifest itself clinically as melena or hematochezia or as iron deficiency anemia. Bleeding from AVMs is self-limiting in 90 % of cases, but recurrences may occur in a subset of patients. Additionally, up to 15 % of patients may present with massive bleeding, requiring emergent intervention [21].

Diagnostic Workup

Initial Assessment

Assuming that the patient is hemodynamically stable, the initial examination of the patient should include a complete history and physical exam. Patients should be thoroughly questioned about associated comorbidities, as well as family and personal history of cancers, bleeding disorders, use of anticoagulation, previous episodes of GI bleeding, and their last colonoscopic examination. Physical exam can demonstrate findings associated blood volume loss, such as tachycardia, hypotension, and orthostatic changes. Basic laboratory data should be obtained, including a complete blood count, coagulation factor levels, and serum iron levels. Microcytic hypochromic anemia, reflecting iron deficiency, may be observed in 10–15 % of cases of patients.

If the patient is unstable, steps should be taken immediately to ensure adequate intravenous access, prepare at least 4–6 units of packed red blood cells, and begin volume resuscitation as soon as possible. This may require immediate transfer to a more optimal medical environment such as the emergency room or the intensive care unit, followed by definitive management via endoscopic, angiographic, or surgical means. Although the focus of this review is colonic AVM, a thorough endoscopic assessment is necessary to rule out neoplastic causes of GI bleeding.

Radiographic and Imaging

Stable patients that can tolerate bowel preparation should undergo endoscopic examination to identify and possibly treat small bleeding AVMs. Unstable patients with massive bleeding may benefit from localization of the bleeding source by ^{99m}Tc-labeled red blood cells radionuclide scanning, followed by selective mesenteric angiography. Tagged red cell scans is very sensitive, detecting even slow bleeds at 0.1 mL/min. However, this technique is limited in colonic AVMs that only intermittently bleed. The angiographic yield (sensitive to 1 mL/min) is low in these patients with delayed or negative radionuclide scans, and therefore should proceed to colonoscopy for diagnosis and treatment [22].

Helical CT angiography (CTA) can detect active bleeding from AVM and is a noninvasive test in patients with obscure bleeding sites. Junquera et al. have shown that CTA has high sensitivity (70 %) and specificity (100 %) in the detection of colonic AVMs in selected populations with experienced radiologists [23]. However, one disadvantage is that CTA is a purely diagnostic test without means for intervention.

Endoscopy

Endoscopic options for diagnosis of AVMs include upper endoscopy, deep small bowel enteroscopy, capsule endoscopy, and colonoscopy. Although AVMs are most commonly found in the colon, a combination of endoscopic techniques may be necessary because AVMs can be located throughout the GI tract. For colonic AVMs, the sensitivity of colonoscopy is estimated to be greater than 80 %, though true sensitivity cannot be calculated without performing the gold-standard angiography on every patient [24]. AVMs typically appear as 2–10 mm, flat, cherry-red lesions consisting of disorganized blood vessels that radiate from a central feeding vessel [25] (Fig. 14.2). Endoscopic biopsy is not indicated in benign appearing lesions due to the increased risk of bleeding.

If bowel preparation can be performed adequately, colonoscopy is safe and yields a specific diagnosis in more than 70 % of cases [26, 27]. In addition, endoscopic examination allows for both diagnosis as well as treatment of bleeding from relatively small AVMs. Due to the self-limiting nature of AVMs, there are concerns for over-treatment, as colonoscopy may be performed after bleeding had already stopped and therefore does not translate into true improvements in outcomes. For example, a retrospective review of 90 patients from a single institution with lower GI bleeding, colonoscopic identification of a definitive or probable source occurred in only 40 % of patients [28]. On the other hand, one hundred patients with lower GI bleeding at our institution was randomized to immediate colonoscopy or standard care algorithm with angiography and expectant colonoscopy, and found that immediate colonoscopy was able to identify a definite source of bleeding more often [29]. However, there were no differences in in-hospital mortality, hospital length of stay, ICU stay, transfusion requirement, risk of surgery, early rebleeding,

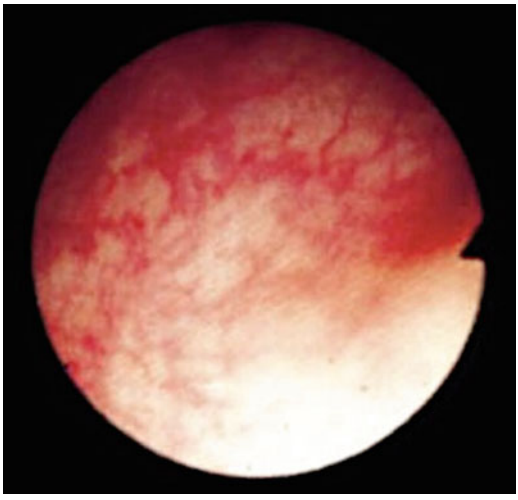

Fig. 14.2 Endoscopic appearance of arteriovenous malformations. GI arteriovenous malformations appear as small flat cherry-red lesions of disorganized vasculature (Reproduced with permission from Gordon FH, et al. Copyright Elsevier [30])

or late rebleeding at 5 years. This data suggests that success of colonoscopy in diagnosis of AVMs can be very operator-dependent.

There are several disadvantages in utilizing an endoscopic approach to diagnosing colonic AVMs. First, inadequate bowel preparation may lead to an incomplete evaluation of the colonic mucosa, which presents a frustrating diagnostic challenge in the face of recurring and intermittent bleeding. Additionally, visualization may be difficult in the face of active bleeding or in cases of over-insufflation. Moreover, low blood pressure or volume may decrease the chance of recognizing a symptomatic AVM.

Angiography

Angiography remains the gold standard for diagnosis of colonic AVMs. Diagnosis of hemorrhage from AVMs on angiography depends on the presence of contrast extravasation or "blush" generally on the anti-mesenteric border of the colon, in conjunction with early venous filling such that both the artery and the vein are silhouetted simultaneously (Fig. 14.3). Vasopressin or coil embolization may be utilized during angiography as potential treatment of bleeding AVMs. Disadvantages of performing angiography include the risk of kidney injury due to administration of intravenous contrast in a patient that is likely volume-depleted, possibility of negative studies in AVMs that only intermittently bleed, and the higher risk of colonic ischemia if proximal injections are performed.

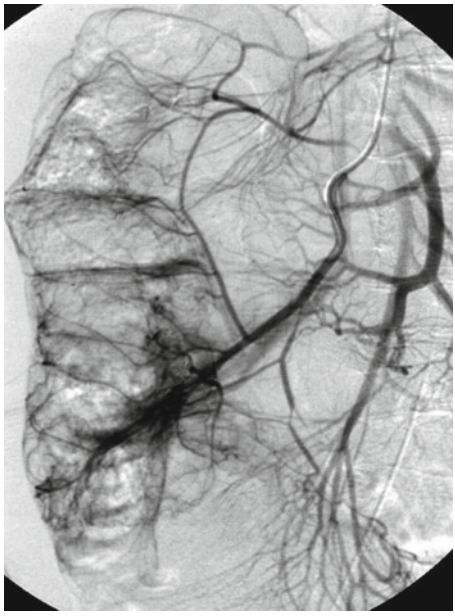

Fig. 14.3 Fluoroscopic appearance of arteriovenous malformations during angiography. Arterial phase of mesenteric angiogram showing arterial and simultaneous early venous filling of vasculature in the cecal wall (Reproduced with permission from Gordon FH, et al. Copyright Elsevier [30])

Management

Nonsurgical Strategies

Patients who present with lower GI bleeding from AVMs need to be assessed immediately for any disruptions to hemodynamic status. Any coagulopathic conditions should be corrected in conjunction with volume resuscitation as needed. In general, patients who are stable should be treated conservatively since the natural history of AVMs is often self-limiting. Additionally, treatment is not warranted in asymptomatic, incidental AVMs found on routine colonoscopy.

In patients undergoing colonoscopy for bleeding from AVMs, endoscopic sclerotherapy is an effective method for control of bleeding [30]. This can be accomplished using a variety of sclerosant material including epinephrine, ethanolamine, etc.[31, 32]. Alternatively, endoscopic laser photocoagulation can be used with a high degree of success [33]. As a last resort, colonoscopic tattoos can mark the bleeding lesions and guide surgical resection if less-invasive methods fail.

Angiography is indicated in patients who are hemodynamically unstable, in whom previous endoscopic intervention has failed, or in those who cannot tolerate surgery. In general, the use of super-selective mesenteric embolization for the treatment of lower GI bleeding is highly successful and relatively safe. In a small institutional study, only 3 of 38 patients treated for GI bleeding experienced ischemic complications, but all were managed conservatively without any interventions [34]. Additionally, angiography is less invasive compared to surgical exploration and can be reattempted. Alternatively, infusion of vasopressin into bleeding vessels is also an effective strategy. In comparing embolization versus intra-arterial vasopressin therapy, Gomes et al. demonstrated that although vasopressin achieved initial control of hemorrhage in 70 % of cases, several patients required surgical intervention for rebleeding, resulting in an overall success of 52 %[35]. Primary control of bleeding after embolization was achieved in 71 % of patients. Among patients who rebled, most were able to undergo repeat embolization, resulting in an overall success of 88 %. This led the authors to conclude that embolization appear to be the preferred method as it allowed for better control of GI hemorrhage as well as repeat attempts if the patient fails.

Surgical Treatment

When endoscopic and angiographic options are exhausted, surgery provides definitive management for patients with lower GI bleeding from AVMs. However, due to its morbidity, surgery should be limited to acute, uncontrollable, or recurrent presentations of GI bleeding. Patients indicated for surgery include those who continue to require more than four units of blood within a 24-h period to maintain hemodynamic stability, those who continue to bleed after 72 h from presentation, or in those

experiencing significant rebleeding within 1 week after the initial episode. Overall, surgical intervention for lower GI bleeding is necessary in 18–25 % of patients who require blood transfusion [36, 37].

Moreover, surgery should be reserved to patients in whom a bleeding source has been definitively identified. Blind segmental resection of the colon, segmental resection based tagged blood cell scan localization only, and emergency subtotal colectomy are associated with significant rates of rebleeding (as high as 33 %) and mortality (33–57 %) [38–40]. However, if the source of bleeding can be localized, limited segmental colectomy can be performed with significantly lower morbidity [38].

Conclusion

In conclusion, colonic arteriovenous malformation is a common etiology of lower GI bleeding, especially in the elderly. Diagnostic tools include radiographic and nuclear medicine scans, colonoscopy, and angiography. For the treatment of non-resolving bleeding from colonic AVMs, endoscopic and interventional options should be exhausted before attempting surgical resection.

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References

1. Margolis A, Heinbecker P, Bernard H. Operative mesenteric angiography in the search for the site of bleeding in unexplained gastrointestinal hemorrhage. A preliminary report. Surgery. 1960;48:534–7.
2. McAllister KA, Grogg KM, Johnson DW, Gallione CJ, Baldwin MA, Jackson CE, et al. Endoglin, a TGF-beta binding protein of endothelial cells, is the gene for hereditary haemorrhagic telangiectasia type 1. Nat Genet. 1994;8(4):345–51.
3. Boley SJ, DiBiase A, Brandt LJ, Sammartano RJ. Lower intestinal bleeding in the elderly. Am J Surg. 1979;137(1):57–64.
4. Foutch PG, Rex DK, Lieberman DA. Prevalence and natural history of colonic angiodysplasia among healthy asymptomatic people. Am J Gastroenterol. 1995;90(4):564–7.
5. Boley SJ, Sammartano R, Adams A, DiBiase A, Kleinhaus S, Sprayregen S. On the nature and etiology of vascular ectasias of the colon. Degenerative lesions of aging. Gastroenterology. 1977;72(4 Pt 1):650–60.
6. Zuckerman GR, Cornette GL, Clouse RE, Harter HR. Upper gastrointestinal bleeding in patients with chronic renal failure. Ann Intern Med. 1985;102(5):588–92.
7. Alhumood SA, Devine DV, Lawson L, Nantel SH, Carter CJ. Idiopathic immune-mediated acquired von Willebrand's disease in a patient with angiodysplasia: Demonstration of an unusual inhibitor causing a functional defect and rapid clearance of von Willebrand factor. Am J Hematol. 1999;60(2):151–7.
8. Duray PH, Marcal JM, Livolsi VA, Fisher R, Scholhamer C, Brand MH. Gastrointestinal angiodysplasia: a possible component of von Willebrand's disease. Hum Pathol. 1984;15(6):539–44.

9. Cody MC, O'Donovan TPB, Hughes Jr RW. Idiopathic gastrointestinal bleeding and aortic stenosis. Am J Dig Dis. 1974;19(5):393–8.
10. King RM, Pluth JR, Giuliani ER. The association of unexplained gastrointestinal bleeding with calcific aortic stenosis. Ann Thorac Surg. 1987;44(5):514–6.
11. Methodologic A. Aortic stenosis, idiopathic gastrointestinal bleeding, and angiodysplasia: is there an association? Gastroenterology. 1988;95:1670–6.
12. Elmunzer BJ, Padhya KT, Lewis JJ, Rangnekar AS, Saini SD, Eswaran SL, et al. Endoscopic findings and clinical outcomes in ventricular assist device recipients with gastrointestinal bleeding. Dig Dis Sci. 2011;56(11):3241–6.
13. Kushnir VM, Sharma S, Ewald GA, Seccombe J, Novak E, Wang I-W, et al. Evaluation of GI bleeding after implantation of left ventricular assist device. Gastrointest Endosc. 2012;75(5):973–9.
14. Demirozu ZT, Radovancevic R, Hochman LF, Gregoric ID, Letsou GV, Kar B, et al. Arteriovenous malformation and gastrointestinal bleeding in patients with the HeartMate II left ventricular assist device. J Heart Lung Transplant. 2011;30(8):849–53.
15. Höchter W, Weingart J, Kühner W, Frimberger E, Ottenjann R. Angiodysplasia in the colon and rectum. Endoscopic morphology, localisation and frequency. Endoscopy. 1985;17(5):182–5.
16. Meyer CT, Troncale FJ, Galloway S, Sheahan DG. Arteriovenous malformations of the bowel: an analysis of 22 cases and a review of the literature. Medicine. 1981;60(1):36–48.
17. Moreto M, Figa M, Ojembarrena E, Zaballa M. Vascular malformations of the stomach and duodenum: an endoscopic classification. Endoscopy. 1986;18(6):227–9.
18. Clouse RE, Costigan DJ, Mills BA, Zuckerman GR. Angiodysplasia as a cause of upper gastrointestinal bleeding. Arch Intern Med. 1985;145(3):458–61.
19. Steger A, Galland R, Hemingway A, Wood C, Spencer J. Gastrointestinal haemorrhage from a second source in patients with colonic angiodysplasia. Br J Surg. 1987;74(8):726–7.
20. Cappell MS. Spatial clustering of simultaneous nonhereditary gastrointestinal angiodysplasia. Dig Dis Sci. 1992;37(7):1072–7.
21. Reinus JF, Brandt L. Vascular ectasias and diverticulosis. Common causes of lower intestinal bleeding. Gastroenterol Clin North Am. 1994;23(1):1–20.
22. Ng DA, Opelka FG, Beck DE, Milburn JM, Witherspoon LR, Hicks TC, et al. Predictive value of technetium Tc 99m-labeled red blood cell scintigraphy for positive angiogram in massive lower gastrointestinal hemorrhage. Dis Colon Rectum. 1997;40(4):471–7.
23. Junquera F, Quiroga S, Saperas E, Pérez-Lafuente M, Videla S, Alvarez-Castells A, et al. Accuracy of helical computed tomographic angiography for the diagnosis of colonic angiodysplasia. Gastroenterology. 2000;119(2):293–9.
24. Richter J, Hedberg S, Athanasoulis C, Schapiro R. Angiodysplasia. Clinical presentation and colonoscopic diagnosis. Dig Dis Sci. 1984;29(6):481–5.
25. Skibba RM, Hartong WA, Mantz FA, Hinthorn DR, Rhodes JB. Angiodysplasia of the cecum: colonoscopic diagnosis. Gastrointest Endosc. 1976;22(3):177–9.
26. Jensen DM, Machicado GA, Jutabha R, Kovacs TO. Urgent colonoscopy for the diagnosis and treatment of severe diverticular hemorrhage. N Engl J Med. 2000;342(2):78–82.
27. Kok K, Kum C, Goh P. Colonoscopic evaluation of severe hematochezia in an Oriental population. Endoscopy. 1998;30(8):675–80.
28. Angtuaco TL, Reddy SK, Drapkin S, Harrell LE, Howden CW. The utility of urgent colonoscopy in the evaluation of acute lower gastrointestinal tract bleeding: a 2-year experience from a single center. Am J Gastroenterol. 2001;96(6):1782–5.
29. Green BT, Rockey DC, Portwood G, Tarnasky PR, Guarisco S, Branch MS, et al. Urgent colonoscopy for evaluation and management of acute lower gastrointestinal hemorrhage: a randomized controlled trial. Am J Gastroenterol. 2005;100(11):2395–402.
30. Gordon FH, Watkinson A, Hodgson H. Vascular malformations of the gastrointestinal tract. Best Pract Res Clin Gastroenterol. 2001;15(1):41–58.
31. Bemvenuti G, Jülich M. Ethanolamine injection for sclerotherapy of angiodysplasia of the colon. Endoscopy. 1998;30(6):564–9.

32. Suzuki N, Arebi N, Saunders BP. A novel method of treating colonic angiodysplasia. Gastrointest Endosc. 2006;64(3):424–7.
33. Gostout CJ, Bowyer BA, Ahlquist DA, Viggiano TR, Balm RK, editors. Mucosal vascular malformations of the gastrointestinal tract: clinical observations and results of endoscopic neodymium: yttrium-aluminum-garnet laser therapy. Mayo Clinic Proceedings; 1988: Elsevier.
34. Nicholson A, Ettles D, Hartley J, Curzon I, Lee P, Duthie G, et al. Transcatheter coil embolotherapy: a safe and effective option for major colonic haemorrhage. Gut. 1998;43(1):79–84.
35. Rose SC, Dunnick NR. Angiographic treatment of gastrointestinal hemorrhage: comparison of vasopressin infusion and embolization. Invest Radiol. 1987;22(4):354–6.
36. Bokhari M, Vernava AM, Ure T, Longo WE. Diverticular hemorrhage in the elderly—is it well tolerated? Dis Colon Rectum. 1996;39(2):191–5.
37. McGuire Jr HH. Bleeding colonic diverticula. A reappraisal of natural history and management. Ann Surg. 1994;220(5):653–6.
38. Browder W, Cerise EJ, Litwin MS. Impact of emergency angiography in massive lower gastrointestinal bleeding. Ann Surg. 1986;204(5):530–6.
39. Zuckerman GR, Prakash C. Acute lower intestinal bleeding: part I: clinical presentation and diagnosis. Gastrointest Endosc. 1998;48(6):606–17.
40. Farner R, Lichliter W, Kuhn J, Fisher T. Total colectomy versus limited colonic resection for acute lower gastrointestinal bleeding. Am J Surg. 1999;178(6):587–90.

Chapter 15
Bleeding Colorectal Tumors

Cristan E. Anderson and Paula I. Denoya

Overview

Colorectal tumors are an uncommon source of an acute life threatening hemorrhage, but a very common cause of occult gastrointestinal bleeding. In fact, asymptomatic anemia is a common indication for workup which ultimately reveals a cancer. This chapter provides a guide to the clinician regarding the presentation, workup, and treatment of bleeding colorectal tumors.

Incidence

Colonic tumors are the third most common source of lower gastrointestinal bleeding. In a study of 1112 patients admitted with lower gastrointestinal bleeding, Gayer et al. [1] found that 12.7 % of the patients had bleeding due to neoplasia. The most common sources of bleeding were diverticulosis (33.5 %) and hemorrhoids (22.5 %). The incidence did not change over time. The incidence of colorectal cancer has been steadily declining in the older population due to the increased prevalence of screening colonoscopy with polypectomy; however, the incidence in young patients continues to increase [2]. Therefore, colorectal cancer must be in the differential of all patients presenting with gastrointestinal bleeding, regardless of age.

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Etiology

Benign colonic tumors which can present with bleeding include hemangiomas, leiomyomas, lipomas, and adenomatous polyps. Polyps may be classified as serrated polyps, hamartomas, which can be associated with various genetic syndromes including Peutz–Jeghers syndrome, juvenile polyposis, and Cronkhite–Canada syndrome, and adenomas which are considered to be precancerous lesions [3]. Additionally, malignant lesions which can present with bleeding may include adenocarcinoma, squamous cell carcinoma, and lymphomas. This chapter focuses on the malignant lesions as they are more commonly responsible for significant bleeding.

Presentation and Evaluation

Bleeding from colorectal tumors can be divided into three broad categories with implications for workup and management: chronic, acute, and massive.

Chronic Bleeding

Chronic bleeding will most likely come to the clinician's attention upon review of laboratory values, either ordered as a routine screening procedure, or when obtained for symptoms, either related or unrelated to anemia. Symptomatic anemia may result in weakness, dizziness, fatigue, or occasionally signs of myocardial ischemia such as arrhythmia, or dyspnea upon exertion. Rarely, anemia may be profound enough to trigger a myocardial event such as angina or even myocardial infarction. Patients will present with an anemia due to occult blood loss. The initial workup of this patient should include a colonoscopy, and most patients will also undergo an upper endoscopy in conjunction with the colonoscopy. If a tumor is found, the anemia will usually be initially managed medically through blood transfusion or iron supplementation as needed while an appropriate preoperative evaluation ensues. The location just distal to the tumor should be tattooed at the time of colonoscopy to allow subsequent identification at surgery, unless the tumor is conclusively seen within the right colon as evidenced by either the ileocecal valve or the appendiceal orifice in view of the tumor. In addition, biopsies must be obtained for pathologic diagnosis. Occasionally, biopsies taken from the edge of the tumor will sample mucosa that has been displaced by the tumor, and will be falsely negative, but the surgeon should try to obtain pathologic confirmation of actual tissue diagnosis if at all possible, especially in a minimally symptomatic patient, as this may influence the extent of resection. In certain cases further genetic testing may be indicated by the pathologic results, such as testing for microsatellite instability, KRAS mutations, or for genetic disorders such as Lynch syndrome or familial adenomatous polyposis. Of course, all patients should have a family history elicited as well as any

personal history of cancer or colitis. If familial genetic syndromes are suspected, the patient should undergo evaluation and testing as this may impact the extent of the resection or indicate additional procedures which would ideally be performed in conjunction with the colectomy [4]. Next, in the case of cancer, the patient should undergo a preoperative staging evaluation [5]. In adenocarcinoma, this would include basic laboratory evaluation such as a carcinoembryonic antigen level [6], liver function tests, and a complete blood count. Additionally, computerized tomographic scan of the abdomen and pelvis with intravenous contrast should be done to evaluate the liver for metastatic disease [7]. In the case of a patient who cannot tolerate intravenous contrast due to renal disease or allergy, consideration could be given to liver evaluation with magnetic resonance imaging, or an ultrasound by an experienced radiologist. In addition to evaluating for metastatic disease, the CT scan will give the surgeon a rough "road map" of what may be encountered intraoperatively such as bulky lymph nodes or locally advanced disease, which may influence the choice of surgical approach. Additionally, the lungs must be evaluated for metastatic disease, which may be done by a chest X-ray, or more commonly by a computerized tomographic scan at the same time as the scan of the abdomen and pelvis. In general, cancer patients are best served by evaluation by a multidisciplinary tumor board, to optimize cancer care; however, this need is most acute in the patient with metastatic disease. Finally, the patient should undergo evaluation for fitness to undergo surgery, and proceed with oncologic resection of the lesion.

Acute Bleeding

The patient with acute bleeding will typically present with complaints of bright red blood per rectum which may or may not be associated with systemic signs of hypovolemia. Laboratory values will reveal a normocytic anemia. The patient should initially be treated as any other acute gastrointestinal bleed, with two large bore intravenous catheters, fluid resuscitation, nothing by mouth, nasogastric lavage to rule out an upper gastrointestinal source, hemodynamic support, and blood transfusion and correction of coagulation abnormalities as necessary. A careful history should be performed with documentation and review of any previous colonoscopy reports, change in bowel habits, personal and family history of cancer or colitis, and usage of any anticoagulant medications. Occasionally, in a malnourished patient or one with unsuspected liver dysfunction, coagulation parameters may be unexpectedly abnormal without use of anticoagulant medication. Next, a careful physical exam should be performed with attention to the abdominal exam which may occasionally reveal a palpable mass or hepatosplenomegaly. Of course, a careful rectal exam is essential, and the surgeon should perform a thorough digital rectal exam, anoscopy, and a rigid sigmoidoscopy, all of which can be done rapidly in the emergency room or office setting without the need for specialized equipment. This is to rule out a hemorrhoidal bleed and possibly identify a distal colon or rectal lesion. If the surgeon has access to flexible endoscopy, a flexible sigmoidoscopy is the ideal

method to evaluate the distal colon or rectum, and with careful lavage, the bleeding source may be able to be identified. Historically, colorectal cancer has been thought to be associated with older age; however, there is evidence that the incidence of rectal cancer in younger patients is increasing significantly, and thus young age should not lure the surgeon into omitting a thorough exam in the symptomatic patient [8]. Locating the source of bleeding is paramount, as if the bleed were to become massive, having a location and possible diagnosis will assist in proper operative intervention. Although some endoscopists may be reluctant to perform flexible endoscopy in an unprepped colon, blood is an excellent cathartic, and while time consuming, thorough lavage will usually remove the blood enough to allow adequate visualization and safe passage of the scope, which would be quite difficult if solid stool were present. If the patient is hemodynamically normal, and responsive to blood transfusion, and sigmoidoscopy reveals no distal source, it may be reasonable to defer definitive colonoscopy and prepare the patient with either enemas or a full bowel prep prior to colonoscopy. However, if the diagnosis is in question, a colonoscopy should be attempted with the understanding that it may not be possible, but in experienced hands the procedure should be safe and may guide therapy. In a randomized trial of 100 patients randomized to either urgent colonoscopy or angiography followed by expectant colonoscopy, the authors found that more lesions were identified in the urgent colonoscopy patients, though there was no significant difference in other outcomes such as mortality, morbidity, amount of blood transfusion, need for further intervention, or recurrent bleeding [9].

Massive Bleeding

Massive bleeding from colorectal neoplasia is rare [10], but the stepwise approach for any massive gastrointestinal bleed should allow the diagnosis to be obtained. First, appropriate resuscitation with isotonic fluid and packed red blood cells should be undertaken, and any coagulation abnormalities should be rapidly corrected. Next a focused history and physical should be obtained, to include a history of similar episodes, previous colonoscopy or cancers, and a careful rectal exam with palpation and sigmoidoscopy, either rigid or flexible. At this point, if the diagnosis is still unknown, the patient should proceed to nuclear medicine for a tagged red cell bleeding scan or to the interventional radiology suite for angiographic localization and embolization as appropriate (Fig. 15.1).

Treatment

As with any disease, treatment can be separated into two broad categories: damage control or palliative, and definitive. If time and the patient's condition permits, the surgeon will attempt definitive care; however, if the situation is such that the patient

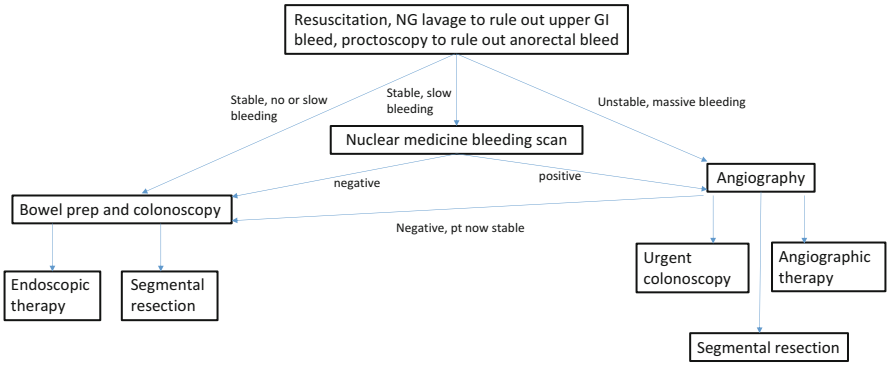

Fig. 15.1 Acute or massive lower GI bleeding algorithm

will not tolerate a definitive procedure without great risk, damage control becomes the best choice, either as the sole intervention, or ideally as a bridge to a definitive procedure.

Damage Control/Palliation

Endoscopic

If the tumor can be well visualized endoscopically, endoscopic control of the bleeding may be possible. There are many options available to the endoscopist, which are covered in more detail in other chapters, including monopolar or bipolar coagulation, infrared coagulation, and endoscopic clipping. Initially, attempting the lift the tumor with a mixture of saline and epinephrine may provide some local control of the bleeding to allow better visualization for a more definitive procedure (Fig. 15.2).

Angiographic

If the source of bleeding can be visualized angiographically, coiling or embolizing the feeding blood vessels may allow control of the bleeding and serve as a bridge to surgical resection (Fig. 15.3). After embolization, the practitioner should monitor the patient closely for signs of bowel ischemia, and if a tumor is suspected, the patient should proceed to colonoscopy for definitive diagnosis followed by segmental colectomy.

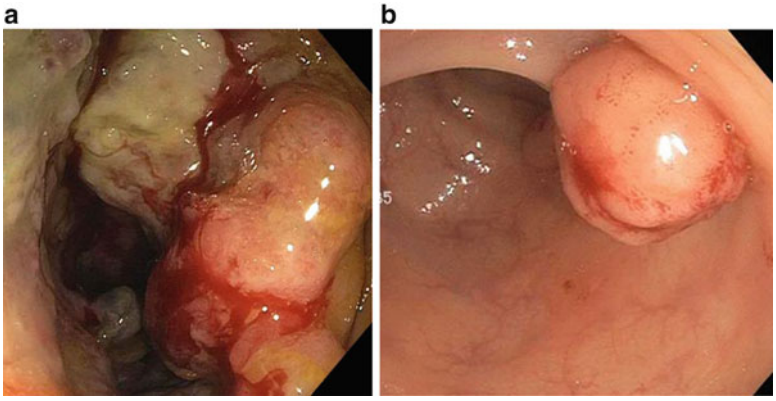

Fig. 15.2 Colonoscopic findings causing iron deficiency anemia (**a**) colon adenocarcinoma (**b**) colon adenoma

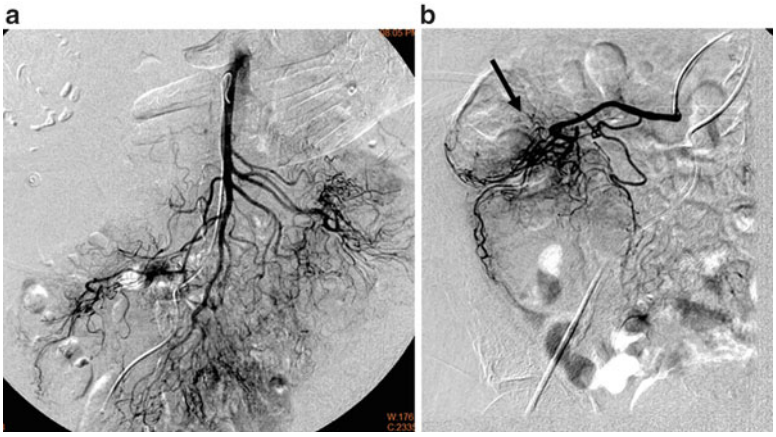

Fig. 15.3 (**a**) Superior mesenteric artery angiography (**b**) superselective angiography of a branch of ileocolic artery (*arrow* shows active bleeding)

Subtotal Colectomy

If the source of bleeding cannot be clearly elucidated and an upper source of bleeding has been ruled out through nasogastric lavage or upper endoscopy, the practitioner may occasionally resort to a subtotal colectomy. Ideally, the patient should have a bleeding scan prior to surgery, to confirm the bleeding source as colonic and appropriately target resection. However, occasionally, if the patient is in extremis or the technology not available, the clinician will proceed with a subtotal colectomy, understanding that if the source is not proximal to the duodenum, and the rectum is cleared, the most common source of bleeding will be the abdominal colon. In this case, the patient should be positioned in stirrups, to allow for a thorough sigmoidoscopic exam as a final effort to identify the bleeding source preoperatively. If the patient is having an emergent operation due to hemodynamic instability, minimally invasive methods should not be

attempted, and the patient approached by midline laparotomy. Intraoperative palpation may reveal a mass as the source of the bleeding, in which case a segmental resection may be attempted with the proximal portion of the bowel matured as an ostomy. If there is a long distal stump, this may be brought out as a mucus fistula. Ideally, a cancer resection should be done if a mass is palpated, as the patient is likely to have an adenocarcinoma and would then benefit from a formal lymphadenectomy. The proximal bowel should be examined for stigmata of bleeding, and if any bleeding is suspected, the entire proximal colon should be removed and an end ileostomy performed. If the bleeding had not been localized preoperatively, the proximal portion of the surgery should be divided first, and examined for stigmata of bleeding. If the surgeon believes the source may be proximal to the ileocecal valve, on table endoscopy should be performed from the distal segment heading proximal to identify the bleeding source. If there is no bleeding proximal to the ileocecal valve, and a mass is not felt, a subtotal colectomy will be the chosen procedure, with end ileostomy.

Segmental Resection

The surgeon should use great caution in performing a segmental resection for a massive bleed. The risk of recurrent massive bleed after segmental resection would be life threatening to the patient. Thus the surgeon should only proceed with this operation if it can be established beyond a doubt that the bleeding is arising from this segment. This will usually be the case only in obvious bleeding colorectal tumors and not in diverticular disease or arteriovenous malformation.

Local Excision

There may occasionally be cases in which local excision can be performed. The most likely situation would be a low lying rectal tumor that can be approached transanally. If the surgeon can remove the portion of the tumor which is bleeding, this approach can allow hemostasis to be obtained and provide tissue for pathologic analysis which will allow the planning of a definitive operation. Rarely, a tumor may be approached endoscopically and adequate hemostasis can be attained to allow visualization for endoscopic local excision. Again, this may allow the endoscopist to both attain hemostasis and obtain tissue for pathologic review. If laparotomy is performed for a lesion proximal to the rectum, segmental resection will almost always be required.

Rectal Packing

Another method of damage control is rectal packing. In an acutely bleeding rectal cancer, this may provide emergent hemostasis to allow the patient to be stabilized so that more definitive management can be planned. Radiation therapy may be an

option, and can be started prior to removing the packing. Packing should be done with either gauze or a hemostatic agent and provide pressure to the rectal wall. Careful documentation should be maintained of what type and quantity of material is used and packing should be performed in a manner which will allow the packing material to be removed transanally intact. If the patient tolerates it, this procedure can be done at the bedside at the time of initial evaluation, or may need to be performed under sedation.

Definitive Treatment

Definitive treatment is the ultimate goal for bleeding colorectal tumors whenever possible. The majority of tumors will be treated with segmental resection, but there will be a limited role for local therapy and radiation in selected patients. The surgeon should always preoperatively examine the patient to determine the optimal placement of an ostomy if it should become necessary. The patient should be examined sitting and standing to elicit the location of various skin folds and creases which would interfere with ostomy placement. If there is a high likelihood of an ostomy and the surgery is not emergent, the patient should preoperatively be assessed and counseled by a trained enterostomal therapist if available.

Segmental Resection

Abdominal Colon

In general segmental resection will be the gold standard for the treatment of colorectal cancers. An adequate cancer resection should include an adequate lymphadenectomy to obtain 12 lymph nodes to allow accurate cancer staging [11]. In addition, the surgeon should attempt to attain an R0 resection with no microscopic residual disease [12]. If this is not technically possible, due to invasion of vital structures, the patient will have a significantly poorer prognosis. In the abdominal colon and upper rectum, the surgeon should obtain a 5 cm margin proximally and distally along the luminal length of the bowel. Upon commencing the operation, the surgeon should confirm the preoperative staging by performing a thorough abdominal exploration, paying attention to the liver and the ovaries in the female for any evidence of metastatic disease. Surgery should be performed in the manner in which the surgeon is most experienced; however, there is evidence that laparoscopic surgery in the stable patient will allow a faster recovery and better long term outcomes. Resection in the surgical plane resulting in a complete mesocolic excision may favorably impact long term survival [13–15]. After surgery, a multidisciplinary team should review the pathology, and determine whether the patient would benefit from adjuvant chemotherapy. In general, the benefit is greatest for patients with positive lymph nodes,

metastatic disease, T4 disease, perforated tumors, and inadequate lymphadenectomy. Patients with peritoneal metastases may benefit from adjuvant treatment with hyperthermic intraperitoneal chemotherapy [16].

Rectum

Prior to performing a definitive resection in a rectal tumor, the tumor must be appropriately staged. As there is a defined role for neoadjuvant chemoradiation in rectal adenocarcinoma, patients must be appropriately selected to determine which ones will benefit from this approach. In addition to the basic colon cancer staging to evaluate for metastatic disease, the patient with rectal cancer should have rectal magnetic resonance imaging to assess for any lymphadenopathy, and endorectal ultrasound to assess the depth of invasion. Patients with evidence of lymphadenopathy or those in which the tumor will not be able to be removed with a 2 mm negative circumferential resection margin should undergo neoadjuvant chemoradiation to downstage the tumor and allow an R0 resection [17]. Additionally, most patients with T3 or T4 tumors will receive chemoradiation. After chemoradiation the tumor should be evaluated for changes in size and location, and the operation planned to ensure the attainment of negative margins. In advanced tumors this may require pelvic exenteration. In patients where there is a concern for a small amount of residual disease after resection, intraoperative radiation therapy may allow targeted destruction of unresectable disease [18].

In the mid and lower rectum, where a total mesorectal excision is performed, a smaller distal margin is sufficient. If possible, the surgeon should aim for a 2 cm distal margin, but if this would require an abdominal perineal resection, smaller negative margins will be acceptable, particularly if the patient is receiving chemoradiotherapy. In the upper rectum, a partial mesorectal excision is acceptable, and the surgeon should aim to remove the proportion of mesorectal tissue which will allow a 5 cm distal bowel resection to be performed, without coning in on the specimen so that the transection is perpendicular to the lumen of the rectum.

Most upper and mid rectal tumors will be able to be approached by an anterior resection. Low rectal tumors can be more challenging due to the confines of the bony pelvis, particularly in a male. The general principle is to perform a total mesorectal excision [19, 20] with a negative distal margin. If this cannot be attained by an abdominal approach due to the inability to complete the dissection transabdominally, the surgeon can complete the distal dissection transperineally. In some cases, this is only possible or desirable by performing an abdominal perineal resection and leaving the patient with a permanent end stoma. In highly selected patients, an intersphincteric resection may be performed if the surgeon has sufficient experience. In this case, the dissection is started at the anal canal, in the intersphincteric groove, and a portion of the internal sphincter is removed in order to complete the distal dissection. A coloanal anastomosis is performed [21]. Again, cancer surgery principles apply, and this procedure is only indicated if it will allow removal of the

cancer with an acceptable functional and oncologic result. As such, the tumor should not invade the external sphincter, negative margins must be obtainable, and the patient must have acceptable preoperative anorectal function to allow continence with the removal of the internal sphincter. This requires careful preoperative evaluation and is perhaps best performed in the highly selected, carefully counseled patient with excellent preoperative function and who did not require neoadjuvant radiation. All patients will notice changes in bowel function after rectal cancer surgery in terms of increased frequency of bowel movements and decreased ability to delay bowel movements, and those with a lower resection will notice the greatest change. The surgeon and patient must weigh whether the functional changes will be acceptable to the patient long term, or if the patient would be best served with a permanent stoma.

In addition to the functional changes of the bowel after rectal surgery, the patient undergoing proctectomy is at risk for nerve damage due to the association of vital structures in a confined space. There may be some benefit to robotic surgery in order to allow greater visualization and increased instrument mobility, although there is a disadvantage in terms of loss of tactile feedback. Barnajian et al. reported no difference in the quality of total mesorectal excision in open, laparoscopic, or robotic cases, but found an improvement in circumferential resection margin in the robotic group [22]. Finally, rectal cancer surgery should be performed by highly experienced surgeons to ensure the patient has an adequate cancer resection with the lowest risk of functional complications [23].

Local Excision of Rectal Tumors

Local excision may be offered as a definitive treatment for benign polyps in the rectum. It may be considered in early rectal cancers for patients who are high risk for radical surgery or refuse radical surgery. In order to perform local excision for a T1 cancer, a full thickness excision should be done with an adequate margin. This is only appropriate for lesions occupying less than 1/3 of the circumference of the bowel wall, due to the risk of luminal narrowing if a larger defect is created and closed. Additionally, the surgeon must remember that T1 cancers have a 12 % chance of associated lymph node metastasis, and the patients should be carefully staged before surgery to evaluate for this possibility. After surgery, the ability to accurately stage the lymph nodes may be confounded by reactive lymphadenopathy. There is a significant risk of local recurrence as well, which has been reported to be as high as 20 % [24]. Due to these factors, the disease free survival and 5 year survival for early rectal cancer treated by local excision is much worse than those treated by radical surgery. This approach should be pursued only when the patient has been well informed of these risks and refuses to undergo definitive surgery or has significant comorbidities that prevent radical surgery. Approaches to local excision would include a traditional transanal excision with an anoscope or transanal minimally invasive approach: transanal endoscopic microsurgery (TEM) or transanal minimally invasive surgery (TAMIS). In general, traditional transanal surgery

is most appropriate for a low lying tumor which can be easily exposed using an anoscope. For higher lying tumors, TEM or TAMIS approaches are more appropriate. In the case of TEM, this involves placing an operating scope transanally and using specialized instruments to remove the tumor [25]. The tumor is optimally positioned toward the floor of the operating room, and the patient position is manipulated to allow this positioning to occur. In TAMIS, a port is placed in the anal canal, similar to a single site laparoscopic surgery port and the rectum insufflated to allow visualization [26]. Nonspecialized laparoscopic or robotic instruments can then be used to remove the tumor. Both of these techniques offer a magnified view and the ability to operate at a greater distance from the anal verge than is possible with a traditional transanal approach.

In the setting of a bleeding rectal tumor, local excision can be considered as a way to manage the acute bleeding and does not preclude proceeding with definitive oncologic resection in the near future, after the patient is optimized for surgery. This approach allows for excellent visualization of the tumor and access to cautery or excision techniques.

Conclusion

Lower gastrointestinal bleeding due to colonic neoplasm is initially treated as any other lower bleed, with a goal of stabilizing the patient and localizing the source. Once this is accomplished, the choice of definitive treatment is made based on location, patient comorbidities, and risk of repeat bleeding. In the setting of acute massive bleeding, subtotal colectomy for abdominal sources and transanal therapy for rectal sources are the most commonly utilized options. In a controlled or chronic bleeding patient, definitive therapy for colorectal cancer should be performed.

References

1. Gayer C, Chino A, Lucas C, Tokioka S, Ymasaki T, Edelman D, Sugawa, C. Acute lower gastrointestinal bleeding in 1,112 patients admitted to an urban emergency medical center. Surgery. 2009;146(4):600–7.
2. Siegel R, Desantis C, Jemal A. Colorectal cancer statistics. CA Cancer J Clin. 2014;64(2): 104–17.
3. Church JM, Kalady MF. Colorectal polyps. In: Corman ML, editor. Corman's colon and rectal surgery. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013. p. 1014–78.
4. Galiatsatos P, Foulkes WD. Familial adematous polyposis. Am J Gastroenterol. 2006;101(2): 385–98.
5. Benson 3rd AB, Venook AP, Bekaii-Saab T, Chan E, Chen YJ, Cooper HS, et al. NCCN clinical practice guidelines in oncology: colon cancer. J Natl Compr Canc Netw. 2014;12(7): 1028–59.
6. Compton CC, Fielding LP, Burgart LJ, Conley B, Cooper HS, Hamilton SR, et al. Prognostic factors in colorectal cancer. College of American Pathologists consensus statement. Arch Pathol Lab Med. 2000;124:979–94.

7. Balthazar EJ, Megibow AJ, Hulnick D, Naidich DP. Carcinoma of the colon: detection and preoperative staging by CT. Am J Roentgenol. 1988;150(2):301–6.
8. Tawadros PS, Paquette IM, Hanly AM, Mellgren AF, Rothenberger DA, Madoff RD. Adenocarcinoma of the rectum in patients under age 40 is increasing: impact of signet-ring cell histology. Dis Colon Rectum. 2015;58(5):474–8.
9. Green BT, Rockey DC, Portwood G, Tarnasky PR, Guarisco S, Branch MS, et al. Urgent colonoscopy for evaluation and management of acute lower gastrointestinal hemorrhage: a randomized controlled trial. Am J Gastroenterol. 2005;100(11):2395–402.
10. Gordon PH. Malignant neoplasms of the colon. In: Gordon PH, Nivatvongs S, editors. Principles and practice of surgery for the colon, rectum, and anus. 3rd ed. New York, NY: Informa Healthcare USA, Inc; 2007. p. 489–643.
11. LeVoyer RE, Gigurdson ER, Hanion AL, Mayer RJ, Macdonald JS, Catalano PJ, et al. Colon cancer survival is associated with increasing number of lymph nodes analyzed: a secondary survey of intergroup trial INT-0089. J Clin Oncol. 2003;21:2912–9.
12. Edge S, Byrd DR, Compton C, Fritz AG, Greene FL, Trotti A, editors. AJCC cancer staging manual. 7th ed. New York: Springer; 2010.
13. West NP, Morris EJA, Rotimi O, Cairns A, Finan PJ, Quirke P. Pathology grading of colon cancer surgical resection and its association with survival: a retrospective observational study. Lancet Oncol. 2008;9:857–65.
14. Kontovounisios C, Kinross J, Tan E, Brown G, Rasheed S, Tekkis P. Complete mesocolic excision in colorectal cancer: a systematic review. Colorectal Dis. 2014;17:7–16.
15. Bertelsen CA, Neuenschwander AU, Jansen JE, Wilhelmsen M, Kirkegaard-Klitbo A, Tenma JR, et al. Disease-free survival after complete mesocolic excision compared with conventional colon cancer surgery: a retrospective, population-based study. Lancet Oncol. 2015;16:161–8.
16. Verwaal VJ, van Ruth S, De Bree E, van Sloothen GW, van Tinteren H, Boot H, et al. Randomized trial of cytoreduction and hyperthermic intraperitoneal chemotherapy veruss systemic chemotherapy and palliative surgery in patients with peritoneal carcinomatosis of colorectal cancer. J Clin Oncol. 2003;21(20):3737–43.
17. Nagtegaal ID, Marijen CAM, Kranenbarg EK, van de Velde CJ, van van Krieken JH. Pathology Review Committee; Cooperative Clinical Investigators. Circumferential margin involvement is still an important predictor of local recurrence in rectal carcinoma: not one millimeter but 2 millimeters is the limit. Am J Surg Pathol. 2002;26(3):350–7.
18. Cima RR. Rectal cancer: locally advanced and recurrent. In: Beck DE, Roberts PL, Saclariddes TJ, et al., editors. The ASCRS textbook of colon and rectal surgery. 2nd ed. New York, NY: Springer; 2011. p. 761–72.
19. Heald RJ, Humband EM, Ryall RDH. The mesorecum in rectal cancer surgery—the clue to pelvic recurrence? Br J Surg. 1982;69:613–6.
20. Nagetegaal ID, van de Velde CJ, van der Worp E, Kapiteijn E, Quirke P, van Krieken JH. Cooperative Clinical Investigators of the Dutch Colorectal Cancer Group Macroscopic evaluation of rectal cancer resection specimen: clinical significance of the pathologist in quality control. J Clin Oncol. 2002;20:1729–34.
21. Rullier E, Laurent C, Bretagnol F, Rullier A, Vendrely V, Zerbib F. Sphincter-saving resection for all rectal carcinomas: the end of the 2 cm distal rule. Ann Surg. 2005;241:465–9.
22. Barnajian M, Pettet D, Kazi E, Foppa C, Bergamaschi R. Quality of total mesorectal excision and depth of circumferential resection margin in rectal cancer: a matched comparison of the first 20 robotic cases. Colorectal Dis. 2014;16:603–9.
23. Wibe A, Eriksen MT, Syse A, Myrvold HE, Søreide O, Norwegian Rectal Cancer Group. Total mesorectal excision for rectal cancer—what can be achieved by a national audit? Colorectal Dis. 2003;5(5):471–7.
24. Doornebosch PG, Ferenschild FT, de Wilt JH, Dawson I, Tetteroo GW, de Graaf EJ. Treatment of recurrence after transanal endoscopic microsurgery (TEM) for T1 rectal cancer. Dis Colon Rectum. 2010;53(9):1234–9.
25. Saclarides TJ, Smith L, Ko ST, Orkin B, Buess G. Transanal endoscopic microsurgery. Dis Colon Recum. 1992;35(12):1183–91.
26. Atallah S, Albert M, Larach S. Transanal minimally invasive surgery: a giant leap forward. Surg Endosc. 2010;24(9):2200–5.

Part III
GI Bleeding from an Unknown Source

Chapter 16
Evaluation of the Guaiac-Positive Patient

Rebecca Burbridge and Melissa Teitelman

Introduction

One of the most common encounters a physician must deal with is the presence of occult gastrointestinal blood loss. The prevalence may reach up to 1 in 20 adults. The detection of occult blood is important because a person may lose up to 150 ml of blood from the proximal gastrointestinal tract before producing overt melena [1]. Before proceeding further, an important distinction must be made between *occult* gastrointestinal blood loss and *obscure* gastrointestinal bleeding. The following definitions were derived from the 2007 American Gastroenterological Association (AGA) Institute position statement on obscure gastrointestinal bleeding [2]:

Occult bleeding: initial presentation of a positive fecal occult blood test (FOBT) results and/or iron-deficiency anemia, when there is no evidence of visible blood to the patient or physician.

Obscure bleeding: bleeding from the gastrointestinal tract that persists or recurs without an obvious etiology after upper endoscopy, colonoscopy, and radiological evaluation of the small bowel (such as by small bowel follow through or enteroclysis).

As stated in the above definition, occult gastrointestinal blood loss is most commonly brought to the physician's attention by a positive fecal occult blood test or iron-deficiency anemia if the blood loss has been chronic. This chapter primarily focuses on the differential diagnosis and systemic approach to the evaluation of the guaiac-positive patient.

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Fecal Occult Blood

The main focus of testing for fecal occult blood has been in the screening for colorectal cancer. Annual testing has been recommended by the American Cancer Society, World Health Organization, and the US Preventative Services Task Force. A positive test is often followed up with endoscopic or radiological evaluation of the gastrointestinal tract. The cumulative effect of this testing method has been shown to reduce mortality rates from colorectal cancer to up to 33 % [3]. However, anywhere from 2 to 16 % of people who are tested for fecal occult blood will have a positive result [4, 5]. The high rate of false-positive results often leads to unnecessary health-care expenses.

Gastrointestinal blood loss must exceed 10 ml/day (normal <2 ml/day) to produce a positive fecal occult blood test. This degree of bleeding (10 ml/day) will produce a positive test only 50 % of the time by most testing methods [6]. Multiple factors determine the likelihood of detecting fecal occult blood. These factors include the sensitivity of the particular test which is being used, the anatomic level of bleeding, the frequency and rate at which the causative lesion bleeds, and bowel motility. All of these factors influence the intraluminal metabolism of hemoglobin.

Commercially Available Fecal Occult Blood Tests

There are three main categories of fecal occult blood testing methods commercially available: guaiac based, heme–porphyrin based, and immunochemical based. Depending on the particular testing method used, occult blood loss can be detected from any location in the gastrointestinal tract.

Guaiac-Based Tests

Guaiac-based fecal occult blood testing is the most commonly used testing method because of its simplicity. Guaiac is a colorless compound that turns blue on exposure to hemoglobin. Guaiac tests are more sensitive for the detection of bleeding from the lower gastrointestinal tract than from the upper gastrointestinal tract because hemoglobin is degraded as it travels down the gastrointestinal tract [7]. The likelihood that a guaiac test will detect fecal occult blood is related to the quantity of hemoglobin in the stool, which in turn is affected by the size and location of the bleeding lesion [8].

A drawback of guaiac-based testing is the high rate of false-positive results (Table 16.1). For this reason, patients are often asked to avoid certain peroxidase-containing foods and red meats for 3 days prior to stool testing. Nonsteroidal anti-inflammatory drugs and aspirin (if taking greater than one adult aspirin per day) should be avoided for 7 days prior to testing unless the patient is on a cardioprotective regimen. Oral iron was once believed to cause false-positive guaiac results. This line

Table 16.1 Substances causing false-positive and false-negative guaiac testing results

False positives	False negatives
Radishes	Vitamin C
Turnips	Antacids
Cantaloupe	Heat
Bean sprouts	Acid pH
Cauliflower	Impaired bowel
Broccoli	Motility
Grapes	"Dry stools"
Artichokes	
Mushrooms	
Horseradish	
Oranges	
Bananas	
Red meats	
NSAIDS/ASA	
Sucralfate	
Cimetidine	
Halogens	
Toilet bowel sanitizer	

of thinking was thought to be secondary to the fact that oral iron gives the stool a dark green/black appearance which may be confused with the blue color of a positive guaiac reaction. However, even in large amounts, oral iron does not cause guaiac to react positively [9]. Like iron, bismuth also gives the stool a dark color, but has no effect on the results of guaiac testing.

Heme–Porphyrin-Based Tests

The heme–porphyrin test is the most sensitive test to detect fecal occult blood loss, but its use is limited by a high false-positive rate. The test utilizes a fluorometric assay to quantify heme and heme-derived porphyrin in stool. Unlike the guaiac-based tests, vegetable peroxidases do not affect the result. However, the presence of myoglobin in red meats will artificially raise the amount of heme–porphyrin in the sampled stool, thus creating a false-positive result. The test is useful for detecting occult bleeding in any part of the gastrointestinal tract, but one major drawback is the inability to perform this test at the bedside as the stool samples must be sent to a reference laboratory for processing.

Immunochemical-Based Tests

The principal behind immunochemical tests is the use of antibodies directed against human globin epitopes to detect colonic blood [10]. Because globin molecules are degraded in the upper gastrointestinal tract, this test is useful only in the evaluation

of lower gastrointestinal bleeding. The test is highly sensitive for the detection of colonic blood [11]; however, it is quite cumbersome for the physician to perform. Room temperature storing of the sample must be avoided as loss of hemoglobin antigenicity may occur. The sample cannot be processed in the physician's office, instead needing to go to a special laboratory for processing.

Differential Diagnosis

Although the focus of fecal occult blood testing is in the screening of colorectal cancer, there are many other causes of occult gastrointestinal bleeding. A detailed history and physical examination often provide the first clues to the etiology. An important component of the history to ascertain is an updated medication list. In particular, nonsteroidal anti-inflammatory drugs [12], potassium chloride, and alendronate all have the potential to injure the gastrointestinal mucosa. The use of anticoagulants may increase the rate of blood loss from preexisting lesions, thereby increasing the incidence of occult bleeding. Some familial conditions may predispose to a patient to bleeding tendencies (i.e., hereditary hemorrhagic telangiectasia or von Willebrand's disease).

In general, any GI lesion from the mouth to the anus may cause occult GI bleeding. It is important to recognize that lesions in the upper GI tract have the potential to cause occult GI bleeding. These lesions may include epistaxis, bleeding gums, esophagitis, peptic ulcers, esophageal and gastric malignancies, hemobilia, and angiodysplasias to name a few. Traditional colonic sources of occult blood loss include large colon polyps, colon adenocarcinoma, inflammatory bowel disease, ischemic bowel, hemorrhoids, and anal fissures.

Iron-Deficiency Anemia

Iron-deficiency anemia is the most common form of anemia worldwide. The anemia is reflective of a chronic blood loss, typically in excess of 5–10 ml/day over many weeks. In the USA, the prevalence of iron-deficiency anemia reaches 1–2 % of the adult population [13]. Iron deficiency without anemia is much more common, presenting in up to 11 % of women and 4 % of men. In women, the anemia is most often identified in the premenopausal years because of menstrual and pregnancy-associated iron losses. In all other age groups, the primary cause of iron-deficiency anemia is chronic blood loss from the gastrointestinal tract. Therefore, investigation of the gastrointestinal tract is essential in the evaluation of iron-deficiency anemia [7].

Table 16.2 Possible causes of occult gastrointestinal bleeding

Infectious causes	Tumors and neoplasms
Ascariasis	Primary adenocarcinoma
Amebiasis	Lymphoma
Hookworm	Leiomyoma
Strongyloidiasis	Large adenoma (>1.5 cm)
Tuberculous enterocolitis	Metastases
Cytomegalovirus	Miscellaneous causes
Inflammatory disorders	Oropharyngeal lesions
Peptic ulcer disease	Medications
Cameron erosions	Long distance running
Celiac sprue	Hemobilia
Whipple disease	Epistaxis
Inflammatory bowel disease	Vascular causes
Erosive gastropathy	Angiodysplasias
Nonspecific colitis	Portal hypertensive gastropathy
Eosinophilic gastroenteritis	Dieulafoy lesion
Cecal ulcer	Gastric antral vascular ectasia
Solitary rectal ulcer	Hemangiomas

Differential Diagnosis

The differential diagnosis of iron-deficiency anemia encompasses many of the same disorders that can cause occult GI blood loss. Although GI blood loss is the most common etiology for iron-deficiency anemia, reduced gastrointestinal absorption of iron and dietary deficiency can also cause iron-deficiency anemia [14]. Diseases associated with generalized malabsorption and/or achlorhydria can predispose to iron-deficiency anemia. Celiac disease has been shown to be present in up to 8.5 % of patients with iron deficiency unresponsive to conventional iron supplementation [15]. Other causes of iron-deficiency anemia that are not associated with blood loss include intravascular hemolysis and gastric bypass for morbid obesity (Table 16.2).

Approach to Evaluation of Occult Gastrointestinal Blood Loss

The initial evaluation of fecal occult blood loss should begin with the colon as this is the most common site of occult blood loss. The choice of the initial tests is often driven by the expertise of the physician ordering the exam, complication rates, costs of the test, and the patient's overall medical condition [16]. Although there is controversy over which test should be initially performed, the consensus is that colonoscopy is the preferred method of choice for direct evaluation of the colon; however, other options are available [17]. These options include air contrast barium

enema, flexible sigmoidoscopy in conjunction with barium enema, and computed tomographic colonography. Air contrast barium enema is very accurate for detecting large colonic lesions when performed by an experienced radiologist; however, the accuracy in detecting smaller lesions is much less when compared to standard colonoscopy [18]. Likewise, CT colonography has not been shown to match the accuracy of colonoscopy when evaluated head to head in studies [19]. It is important to remember that synchronous upper and lower gastrointestinal tract lesions are rare. Therefore, further evaluation is not needed if the potential source is found on initial examination.

When the colon does not yield an etiology for the source of occult blood loss, attention must then be turned to the upper gastrointestinal tract (proximal to the third portion of the duodenum). Studies have demonstrated that significant potential upper gastrointestinal sites of bleeding have been identified in patients with a normal colonoscopy and a positive fecal occult blood test [20]. As stated earlier, it is important to remember that significant upper GI tract lesions can bleed sufficiently to produce a positive guaiac result [21]. Initial upper gastrointestinal tract testing should start with an upper endoscopy. If iron-deficiency anemia is present, small bowel biopsies should be performed to exclude celiac disease.

If the colonoscopy and upper endoscopy do not reveal an etiology of the occult bleeding source, consideration needs to be given to evaluation of the small intestine distal to the reach of the standard upper endoscope. However, this depends on the clinical scenario. For the positive fecal occult blood test in the absence of iron-deficiency anemia, careful observation is recommended as the prognosis appears to be favorable. When iron-deficiency anemia is present and no etiology is found after initial investigation, a trial of iron supplementation is warranted. If the anemia fails to correct with iron supplementation, attention must then be focused on the mid-to-distal small intestine. Evaluation should proceed with capsule endoscopy or radiographic imaging to localize the potential source of bleeding followed by standard enteroscopy or balloon enteroscopy if treatment needs to be performed. Endoscopic evaluation of the mid-to-distal small intestine is discussed in a later chapter.

References

1. Schiff L, Stevens RJ, Shapiro N, Goodman S. Observations on the oral administration of citrate blood in man. Am J Med Sci. 1942;203:409.
2. Raju GS, Gerson L, Das A, Lewis B. AGA Institute medical position statement on obscure gastrointestinal bleeding. Gastroenterology. 2007;133(5):1694–6.
3. Mandel JS, Church TR, Bond JH. Colorectal cancer mortality: effectiveness of biennial screening for fecal occult blood. J Natl Cancer Inst. 1999;91(5):434–7.
4. Levin B, Hess K, Johnson C. Screening for colorectal cancer. A comparison of 3 fecal occult blood tests. Arch Intern Med. 1997;157:970.
5. Mandel JS, Bond JH, Church TR, Snover DC, Bradley GM, Schuman LM et al. Reducing mortality from colorectal cancer by screening for fecal occult blood. N Engl J Med. 1993;328:1365.

6. Stroehlein JR, Fairbanks VF, McGill DB, Go VL. Hemoccult detection of fecal occult blood quantitated by radioassay. Am J Dig Dis. 1976;21:841.
7. Rockey D. Occult gastrointestinal bleeding. N Engl J Med. 1999;341:38–46.
8. Dybdahl JH, Daae L, Larsen S. Occult faecal blood loss determined by a 51 Cr method and chemical tests in patients referred for colonoscopy. Scand J Gastroenterol. 1984;19:245.
9. Laine LA, Bentley E, Chandrasoma P. Effect of oral iron therapy on the upper gastrointestinal tract. A prospective evaluation. Dig Dis Sci. 1988;33:172.
10. Allison JE, Tekawa IS, Ransom LJ, Adrain AL. A comparison of fecal occult-blood tests for colorectal cancer screening. N Engl J Med. 1996;334:155.
11. Saito H. Screening for colorectal cancer by immunochemical fecal occult blood testing. Jpn J Cancer Res. 1996;87:1011.
12. Bowen B, Yuan Y, James C, Rashid F, Hunt RH. Time course and pattern of blood loss with ibuprofen treatment in healthy subjects. Clin Gastroenterol Hepatol. 2005;3:1075.
13. Looker AC, Dalman PR, Carroll MD, Gunter EW, Johnson CL. Prevalence of iron deficiency in the United States. JAMA. 1997;277(12):973–6.
14. Annibale B, Capurso G, Chistolini A, D'Ambra G, DiGiulio E, Monarca B et al. Gastrointestinal causes of refractory iron deficiency anemia in patients without gastrointestinal symptoms. Am J Med. 2001;111(6):439–45.
15. Corazza GR, Valentini RA, Andreani ML, D'anchino M, Leva MT, Ginaldi L et al. Subclinical coeliac disease is a frequent cause of iron deficiency anaemia. Scand J Gastroenterol. 1995;30(2):153–6.
16. Kim LS, Koch J, Yee J, Halvorsen R, Cello JP, Rockey DC. Comparison of patients' experiences during imaging tests of the colon. Gastrointest Endosc. 2001;54:67.
17. Rockey DC, Koch J, Yee J, McQuaid KR, Halvorsen RA. Prospective comparison of air-contrast barium enema and colonoscopy in patients with fecal occult blood: a pilot study. Gastrointest Endosc. 2004;60:953.
18. Rockey DC, Paulson E, Niedzwiecki D, Davis W, Bosworth HB, Sanders L et al. Analysis of air contrast barium enema, computed tomographic colonography, and colonoscopy: prospective comparison. Lancet. 2005;365:305.
19. Cotton PB, Durkalski VL, Pineau BC, Palesch YY, Mauldin PD, Hoffman B et al. Computed tomographic colonography (virtual colonoscopy): a multicenter comparison with standard colonoscopy for detection of colorectal neoplasia. JAMA. 2004;291:1713.
20. Rockey DC, Cello JP. Evaluation of the gastrointestinal tract in patients with iron-deficiency anemia. N Engl J Med. 1993;329(23):1691–5.
21. Rockey DC, Auslander A, Greenberg PD. Detection of upper gastrointestinal blood with fecal occult blood tests. Am J Gastroenterol. 1999;94:344.

Chapter 17
Endoscopic Techniques for Evaluating Small Bowel Blood Loss: Video Capsule and Device-Assisted Enteroscopy

Daniel Wild

Introduction

The small bowel remains the least-explored portion of the alimentary tract though the demand for direct luminal evaluation of the small bowel is increasing, most often to search for a source of bleeding, which is found in the small bowel in approximately 5% of cases [1]. Several of the small bowel's anatomic features make direct luminal evaluation difficult. Estimates of its average length vary widely between radiographic, cadaveric, and surgical studies but it extends for approximately 450 cm (14.7 ft) in most average-sized adults, a feature that presents a formidable obstacle to endoscopic exploration [2]. Compounding its length is its considerable elasticity and the fact that, except for the duodenum, it lacks retroperitoneal fixation which allows it to float relatively freely within the abdomen. Flexible endoscopes are therefore stymied by stretching of the bowel and repeated looping of the scope. Given these obstacles, investigation of the small bowel lumen has lagged behind the advances in colonoscopy and esophagogastroduodenoscopy. Physicians have generally relied on radiographic procedures for imaging the small bowel and, if direct evaluation was required, a laparoscopy with manual small bowel manipulation with or without endoscopy directed through the mouth or an enterotomy was required.

The first dedicated technique used for direct endoscopic evaluation of the small bowel distal to the duodenum was sonde enteroscopy which was first described in 1986 [3]. This cumbersome scope was 2.7 m in length and only 5 mm in diameter, thin enough to allow for transnasal passage. It was limited by non-deflectable tip and the absence of a working channel and with it, the inability to perform therapeutic intervention. These lengthy procedures required unsedated patients to remain

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under direct observation for several hours. Given these limitations, sonde enteroscopy was not widely adopted and considerable room for improvement existed.

The state of small bowel endoscopy changed dramatically with the release and widespread adoption of two revolutionary techniques in 2001: the wireless video capsule endoscope (VCE) and the double balloon enteroscope (DBE). This evolution of equipment and techniques has continued with the development of spiral enteroscopy (SE) in 2006 and single balloon enteroscopy (SBE) with both a balloon overtube in 2007 and then a through-the-scope balloon system in 2013. Together, this array of techniques to perform device-assisted enteroscopy (DAE) now allows for direct evaluation and deployment of the full complement of luminal therapies along the entire length of small intestine.

Video Capsule Endoscopy

Since its approval and release to the market in 2001, video capsule endoscopy (VCE) has been widely adopted by providers and still remains the most widely used modality for direct inspection of the small bowel lumen. Currently, there are three approved, commercially available VCE systems in the USA: PillCam SB (Given Imaging, Israel); Endocapsule (Olympus Corporation, PA); and MiroCam (Medivators, MN), all of which are very similar.

Technique

Each system requires the ingestion of a small camera capsule that is approximately 10×25 mm. The capsule passes freely through the intestinal tract, transmitting images wirelessly to a small recorder pack that is worn by the patient throughout the exam. Some of the systems allow for real-time viewing of the images but most studies are viewed in their entirety after the images have all been captured. The recording time is limited by the battery life of the capsules which ranges from 8 to 12 h, a duration that allows for a complete exam of the entire small bowel in more than 80 % of procedures [4]. When viewed, the images can be seen singly, doubly or 4 at a time and at speeds that range from 1 to 40 frames per second. Most experienced VCE readers can read an exam in 20–30 min.

A VCE study is designed to evaluate the entire small bowel so it is only considered complete if it reaches the cecum. Progress through the small bowel can be unpredictable and delayed in patients with decreased motility. The use of bowel preparation prior to capsule ingestion remains controversial and the data on this topic do not allow for a clear consensus. Several studies have investigated the benefits of using a full or partial purgative prep prior to capsule ingestion and though there is considerable heterogeneity among prep ratings, 2 meta-analyses suggest that some prep prior to VCE improves image quality and visualization [5, 6].

Indications, Contraindications, and Complications

VCE is most commonly used to evaluate patients with OGIB and its benefit for this purpose is undeniable. Its other widely accepted use is to evaluate for Crohn's disease in patients with suspicious symptoms and an unremarkable colonoscopy. VCE can also be used for surveillance in patients with polyposis syndromes that can involve the small bowel including familial adenomatous polyposis (FAP) and Peutz–Jeghers Syndrome.

The only risk of VCE is that of capsule retention in the small intestine. This does not occur in patients with normal small bowel anatomy but is a consideration in patients suspected to have masses or strictures (as may be the case with Crohn's disease). This risk of retention is approximately 1 % [4]. When retention occurs it is generally asymptomatic and because, in most cases, the capsule continues to float freely within the small bowel lumen, it rarely causes bowel obstruction. If there is high pretest concern for capsule retention, a patency capsule (Agile Patency Capsule, Given Imaging, Israel) can be performed. This device is a biodegradable "dummy" capsule with the same dimensions as a video capsule. It is equipped with radiofrequency identification tag that can be detected with a scanner in order to determine whether the capsule is still present within the abdomen. It starts to dissolve 30 h after ingestion and is completely dissolved in 40–80 h.

Efficacy

In a review of 14 studies, encompassing almost 400 patients comparing the performance of VCE compared to other modalities to investigate the cause of OGIB, VCE proved superior to both push enteroscopy (diagnostic yield 63 % vs. 28 %) and small bowel barium radiography (diagnostic yield 67 % vs. 8 %) with a number needed to test to achieve one additional clinically significant finding with VCE over these modalities of 3 [7]. This study also revealed VCE to perform better than both magnetic resonance imaging of the small bowel and computed tomography enteroclysis.

A large review of 227 studies involving close to 23,000 VCE exams, the majority of which were performed for the evaluation of OGIB, the diagnostic yield of these exams was 60 % and vascular abnormalities, most notably small bowel angioectasias, were the most common finding, found in half of exams performed for OGIB [4].

Double Balloon Enteroscopy

Hinori Yamamoto first reported the technique of double balloon enteroscopy in 2001 and a dedicated double balloon enteroscopy (DBE) system was released commercially in 2003 (Fujinon Inc, Japan) [8]. This system's standard scope has a 200 cm working length and diameter of 8.5 mm. A therapeutic enteroscope with a larger diameter 9.4 mm which allows for a larger working channel of 2.8 mm is also available.

Technique

A soft, inflatable latex balloon is attached to the tip of the scope and this balloon is controlled with a designated air pump. A soft overtube that is 145 cm in length and has a diameter of 12.2 mm with a second inflatable latex balloon at its tip is back loaded over the scope. The scope and overtube are advanced into the small bowel using multiple successive maneuver cycles: first the enteroscope is passed into the small bowel until forward progress ceases; the enteroscope balloon is then inflated to anchor its position within the small bowel; the overtube is then advanced forward to the end of the enteroscope at which time its balloon is also inflated; the scope with its balloon inflated and overtube with its balloon inflated are then withdrawn to straighten the small bowel; the scope's balloon is then deflated and the scope is again pushed forward thus initiating the cycle again. Fluoroscopy can be used to help visualize and remove loops in the small intestine. This procedure can be performed with either an oral (anterograde) or anal (retrograde approach) though the latter is more difficult because of the several feet of colon that must be traversed before accessing the ileum.

Indications, Contraindications, and Complications

DBE is most commonly performed for the evaluation of small bowel bleeding. It has a variety of other uses including: foreign body retrieval for objects that have migrated beyond the pylorus; polyp surveillance and resection in patients with polyposis syndromes that involve the small bowel; enteral feeding tube placement; dilation of established strictures and reaching excluded areas in patients with altered anatomy including ERCP access in those who have undergone Roux-en-Y gastric bypass.

In anyone who is medically stable enough to undergo sedation and endoscopic evaluation, there are no clear contraindications to DBE though the depth of the exam can be limited in patients with dense intra-abdominal adhesions. DBE has an excellent safety profile with a major complication rate of less than 1 % in US and non-US centers. In addition to expected endoscopic complications like perforation and bleeding, acute pancreatitis remains a rare and perplexing complication of DBE. Most attribute this to balloon inflation near the ampulla resulting in temporary increases in pressure within the pancreatic duct though this complication has also been described in retrograde procedure so the mechanism is still poorly understood [11]. The duration and nature of these procedures, generally mandates that DBE be performed under general anesthesia or with monitored anesthesia care both of which have their own rare complications.

Efficacy

DBE is difficult and time-consuming to learn and perform with a mean procedure time of 102 min in a multicenter US study [9]. Despite this limitation, the procedure typically allows for very deep insertion into the small bowel with mean depths of

insertion of 360 cm for anterograde procedures and 165 cm for retrograde procedures in this same US trial. Japanese and European centers generally have more experience and expertise with the technique than their American counterparts and a review of 66 studies spanning the first decade of DBE showed that a complete exam of the entire small bowel with either an oral or combined oral and anal approach was possible in 44 % of procedures [10].

Like VCE, the majority of DBE exams are performed for OGIB with a suspected small bowel source. The overall diagnostic yield of these exams is high, approaching 70 % with findings varying by the region of the study. The most dominant findings in studies conducted in Western nations are vascular abnormalities, most typically angioectasias, which comprise 66 % of the abnormalities found. Unlike with VCE, DBE and other device-assisted modalities allow for full therapeutic capability so when vascular lesions like angioectasias are encountered, they can be treated, most typically with argon plasma coagulation [Figs. 17.1, 17.2, 17.3, and 17.4]. On the contrary, inflammatory changes surpass vascular abnormalities (38 % vs. 27 %) in studies from Eastern centers. Neoplasms are also more commonly encountered in Eastern centers, 26 %, than in those in the West, 14 % [10].

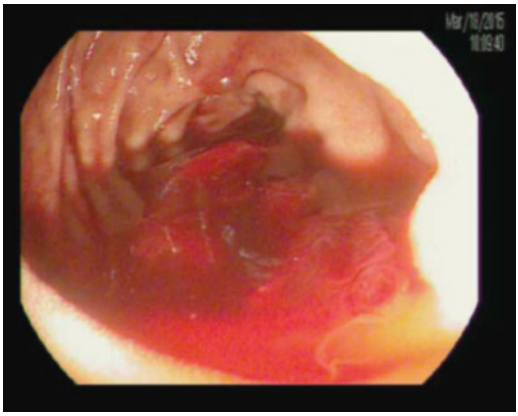

Fig. 17.1 Blood and clot in lumen of small bowel from a briskly bleeding angioectasia

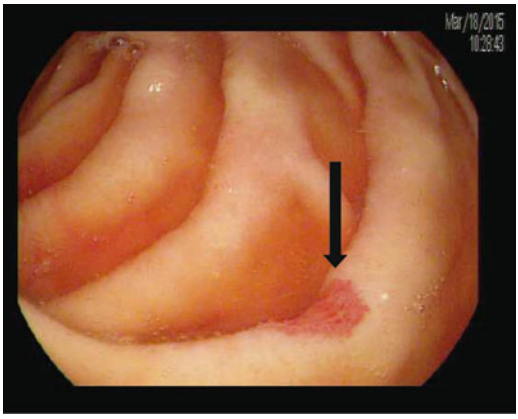

Fig. 17.2 Angioectasia revealed after blood is cleared

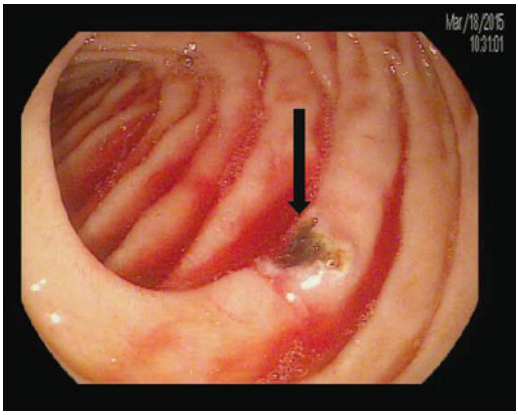

Fig. 17.3 Angioectasia successfully ablated with argon plasma coagulation

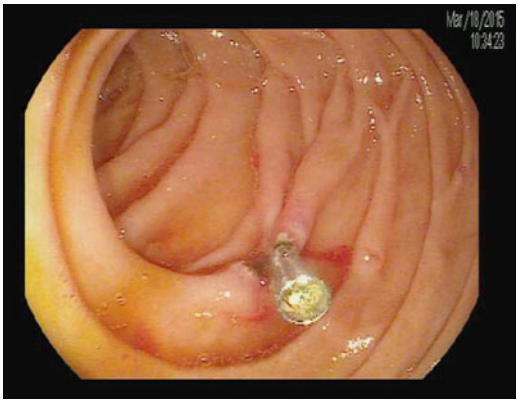

Fig. 17.4 Hemostatic clip placed across angioectasia site as an additional hemostatic measure

Single Balloon Enteroscopy

Single balloon enteroscopy (SBE) was developed in an effort to allow for deep small bowel insertion with a shorter procedure time and easier learning curve than DBE.

Technique

There are two currently available SBE systems, each of which utilizes a slightly different technique. The first system utilizes the EVIS EXERA II SIF-Q180 enteroscope and the Single Use Splinting Tube (Olympus Corporation, PA). This utilizes a 140-cm balloon-tipped overtube but unlike DBE, the scope is a standard 200-cm enteroscope without an additional balloon at its tip. The tip of the scope is used as

an anchor by deflecting it maximally which then allows for the overtube balloon to be deflated and advanced. The balloon is then inflated, allowing the scope tip to be straightened and both scope and overtube to be withdrawn, thus pleating the small bowel. This maneuver is repeated until further advancement is no longer possible.

More recently, the Navi-Aid AB (SMART Medical Systems, Israel) has allowed SBE to be performed using a through-the-scope balloon instead of a balloon overtube [12]. Currently, because of the balloon's size, this procedure necessitates using an adult colonoscope with a 3.8 mm working channel. Once the scope is advanced into the small bowel, either from an anterograde or retrograde approach, the balloon is passed through the channel and advanced forward into the small bowel lumen. The balloon is then inflated, anchoring itself distal to the scope in the small bowel lumen. The scope is then advanced while the balloon is simultaneously withdrawn until the two meet. The balloon is then deflated and advanced again into the small bowel lumen. The cycle is repeated until maximal insertion is reached [Figs. 17.5, 17.6, and 17.7].

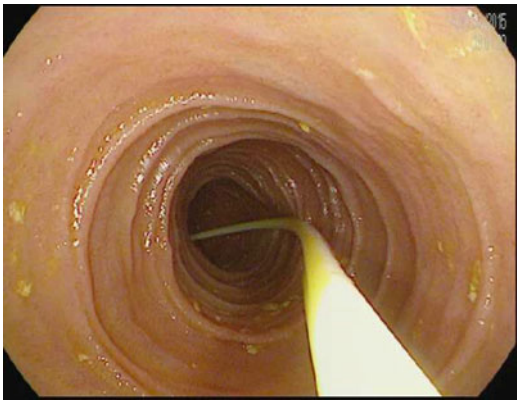

Fig. 17.5 Navi-Aid balloon catheter traversing the small bowel lumen ahead of the colonoscope

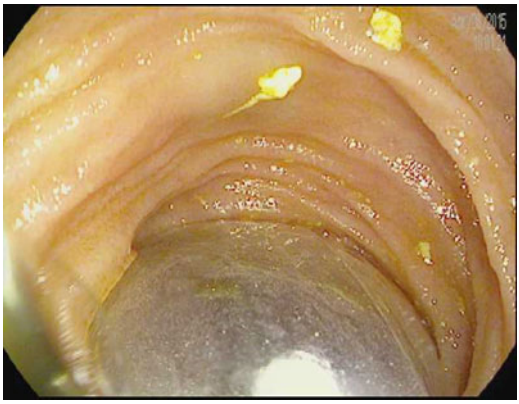

Fig. 17.6 Navi-Aid balloon inflated, retracting the bowel back towards the scope as the scope is simultaneously advanced

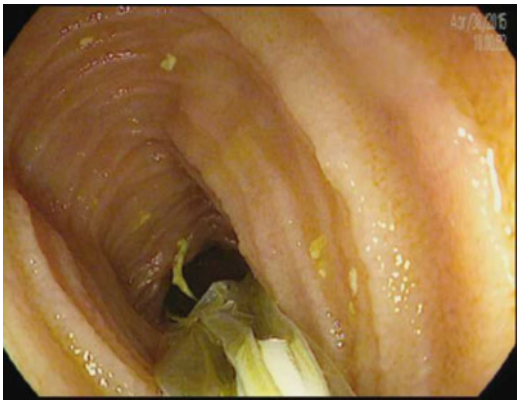

Fig. 17.7 Navi-Aid balloon deflated in preparation for a repeated maneuver

Indications, Contraindications, and Complications

SBE shares the same indications as DBE but is often used when time or ease of use are more important than achieving maximal depths of insertion as may be the case is a lesion is suspected to be in the proximal small bowel based on previous imaging. Operator training and instrument availability also factor in to the decision to use SBE over DBE

SBE is widely considered safe with the majority of studies showing no significant complications, though perforations have been described [13–18].

Efficacy

In general, SBE allows for quicker but less deep insertion into the small bowel. Mean times for anterograde procedures range from 49 to 83 min and average insertion depths for anterograde and retrograde procedures are 132 and 73 cm respectively [13, 14]. In expert hands, complete small bowel inspection is possible (with a bidirectional approach) in up to 22 % of patients [15]. Diagnostic yields for SBE range from 47 to 58 % with therapy being performed in 24 to 48 % of cases [13–15].

Spiral Enteroscopy

Originally devised as a colonoscopy-assist device, when the potential to use a spiral overtube to advance an endoscope into the small bowel was realized, the original overtube was modified and refined to its current form and the technique of spiral enteroscopy (SE) was born.

Technique

This technique, first published in 2008, adopts a different principle to drive an endoscope deeply into the small bowel [19]. During the anterograde procedure, the Discovery SB overtube (Spirus Medical, MA) which is covered with soft, screw-like spirals, is fitted over an Olympus SIF-180 enteroscope. When the overtube and scope are coupled, they are advanced together by spiral rotation of the overtube which pleats the small bowel back across the scope. When uncoupled, the overtube acts as an anchor, holding the pleated small bowel in place, while the scope is then advanced further using the more standard push technique. The procedure can also be performed with a retrograde approach using the larger Vista overtube (Spirus Medical, MA) and either a standard pediatric colonoscope or designated enteroscope. In this approach, the spiral overtube is used primarily to straighten and splint the colon in order to prevent looping of the scope within the colon so the ileum can be entered more deeply. Though very difficult and time-consuming, it is possible to maneuver both the overtube and scope into the ileum in which case retrograde advancement into the ileum can be achieved with spiral turning.

Indications, Contraindications, and Complications

SE shares the same indications as the other device-assisted techniques. Here again, some depth of insertion may be sacrificed in favor of reduced procedural times and operator training and equipment availability are factors.

Like DBE and SBE, there are no clear contraindications other than those that would preclude deep sedation and endoscopy in general. Abdominal adhesions can also limit the depth of insertion possible with SE. Because of the large diameter of the overtube, a larger bite block is required to allow for safe passage of the overtube though the patient's mouth. Rarely, patients with limited jaw flexibility, micrognathia or other facial abnormalities, may not be able to accommodate the bite block's large size.

Though the relatively large size of the overtube and, at times, vigorous turning this technique demands led some to fear that SE would be wrought with complications, this procedure has proven very safe with a mean perforation rate across the literature of only 0.34 % [21]. Unlike with DBE, acute pancreatitis has not been described following SE.

Efficacy

SE typically allows for deep small bowel insertion with relatively short procedure times with reported mean depths of insertion for anterograde procedures ranging from 250 to 268 cm achievable in 43–45 min [19, 20]. When SE and DBE have been

directly compared, DBE has been proven to allow for deeper insertion into the small bowel for both anterograde and retrograde approaches, 346 cm vs. 268 cm and 209 cm vs. 78 cm respectively and complete small bowel inspection is more likely with DBE than SE in skilled hands, 92 % vs. 8 %, but importantly, both techniques have similar diagnostic and therapeutic yields [22].

Summary

This is an exciting time for the evolving field of small bowel enteroscopy. Currently, there are several available complementary techniques that allow for direct inspection of and therapy within the small bowel lumen. VCE remains the primary diagnostic modality because of it wide availability, high likelihood of visualizing the entire small bowel, and very low complication rates. When VCE findings mandate therapeutic intervention or clinical circumstances indicate a high probability of small bowel bleeding, inflammation, or neoplasm, DAE can be performed to target lesions deep in the small bowel lumen. DBE was the first modern technique and is still the most widely used. In expert hands, DBE can allow access to the entire small bowel though these exams are difficult and time-consuming to perform. The more recently developed techniques of SBE and SE allow access to large portions of the small bowel, typically in less time than is required for DBE. These procedures have shown that vascular lesions, most notably angioectasias, comprise the most frequent small bowel abnormalities while neoplasm and inflammatory changes remain less common but important small bowel pathologies.

References

1. Gerson L, Fidler J, Cave D, Leighton J. ACG clinical guideline: diagnosis and management of small bowel bleeding. Am J Gastroenterol. 2015;110:1265–87.
2. Hosseinpour M, Behdad A. Evaluation of small bowel measurement in alive patients. Surg Radiol Anat. 2008;30(8):653–5. PMID:18685804.
3. Tada M, Shimizu S, Kawai K. A new transnasal sonde type fiberscope (SSIF type VII) as a pan-enteroscope. Endoscopy. 1986;18(4):121–4.
4. Liao Z, Gao R, Xu C, Li ZS. Indications and detection, completion, and retention rates of small-bowel capsule endoscopy: a systematic review. Gastrointest Endosc. 2010;71(2):280–6. PMID:20152309.
5. Kotwal VS, Attar BM, Gupta S, Agarwal R. Should bowel preparation, antifoaming agents, or prokinetics be used before video capsule endoscopy? A systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2014;26(2):137–45. PMID: 24220156.
6. Rokkas T, Papaxoinis K, Triantafyllou K, Margantinis G, Pistiolas D. Does purgative preparation influence the diagnostic yield of small bowel video capsule endoscopy?: A meta-analysis. Am J Gastroenterol. 2009;104(1):219–27.
7. Triester SL, Leighton JA, Leontiadis GI, Fleischer DE, Hara AK, Heigh RI, et al. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with obscure gastrointestinal bleeding. Am J Gastroenterol. 2005;100(11):2407–18.

8. Yamamoto H, Sekine Y, Sato Y, Higashizawa T, Miyata T, Iino S, et al. Total enteroscopy with a nonsurgical steerable double-balloon method. Gastrointest Endosc. 2001;53(2):216–20.
9. Mehdizadeh S, Ross A, Gerson L, Leighton J, Chen A, Schembre D, et al. What is the learning curve associated with double-balloon enteroscopy? Technical details and early experience in 6 U.S. tertiary care centers. Gastrointest Endosc. 2006;64(5):740–50.
10. Xin L, Liao Z, Jiang YP, Li ZS. Indications, detectability, positive findings, total enteroscopy, and complications of diagnostic double-balloon endoscopy: a systematic review of data over the first decade of use. Gastrointest Endosc. 2011;74(3):563–70. PMID: 21620401.
11. Gerson LB, Tokar J, Chiorean M. Complications associated with double balloon enteroscopy at nine US centers. Clin Gastroenterol Hepatol. 2009;7(11):1177–82. PMID: 19602453.
12. Ali R, Wild D, Shieh F, Diehl DL, Fischer M, Tamura W, et al. Deep enteroscopy with a conventional colonoscope: initial multicenter study by using a through-the-scope balloon catheter system. Gastrointest Endosc. 2015;82(5):855–60.
13. Upchurch BR, Sanaka MR, Lopez AR, Vargo JJ. The clinical utility of single-balloon enteroscopy: a single-center experience of 172 procedures. Gastrointest Endosc. 2010;71(7):1218–23. PMID: 20409544.
14. Frantz DJ, Dellon ES, Grimm IS, Morgan DR. Single-balloon enteroscopy: results from an initial experience at a U.S. tertiary-care center. Gastrointest Endosc. 2010;72(2):422–6. PMID: 20541189.
15. May A, Färber M, Aschmoneit I, Pohl J, Manner H, Lotterer E, et al. Prospective multicenter trial comparing push-and-pull enteroscopy with the single- and double-balloon techniques in patients with small-bowel disorders. Am J Gastroenterol. 2010;105(3):575–81.
16. Ramchandani M, Reddy DN, Gupta R, Lakhtakia S, Tandan M, Rao GV, et al. Diagnostic yield and therapeutic impact of single-balloon enteroscopy: series of 106 cases. J Gastroenterol Hepatol. 2009;24(10):1631–8.
17. Khashab MA, Lennon AM, Dunbar KB, Singh VK, Chandrasekhara V, Giday S, et al. A comparative evaluation of single-balloon enteroscopy and spiral enteroscopy for patients with midgut disorders. Gastrointest Endosc. 2010;72(4):766–72.
18. Aktas H, de Ridder L, Haringsma J, Kuipers EJ, Mensink PB. Complications of single-balloon enteroscopy: a prospective evaluation of 166 procedures. Endoscopy. 2010;42(5):365–8.
19. Akerman PA, Agrawal D, Cantero D, Pangtay J. Spiral enteroscopy with the new DSB overtube: a novel technique for deep peroral small-bowel intubation. Endoscopy. 2008;40(12):974–8. PMID: 19065477.
20. Morgan D, Upchurch B, Draganov P, Binmoeller KF, Haluszka O, Jonnalagadda S, et al. Spiral enteroscopy: prospective U.S. multicenter study in patients with small-bowel disorders. Gastrointest Endosc. 2010;72(5):992–8.
21. Chavalitdhamrong D, Adler DG, Draganov PV. Complications of enteroscopy: how to avoid them and manage them when they arise. Gastrointest Endosc Clin N Am. 2015;25(1):83–95. PMID: 25442960.
22. Messer I, May A, Manner H, Ell C. Prospective, randomized, single-center trial comparing double-balloon enteroscopy and spiral enteroscopy in patients with suspected small-bowel disorders. Gastrointest Endosc. 2013;77(2):241–9. PMID: 23043851.

Chapter 18
Provocative Angiography

Mayur B. Patel, Charles Y. Kim, and Michael J. Miller

Introduction

Determination of the site and etiology of lower gastrointestinal (GI) bleeding may lead to frustration for internists, gastroenterologists, surgeons, diagnostic, and interventional radiologists. The intermittent nature, variable severity, and changes in patient hemodynamic status can result in multiple rounds of diagnostic imaging without an answer. This is especially true in the setting of negative upper endoscopy and limited lower endoscopy due to the amount of blood within the colon. Despite significant blood loss, traditional diagnostic examinations such as tagged red cell scans may be negative or positive without definitive localization of the responsible site. Mesenteric angiography is the definitive imaging tool for localization of the bleeding site. This can, however, lend to confusion when multiple vascular lesions are identified without visible bleeding. With the addition of super-selective microcatheter embolization, angiography has become both diagnostic and therapeutic, and in many institutions, the first-line intervention for the management of lower GI bleeding. The main limitations of angiographic detection are the temporal relation of the arteriogram to the intermittent nature of the bleed, as well as the volume of bleeding. To help improve the sensitivity of angiography, practices have combined catheter-based delivery of pharmacologic agents with intermittent angiography in hopes of increasing the yield of angiography without compromising safety or efficacy. Now, known as provocative angiography, this technique has been applied to assess fore-, mid-, and hindgut bleeding that is refractory to traditional diagnostic and therapeutic modalities.

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Review

In 1982 Rösch [1] first described "pharmacoangiography" to address difficult lower GI bleeding. In his retrospective review of four cases in three patients they described the use of tolazoline, heparin, and streptokinase to improve the detection of the anatomical site of bleeding followed by surgical resection of the offending source. The agents were administered either independently or together resulting in active extravasation of contrast. The theory behind the approach was that vasoconstriction, platelet aggregation, and the creation of a soft intravascular plug resulted in transient hemostasis. Presumably, this patient population teeters on a line between hemostasis and bleeding, such that intentional vasodilation, anticoagulation, and/or fibrinolysis can help reactivate and identify hemorrhage.

In 1987, Koval [2] reported the impact of applying more aggressive angiographic techniques. In 63 consecutive patients referred for angiography, multiple factors were retrospectively reviewed. Incorporation of pharmacologic augmentation of mesenteric angiography in the setting of lower GI bleeding improved the diagnostic yield from 32 % (12/37) to 65 % (17/26) with the use of heparin, tolazoline, and streptokinase. Streptokinase was used in two patients and a positive result was found in one of the two. Of the ten patients given agents, eight had a lesion identified angiographically. Another factor predictive of positive angiography was the requirement of transfusion of ≥3 units of packed red blood cells in the 48 h prior to angiography. This correlated with a positive study in 66 % of cases compared with 17 %, in those requiring <3 units of packed red blood cell transfusion.

Glickerman [3] reported the first use of urokinase to identify bleeding in the midgut distribution in 1998. They described management of a patient who had been transfused over 150 units of packed red blood cells, undergone seven angiographic procedures, two exploratory laparotomies with one resection, yet continued to bleed. They performed the provocative arteriogram with selective arterial injection into the superior mesenteric artery with 10,000 U heparin, 1,000,000 U urokinase, and 25 mg tolazoline. Among the numerous vascular ectasias, they were able to pinpoint the entity responsible for bleeding. A 3 French catheter was later placed prior to surgery to allow for staining of the distribution with methylene blue which aided in the resection. In the ensuing 9 months, the patient experienced no further bleeding.

Heparin infusion has been used to unmask or amplify bleeding in order to identify a bleeding site angiographically. Following a papaverine augmented angiogram identifying 6 out of 18 GI bleeding patients, 24 h heparin administration in the remaining patients localized six additional bleeds. Thus, 12 out of 18 bleeds (67 %) were localized angiographically by Mernagh [4]. This is similar to the yield obtained by Koval.

In 1998, Malden et al. [5] published the results of the first prospective use of provocative radiography, specifically scintigraphy. From September 1991 to May 1996 ten examinations were performed in 9 patients that had two or more hospitalizations for substantial GI bleeding, defined as bleeding requiring hospitalization, transfusion, or a 6 % decrease in hematocrit. All recruited patients could tolerate angiography and/or surgical intervention, if needed. All patients had a negative angiogram within 4 months, and all patients had negative upper endoscopy, lower

endoscopy, and a small bowel study (enteroclysis, enteroscopy, or single-contrast barium study). Patients were given systemic heparin and urokinase and scintigraphy was performed. Four of the patients had positive scintigraphy within the first 4 h. However, positive angiography and intervention occurred in only two of the four. Thus only two of the ten studies yielded a positive result with the use of systemically heparin and urokinase.

A few series have looked at arterial catheter directed provocation of lower GI hemorrhage. Bloomfeld [6] reported a diagnostic success with two of seven patients (29 %) utilizing intra-arterial tolazoline, heparin, and/or urokinase in a provocative angiographic study. Ryan et al. [7] reported 6 out of 16 patients (38 %) were positive after provocation with systemic heparin, and selective tolazoline and intra-arterial tPA. Three of these patients were treated with super-selective embolization, but one of these patients required a resection 2 months later for recurrent bleeding. The three remaining positive provocations were treated nonoperatively. Interestingly, of the ten patients who were negative during provocation, two had vascular abnormalities, and five rebled. Widlus and Salis [8] described inducing colonic hemorrhage in eight out of nine patients (89 %) with occult, recurrent, massive lower GI bleeding using reteplase as the fibrinolytic agent. Microcoil embolization was successful in five, and failed in one, who required a colon resection. Hemorrhage spontaneously stopped in two patients. All patients underwent a colonoscopy within 10 days and were without significant findings.

Based upon the available data, an assumption that reteplase may be the optimal agent for the induction of bleeding may be considered. However, equivalent dosing of the medications as well as other factors may have contributed to the variability in sensitivities. Of the fibrinolytic agents available, reteplase has lower fibrin specificity than tPA, however, it has superior clot penetration. Likely, the economic impact of stocking these medications in pharmacy formularies precludes the availability of both at a single institution. Notably, tolazoline is no longer available in our market, and nitroglycerin has replaced it.

Complications and Risk Assessment

Potential complications may occur such as hypotension, puncture site hematoma, and post-procedural hemorrhage requiring transfusion. None of the literature on provocative angiography have reported any episodes of the most feared complications associated with provocative angiography: uncontrollable GI, central nervous system, or nontarget bleeding. This may be related to the fact that tPA is primarily metabolized by the liver, and with mesenteric arterial injection, there is a very high first-pass metabolism of tPA, which theoretically will result in markedly lower systemic concentrations as compared to intravenous infusion. However, careful patient selection is still crucial. Patients should be screened prior to provocation for basic exclusionary criteria for fibrinolytic therapy (Table 18.1). The presence of portal hypertension is a relative contraindication, because provocation of an occult portal

Table 18.1 Contraindications to provocative angiography

Absolute contraindications	Relative contraindications
Transient ischemic attack within 2 months	Recent major surgery, trauma, cardiopulmonary resuscitation
Cerebrovascular accident within 6 months	Uncontrolled hypertension
Intracranial neoplasm	Endocarditis
Craniotomy within 3 months	Pregnancy and postpartum period
Mobile left heart thrombus	Severe cerebrovascular disease
Intestinal surgery within 3 months	Portal hypertension

venous source of hemorrhage, such as esophageal or gastric varices, typically cannot be readily controlled without a change in endovascular approach (i.e., TIPS) or modality (i.e., endoscopy). Due to potentially substantial amounts of contrast needed to complete the examination, close attention to renal function is required. Proper hydration and resuscitation of the patient is recommended. Other factors for consideration include life-threatening contrast reaction, as well as the surgical candidacy of the patient. This can be a time-consuming examination requiring the patient being able to lay supine and follow commands, using pain and sedative medications as adjuncts. To facilitate the procedure, general anesthesia may need to be considered. Both the interventionalist and the surgeon need to have a well-thought-out plan prior to the initiation of provocative angiography. At our institution, provocative angiography is only done with the approval of the surgical service.

Methods

Our provocative angiography protocol involves first performing conventional diagnostic mesenteric angiography on fore-, mid-, and hindgut distributions (celiac, superior mesenteric, and inferior mesenteric arteries). Unless the patient is unstable, the majority of patients have undergone scintigraphic imaging to determine the vascular distribution of concern. In the event scintigraphy has identified a bleeding site, the relevant vascular distribution is targeted for provocation. If there is no bleeding on scintigraphy, the superior mesenteric artery is targeted due to the opportunity to cover a greater length of the lower GI tract with vasodilator and fibrinolytic. Others such as Wildus [8] have suggested starting with the inferior mesenteric artery, due to the relative difficulty entering this vessel, as compared to the superior mesenteric and celiac distributions.

Just as there is variation of techniques between institutions, we have had variable approaches to provocative angiography. Over time, we have made an attempt to standardize our approach, in order to improve safety and provide consistency in our own internal reviews. Our current algorithm is depicted in a flowchart (Fig. 18.1).

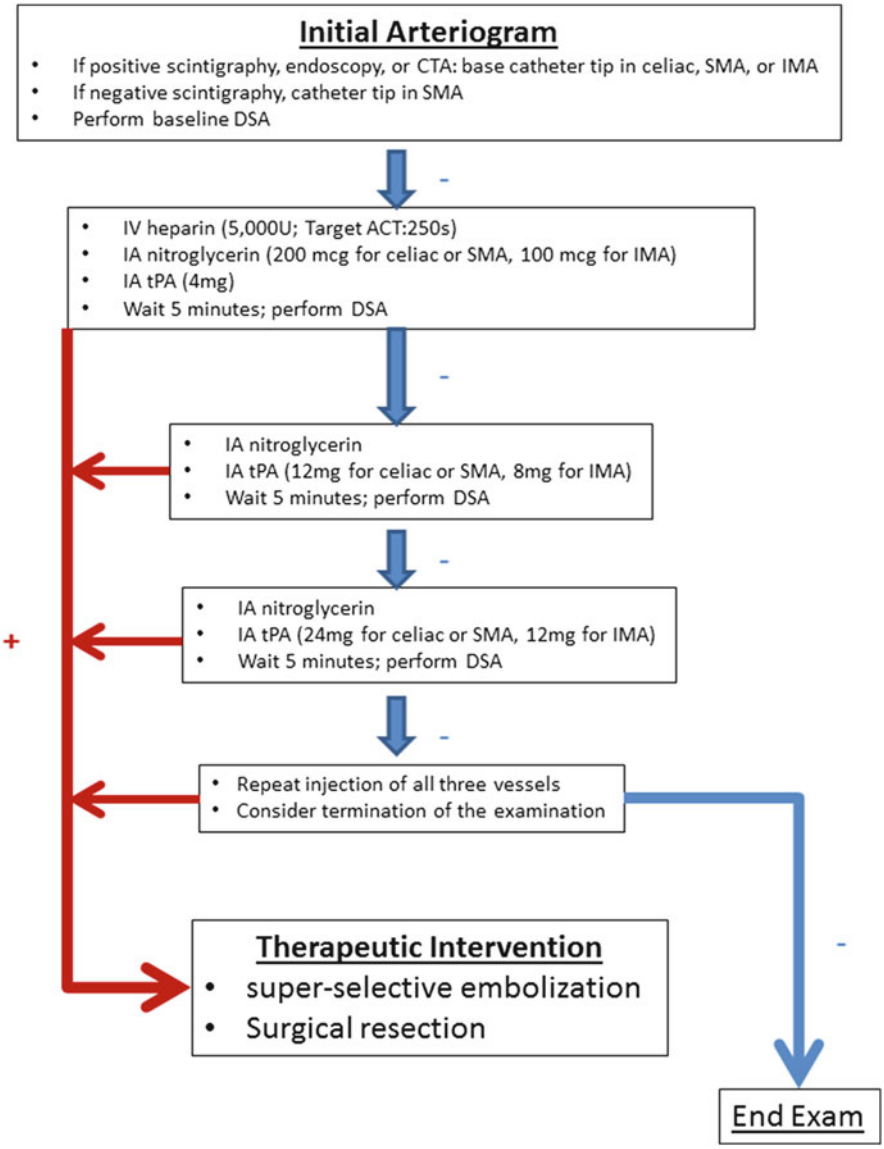

Fig. 18.1 Provocative angiography algorithm

This regimen is then repeated for the second most suspicious distribution. Angiography is acquired with the injection rates of 5–7 mL/s into either the celiac or superior mesenteric arterial distribution for a total injection of 20 mL. In the inferior mesenteric arterial distribution, 3 mL/s or hand injection for a total of 10 mL is injected. This allows for adequate opacification of the distal vascular bed where the bleeding originates (Fig. 18.2a, b, c and d).

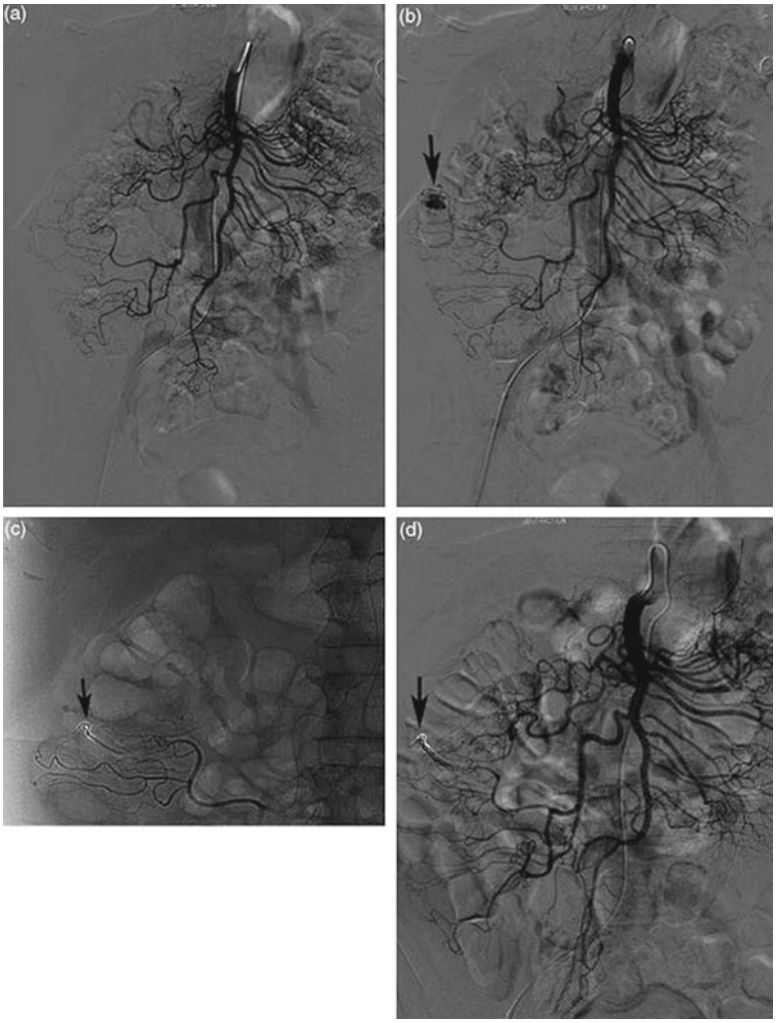

Fig. 18.2 (**a**) 53-year-old male presents with positive scintigraphy in the hepatic flexure, transient hypotension with prior bleeding episode, and one previous negative arteriogram. Initial injection of the superior mesenteric artery is normal without extravasation. (**b**) Injection of the superior mesenteric artery following the administration of 5000 U heparin, 200 mcg nitroglycerin, and 4 mg tPA demonstrates active bleeding (*arrow*) from a branch from the right colic which was suspected on scintigraphy. (**c**) Injection through the microcatheter following placement of coils (*arrow*) within the arcuate branches supplying the area of extravasation. (**d**) Completion arteriogram demonstrates coils (*arrow*) with no further bleeding and preserved collateral supply to the region of colon

Conclusions

Certainly, this is a multidisciplinary endeavor, not limited to the interventionalist, and involves a consensus of surgical, medical, and radiological colleagues. Rates of diagnostic success are certainly variable due to lack of standardized protocols for provocative studies (Table 18.2). The optimal type, dosing, and combination of vasodilator, anticoagulant, and fibrinolytic agents are unclear. Other factors such as

Table 18.2 Provocative angiography series

References	Class study	Agents	Dose	Delivery[a]	Diagnostic extravasation (%)	Therapeutic modality
Widlus [8]	Retrospective	Reteplase	(a) 5 U in 20 mL NS over 1 min	(a) Arterial	8/9 (89)	5 Embolized 1 Embolized then required operation 2 Spontaneous cessation
Ryan [7]	Retrospective	(a) Heparin (b) Tolazoline (c) tPA	(a) 3000–10,000 U (b) 25–100 mg (c) 10–50 mg over 15 min	(a) IV (b) Arterial (c) Arterial	6/16 (38)	2 Embolized 1 Embolized then required operation 2 Estrogen1 Medical
Mernagh [4]	Retrospective	(a) Papaverine (b) Heparin	(a) 65 mg (b) 5000 U Bolus then 24-h infusion to PTT 60–85 s	(a) Arterial (b) IV	12/18 (67)	All confirmed with endoscopy or surgery
Bloomfeld [6]	Retrospective	(a) Tolazoline (b) Heparin (c) Urokinase	(a) 25 mg (b) 1000–10,000 U (c) 250,000 U aliquots to max total dose of 1,000,000 U	(a) Arterial (b) Arterial (c) Arterial	2/7 (29)	2 Operation
Malden [5][b]	Prospective	(a) Heparin (b) Urokinase	(a) 10,000 U bolus then 500 U/h × 3 h (b) 250,000 U/h bolus then 250,000 U/h × 3 h	(a) IV (b) IV	2/9 (22)	1 Embolized 1 Operation
Koval [2]	Retrospective	(a) Heparin (b) Tolazoline (c) Streptokinase	(a) 5000–10,000 U (b) NRc. NR	(a) IV (b) Arterial (c) Arterial	8/10 (80)	NR

Abbreviations: *IV* intravenous, *NR* not reported, *NS* normal saline

[a]Arterial delivery implies selective celiac, superior mesenteric, or inferior mesenteric arterial delivery; IV implies systemic intravenous delivery

[b]Provocative scintigraphy study

time from active bleeding, institutional, and operator experience all impact the variable success rate reported in the literature. Therapeutic success is also broadly defined and, at least, should be stratified into embolization and surgical. At times, success may be of a hybrid form, where bleeding sites can be marked with methylene blue [9] or fluoroscopically locatable coils [10]. Although provocative angiography appears to be performed safely, the decision to proceed requires thoughtful consideration. Prospective data is scant and a large-scale study would further define the role of provocative angiography.

References

1. Rösch J, Keller FS, Wawrukiewicz AS, Krippaehne WW, Dotter CT. Pharmacoangiography in the diagnosis of recurrent massive lower gastrointestinal bleeding. Radiology. 1982;145(3):615–9.
2. Koval G, Benner KG, Rösch J, Kozak BE. Aggressive angiographic diagnosis in acute lower gastrointestinal hemorrhage. Dig Dis Sci. 1987;32(3):248–53.
3. Glickerman DJ, Kowdley KV, Rosch J. Urokinase in gastrointestinal tract bleeding. Radiology. 1988;168(2):375–6.
4. Mernagh JR, O'Donovan N, Somers S, Gill G, Sridhar S. Use of heparin in the investigation of obscure gastrointestinal bleeding. Can Assoc Radiol J. 2001;52(4):232–5.
5. Malden ES, Hicks ME, Royal HD, Aliperti G, Allen BT, Picus D. Recurrent gastrointestinal bleeding: use of thrombolysis with anticoagulation in diagnosis. Radiology. 1998;207(1):147–51.
6. Bloomfeld RS, Smith TP, Schneider AM, Rockey DC. Provocative angiography in patients with gastrointestinal hemorrhage of obscure origin. Am J Gastroenterol. 2000;95(10):2807–12.
7. Ryan JM, Key SM, Dumbleton SA, Smith TP. Nonlocalized lower gastrointestinal bleeding: provocative bleeding studies with intraarterial tPA, heparin, and tolazoline. J Vasc Interv Radiol. 2001;12(11):1273–7.
8. Widlus DM, Salis AI. Reteplase provocative visceral arteriography. J Clin Gastroenterol. 2007;41(9):830–3.
9. Glickerman DJ, Kowdley KV, Rosch J. Urokinase in gastrointestinal tract bleeding. Radiology. 1988;168(2):375–6.
10. Shetzline MA, Suhocki P, Dash R, Rockey DC. Provocative angiography in obscure gastrointestinal bleeding. South Med J. 2000;93(12):1205–8.

Chapter 19
The Unstable Patient with Obscure Gastrointestinal Bleeding: Surgical and Nonsurgical Management

Rebecca P. Petersen and Aurora D. Pryor

Obscure Gastrointestinal Bleeding: Definitions, Causes, and Epidemiology

Obscure gastrointestinal bleeding (OGIB) is defined as intermittent or persistent loss of blood that occurs or reoccurs after evaluation by upper gastrointestinal and lower gastrointestinal endoscopy [1]. The clinical presentation can vary dramatically, from occult blood loss that is only detectible by hemoccult testing, manifesting as iron deficiency to overt clinical manifestations of hematemesis, melena, or hematochezia requiring transfusion and hospitalization. The differential diagnosis of OGIB is extensive and the most common causes are listed in Table 19.1 [2]. Overall, OGIB represents approximately 5 % of all episodes of gastrointestinal bleeding [1, 2, 19]. Importantly, the most common causes of OGIB vary with age. Among patients less than 25 years old, the most common etiology is Meckel's diverticulum and other embryonic remnants. Among patients aged 30–50 years, various small bowel tumors tend to predominate, and older patients greater than 50 years old tend to have vascular pathology leading to bleeding [3, 4].

Provided the patient is hemodynamically stable, it is useful to try and narrow the potential etiologies prior to engaging in diagnostic procedures, as the differential diagnosis for OGIB is extensive. Detailed medical history regarding prior episodes, travel history, concomitant medical conditions such as pancreatic disease, coagulopathies, HIV status, family history of GI bleeding, and prior surgical procedures including vascular and gastrointestinal bypass surgery are important. Also, patients

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Table 19.1 Common causes of obscure gastrointestinal bleeding

Missed upper or lower gastrointestinal source
Vascular anomalies: lymphangioma, extraluminal AVM, submucosal vessel, angiodysplasia/ectasia
Neoplasm: primary, metastasis, or invasion by local spread, lipoma, GIST
Complications from previous surgery
Aorto-enteric fistula: primary or secondary, also iliac-enteric
Extraluminal source: hemobilia, hemosuccus pancreaticus
Inflammation: celiac disease, IBD (Crohn's), sarcoidosis
Meckel's diverticulum, or other ectopic tissue
Other small bowel diverticuli or duplication cysts
Intussusception
Medical: coagulopathy, liver disease with small bowel varices, drug induced
Infectious: CMV, TB, whipworm, salmonella

should be asked about intake of anticoagulants or ulcerogenic medications [19]. A detailed approach to the history can often define the appropriate diagnostic approach to the patient and improve the chances of an accurate diagnosis.

Initial Management and Approach to the Unstable OGIB Patient

Patients with unstable OGIB present similarly to common unstable acute causes of gastrointestinal bleeding. Thus, the initial medical management and stabilization should be similar to standard management for gastrointestinal bleeding as patients could be presenting with a de novo source. Initial maneuvers should include assessment of hemodynamic volume status, obtaining adequate intravenous access, and gastrointestinal lavage as appropriate. Additionally, appropriate bloodwork should be performed, typical pharmacotherapeutic measures should be instituted, and patients should be placed on NPO status.

All patients with overt OGIB require admission to the hospital, which for the OGIB patient affords an excellent opportunity to engage in directed diagnostic testing. As previously noted, diagnostic testing should be directed according to potential risk factors based on a detailed medical history. An algorithmic approach to the diagnostic evaluation is useful to avoid unnecessary testing and to focus the evaluation (Fig. 19.1). Among all patients, the most likely etiology of OGIB is an upper or lower gastrointestinal tract source that was initially missed on prior endoscopic examination. A review of published studies suggests that between 35 and 75 % of presumed OGIB lesions are actually found on repeat upper or lower endoscopy [5–13]. Hence, once hemodynamic stability has been achieved, the first maneuver for all patients should be to repeat the previous esophageal, gastric, and duodenoscopy, and then colonoscopy if negative. Often times etiologies such as tiny Dieulafoy's lesions,

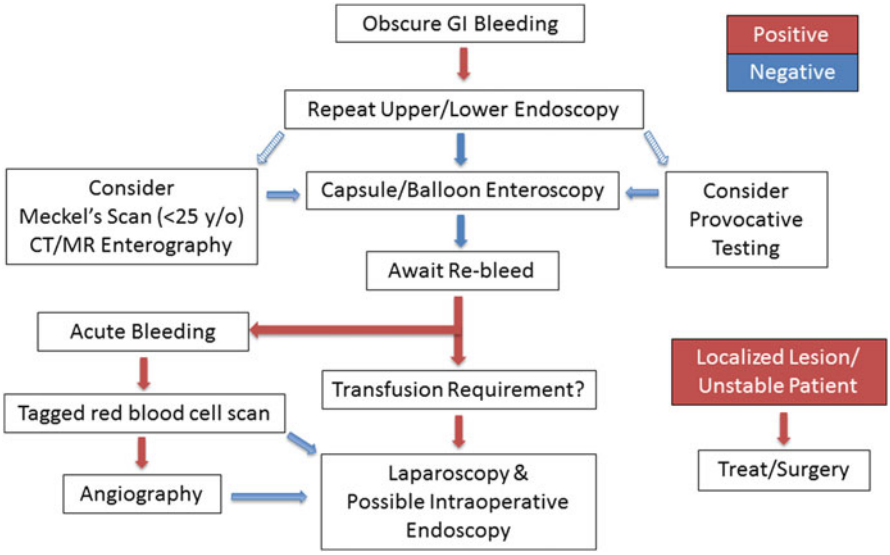

Fig. 19.1 Diagnostic algorithm

Cameron's ulcers (lesions in hiatal hernias), collapsed esophageal or gastric varices are missed [19]. Ideally, the repeat endoscopy should be performed within 48 h of the current acute bleeding event to achieve the greatest diagnostic success.

If the repeat endoscopies are negative, we recommend the next diagnostic maneuver be stratified by age and any other pertinent medical history. In the absence of other clear risk factors for other causes, younger patients should undergo nuclear imaging for a Meckel's diverticulum. Middle-age patients (30–50 years old) should be considered for push, double–balloon, or capsule enteroscopy, depending on the available diagnostic equipment. Older patients (greater than 50 years old) should be considered for evaluation of a vascular etiology, including vascular ectasias, hemangiomas, and Dieulafoy's malformation. As the initial diagnostic maneuver in the older patient, either an enteroscopic approach or an angiographic approach can be considered.

Among stable older patients without active bleeding, push or pill enteroscopy is preferred as angiograms and tagged red blood cell scanning are only effective when active bleeding is suspected. In some cases in which hemodynamic instability is not a concern or previous enteroscopic imaging has been performed, consideration can be given to a diagnostic challenge with an anticoagulant. It is important to select an anticoagulant that can be easily reversed in the event of severe bleeding. Typically administering up to 5000 IU of unfractionated heparin is a reasonable approach, as it can be reversed with protamine in a ratio of 1 mg per 100 IU of unfractionated heparin, up to a maximum dose of 50 mg. Importantly, patients receiving NPH insulin may have a severe anaphylactic reaction to protamine, and hence diabetes should be considered a relative contraindication to this approach. A challenge should be performed in a coordinated effort with the appropriate radiology resources in anticipation

of further angiographic imaging once bleeding occurs. If the source can be treated endovascularly after diagnostic angiography, we strongly recommend this approach before proceeding to surgery.

If these initial tests are unrevealing or do not localize a source, it is not in the best interest of the patient to proceed with an undirected open surgical approach to diagnosis. Historical data have suggested that open laparotomy was only diagnostic in 30 of 100 cases, and of these 30, 17 (58 %) likely would have been made with noninvasive techniques available today [14]. A more recent series found that while a diagnosis was made in 29 of 53 OGIB cases by open laparotomy, 15 additional cases were diagnosed by enteroscopy, and importantly 29 % of patients had a rebleeding episode with overall mortality 7.5 % [15]. Thus, we prefer to consider less invasive approaches to diagnosis when available. Over the past 10 years, noninvasive diagnostic techniques such as multiphase computed tomographic (CT) or magnetic resonance (MR) enterography have been introduced and are highly effective in identifying small bowel lesions, but may be limited by opaque debris, inadequate distension, gastric retention, etc. [20–22]. CT or MR enterography may be considered when capsule endoscopy is incomplete, negative, or contraindicated [22]. In the absence of a clear diagnosis after initial stratified testing in an otherwise stabilized patient, we prefer either to wait for another episode of bleeding or to consider provocative testing with an anticoagulant.

Laparoscopic Approach to Diagnosis and Management of OGIB

If a source is localized by noninvasive or angiographic imaging or the patient continues to be hemodynamically unstable or require transfusion, we recommend an initial diagnostic laparoscopic approach coupled with use of intraoperative endoscopy if necessary (Fig. 19.2). Specifically, for a patient with a non-localized lesion, a diagnostic laparoscopy should be performed. Of course, if the patient has an absolute contraindication to laparoscopy a laparotomy is then recommended. Access is achieved either with an open technique with insertion of the Hasson cannula at the umbilicus or by an insertion of a Veress needle. Additional 5 mm ports are initially placed in the lower quadrants to facilitate running of the small bowel from the ligament of Treitz to the cecum. Additional ports can be placed or the 5 mm ports may be exchanged over for 12 mm ports if necessary depending on the intraoperative findings (Fig. 19.3). All four quadrants of the abdomen are initially explored and attention is then turned to a thorough investigation of the small bowel from the stomach to the cecum. If an obvious etiology is identified a suture may be placed to mark the region. It is important to realize that intralumenal blood clots may resemble a mass upon extra-lumenal exploration. Prior to resection, the surgeon must be confident that indeed the identified pathology is the cause of the ongoing hemorrhage.

If there is no obvious source identified after running the small bowel and closely investigating the colon, intraoperative endoscopy should be performed. Enteroscopy may be performed orally, anally, or through an enterotomy. If investigation is initially

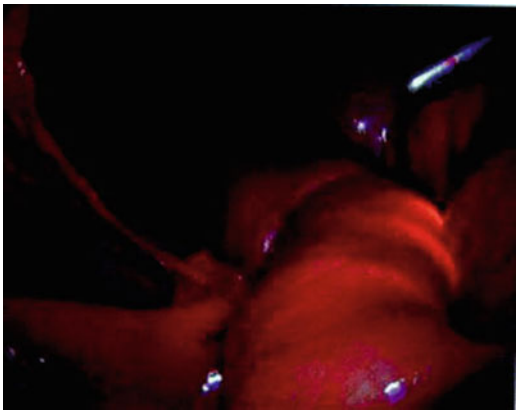

Fig. 19.2 Intraoperative enteroscopy. An endoscope, preferably an enteroscope, is passed transorally and the bowel is run over the scope with the assistance of laparoscopic graspers. Lesions identified with this approach can be diagnosed and treated in the same setting

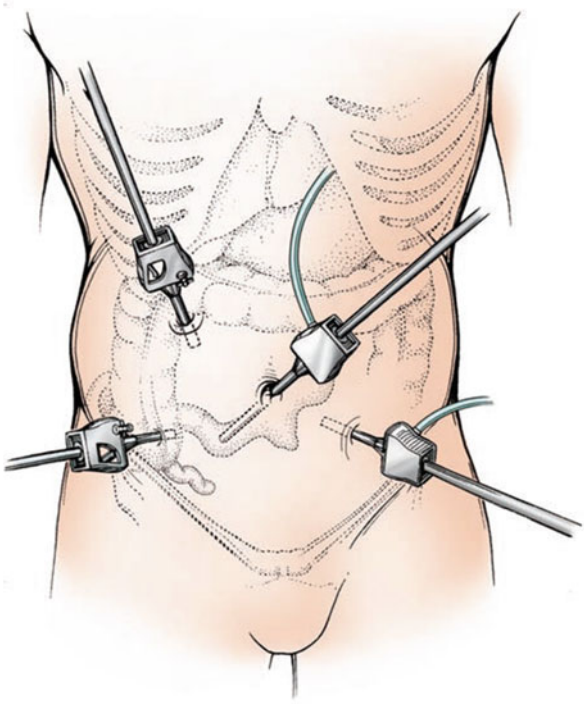

Fig. 19.3 Diagnostic laparoscopy. Initial setup includes three or four 5-mm trocars to facilitate full exploration of the abdomen. If pathology is identified, one or more trocars may be upsized to allow for passage of a surgical stapler and specimen extraction

taken via a natural orifice then a colonoscope or enteroscope may be preferentially used. The investigated bowel is telescoped over the scope as it advances. If no obvious pathology is identified then bowel clamps can be placed distally or proximally to mark the limits of the natural orifice endoscopy. Next, the small bowel is eviscerated from an umbilical incision which may need to be extended and an enterotomy is made following

placement of a purse string suture in an effort to avoid gross contamination. The gastroscope is then inserted and the small bowel is thoroughly examined using a telescoping technique between the previously placed laparoscopic proximal and distal clamps which designate the limits of the natural orifice endoscopy. Usually two surgeons are required. If the source is identified then resection may be performed laparoscopically (Fig. 19.4).

Several case reports and small case series have been described using this technique [16–18]. However, given the rarity of OGIB, there have been no large cohort series described thus far.

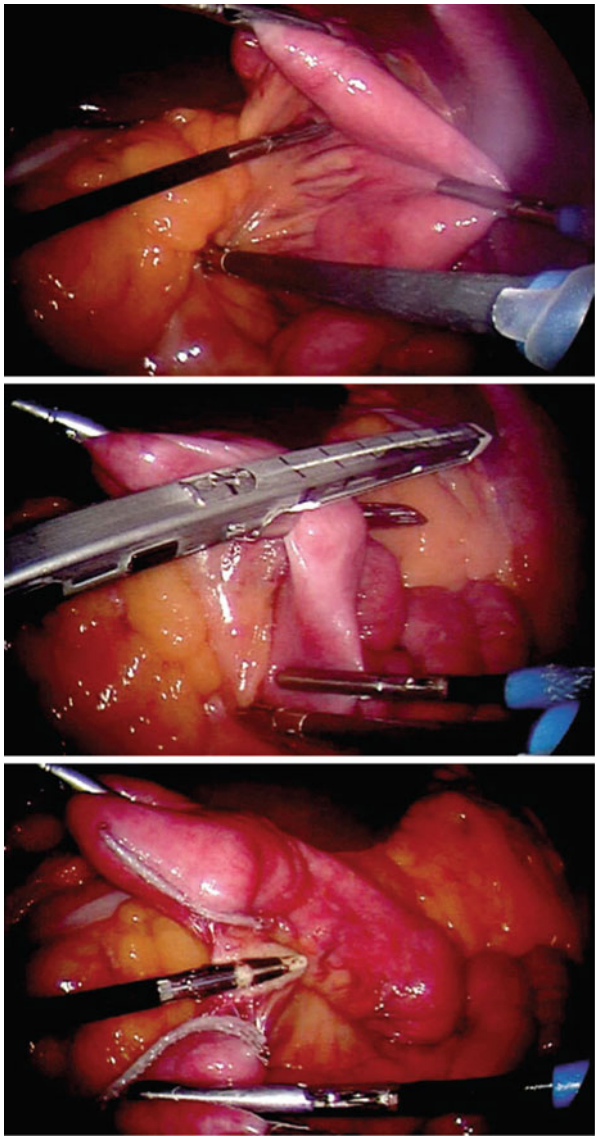

Fig. 19.4 Laparoscopic small bowel resection. A mesenteric window is created bluntly at the resection point (**a**). The bowel is transected with a surgical stapler (**b**). The mesentery is divided with an electrosurgical device (**c**). The anastomosis is then completed with surgical staplers ± sutures

Summary

OGIB is one of the most challenging diagnostic scenarios for gastroenterologists and surgeons alike. As the differential diagnosis is large and the causes are rare, a focused approach toward diagnostic testing should be taken, guided by key aspects of the medical history. Importantly, a second round of standard upper and lower endoscopy should be considered for all patients as the most common cause of OGIB is a previously missed lesion on routine endoscopy.

Further evaluation should be guided by medical history and the patient's clinical condition. Stable patients should be evaluated with capsule, push, or double-balloon enteroscopy, depending on available resources. Consideration should also be given to performing either CT or MR enterography. Patients with active bleeding that are not hemodynamically unstable should be evaluated with noninvasive and angiographic imaging as open diagnostic laparotomy carries a significant risk of morbidity and mortality, and frequently the diagnosis can be made using less invasive techniques. For some patients, a challenge with a reversible anticoagulant can be considered in coordination with the appropriate imaging resources. Finally, if surgery for OGIB is required to evaluate the small bowel, we recommend a combined laparoscopic and endoscopic approach as the first-line approach.

References

1. Zuckerman GR, Prakash C, Askin MP, Lewis BS. AGA technical review on the evaluation and management of occult and obscure gastrointestinal bleeding. Gastroenterology. 2000;118:201–21.
2. Concha R, Amaro R, Barkin JS. Obscure gastrointestinal bleeding: diagnostic and therapeutic approach. J Clin Gastroenterol. 2007;41(3):242–51.
3. Mujica VR, Barkin JS. Occult gastrointestinal bleeding. General overview and approach. Gastrointest Endosc Clin NA. 1996;6:833–45.
4. Lewis BS, Kornbluth A, Waye JD. Small bowel tumours: yield of enteroscopy. Gut. 1991;32:763–5.
5. Descamps C, Schmit A, van Gossum A. "Missed" upper gastrointestinal tract lesions may explain "occult" bleeding. Endoscopy. 1999;31:452–5.
6. Spiller RC, Parkins RA. Recurrent gastrointestinal bleeding of obscure origin: report of 7 cases and a guide to logical management. Br J Surg. 1983;70:489–93.
7. Barkin JS, Lewis BS, Reiner DK, Waye JD, Goldberg RI, Phillips RS. Diagnostic and therapeutic jejunoscopy with a new, longer enteroscope. Gastrointest Endosc. 1992;38:55–8.
8. Chong J, Tagle M, Barkin JS, Reiner DK. Small bowel push-type fiberoptic enteroscopy for patients with occult gastrointestinal bleeding or suspected small bowel pathology. Am J Gastroenterol. 1994;89:2143–6.
9. Zaman A, Katon RM. Push enteroscopy for obscure gastrointestinal bleeding yields a high incidence of proximal lesions within reach of a standard endoscope. Gastrointest Endosc. 1998;47:372–6.
10. Chak A, Koehler MK, Sundaram SN, Cooper GS, Canto MI, Sivak MV Jr. Diagnostic and therapeutic impact of push enteroscopy: analysis of factors associated with positive findings. Gastrointest Endosc. 1998;47:18–22.

11. Willis JR, Chokshi HR, Zuckerman GR, Aliperti G. Enteroscopy-enteroclysis: experience with a combined endoscopic-radiographic technique. Gastrointest Endosc. 1997;45:163–7.
12. Vakil N, Huilgol V, Khan I. Effect of push enteroscopy on transfusion requirements and quality of life in patients with unexplained gastrointestinal bleeding. Am J Gastroenterol. 1997;92:425–8.
13. Chen RY, Taylor AC, Desmond PV. Push enteroscopy: a single centre experience and review of published series. ANZ J Surg. 2002;72:215–8.
14. Retzlaff JA, Hagedorn AB, Bartholomew LG. Abdominal exploration for gastrointestinal bleeding of obscure origin. JAMA. 1961;177:104–7.
15. Lewis MP, Khoo DE, Spencer J. Value of laparotomy in the diagnosis of obscure gastrointestinal haemorrhage. Gut. 1995;37:187–90.
16. Ba MC, Qing SH, Huang XC, Wen Y, Li GX, Yu J. Application of laparoscopy in diagnosis and treatment of massive small intestinal bleeding: report of 22 cases. World J Gastroenterol. 2006;12:7051–4.
17. Pei K, Zemon H, Venbrux A, Brody F. Laparoscopic techniques for occult gastrointestinal bleeding. J Laparoendosc Adv Surg Tech. 2005;15:615–9.
18. Lee K, Yeung C, Tam Y, Ng WT, Yip KF. Laparoscopy for definitive diagnosis and treatment of gastrointestinal bleeding of obscure origin in children. J Pediatr Surg. 2000;35:1291–3.
19. Heil U, Jung M. The patient with recidivent obscure gastrointestinal bleeding. Best Pract Res Clin Gastroenterol. 2007;21:393–407.
20. Barlow JM, Goss BC, Hansel SL, et al. CT enterography: technical and interpretive pitfalls. Abdom Imaging. 2015;40:1081–96.
21. Lin S, Rockey DC. Obscure gastrointestinal bleeding. Gastroenterol Clin North Am. 2005;34:679–98.
22. Rondonotti E, Marmo R, Petracchini M, et al. The American Society for Gastrointestinal Endoscopy (ASGE) diagnostic algorithm for obscure gastrointestinal bleeding: Eight Burning questions from everyday clinical practice. Dig Liver Dis. 2013;45:179–85.

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DOI 10.1007/978-3-319-40646-6