A Multidisciplinary Approach to Gastrointestinal Bleeding in Cancer Patients

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Abstract Gastrointestinal bleeding remains one of the most challenging areas in medicine today, especially in the patient with cancer. New techniques and technology have added much to the diagnosis and management of gastrointestinal bleeding. Although gastroenterologists remain at the center of the evaluation of these patients, the incorporation of new techniques has meant that interventional radiologists and nuclear medicine specialists often have important roles in assessing and treating these patients as well. Because patients with cancer are members of a unique group, gastrointestinal bleeding may also require intervention by surgical oncologists, medical oncologists, and radiation oncologists. This review will address the multidisciplinary approach required for the proper diagnosis and management of gastrointestinal bleeding in patients with cancer.

Gastrointestinal bleeding can be a serious problem in patients with cancer. In addition to various types of cancer of the gastrointestinal tract, common causes of upper and lower gastrointestinal bleeding include peptic ulcer disease, Mallory-Weiss tears, esophageal varices, diverticulosis, and angiodysplasia. With the development of strategies for endoscopic diagnosis and management of gastrointestinal bleeding as well as new pharmacologic agents, few patients will require more invasive procedures.

Upper Gastrointestinal Bleeding

Upper gastrointestinal (UGI) bleeding is usually heralded by melenic stools and either bright-red or "coffee ground" emesis. When bleeding is unusually brisk, bright-red blood or maroon-colored stool may be passed per rectum, which may confuse the clinician as to the correct location of the bleeding site. For subacute or chronic bleeding from the UGI tract, stools may remain brown but be positive for chemical tests for occult blood.

All patients with UGI bleeding require initial assessment for hemodynamic stability. For massive acute UGI bleeding, patients often require resuscitation with intravenous fluids and blood products, as well as close monitoring of vital signs. This process often begins in the emergency department and, depending upon the degree of blood loss and the initial response to resuscitation, may continue in the intensive care unit. Cases of subacute and chronic UGI bleeding may be evaluated electively, either in the hospital or on an outpatient basis. It is not uncommon for a patient with cancer and subacute or chronic UGI bleeding to be admitted to the hospital, where transfusion of blood products can be given and a more rapid diagnostic evaluation performed.

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CAUSES

In an extensive survey assessing UGI bleeding, the majority of cases in the general population were caused by acute gastritis, peptic ulcer disease, esophagitis, Mallory-Weiss tears, or esophageal varices [1]. The causes of UGI bleeding are similar in cancer patients.

In a prospective evaluation of 65 patients with cancer and UGI bleeding at Memorial Sloan-Kettering Cancer Center (MSKCC), 40% of patients were found to be bleeding from hemorrhagic gastritis and 22% from benign peptic ulcer disease—both common causes in hospitalized non-cancer patients [2]. However, patients can directly bleed from cancer of the gastrointestinal tract, including esophageal cancer, gastric cancer (Figure 1), gastric lymphoma, gastrointestinal stromal tumors, and metastatic tumors involving the stomach. In the MSKCC study, 28% of the patients with UGI bleeding had tumors in the stomach (Figure 2), but these tumors were thought to be the source of bleeding in only 15%

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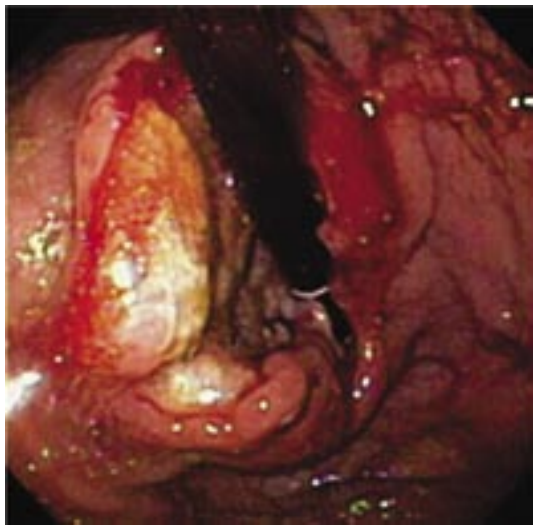

Figure 1 Gastric Cancer

A retroflexed view of an ulcerated, bleeding gastric cardia adenocarcinoma.

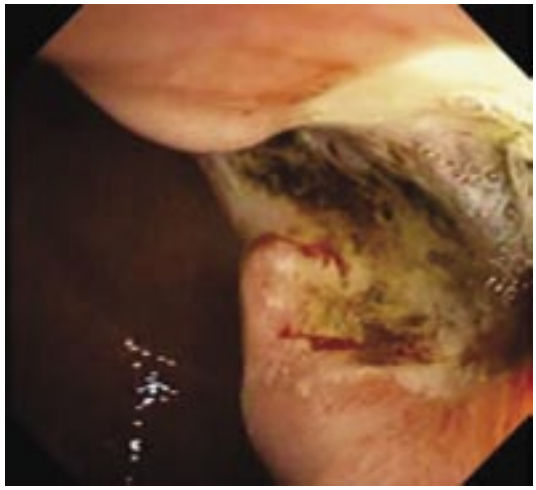

Figure 2 Stomach Tumor

An ulcerated gastric cancer in the body of the stomach.

of patients. In general, tumor bleeding does not present with massive UGI bleeding, but more commonly, the bleeding is chronic, presenting as dark stools or occult blood-positive stools.

Patients with cancer may have portal hypertension on the basis of tumor involvement in the liver. In addition, occlusion of the portal vein, which is relatively common in patients with carcinoma of the pancreas or portal-vein thrombosis, may be secondary to cancer-induced hypercoagulability. Esophageal and gastric varices can develop and bleed. Thus, portal hypertension should be included in the differential diagnosis of UGI bleeding in cancer patients, even without evidence of cirrhosis or massive replacement of the liver with tumor.

Diagnosis and Treatment of UGI Bleeding

When UGI bleeding is suspected, nasogastric aspiration is often used to aid in assessing the degree of bleeding and to help identify the location of the hemorrhage. There have been many studies looking at the diagnostic value of the nasogastric aspirate (NGA). The presence of blood or fluid with a "coffee-ground" appearance was found to be an independent predictor of active UGI bleeding or a non-bleeding visible vessel (Figure 3) [3]. A more recent retrospective review of more than 500 patients showed that a bloody NGA was significantly associated with a "high-risk" lesion identified at endoscopy: spurting blood, oozing of blood, or a visible vessel [4]. However, the specificity of a bloody NGA for such a lesion was only 75.8%, and the negative predictive value was only 77.9%. Conversely, 14.7% of patients with a clear or bile-stained NGA still were found to have a high-risk lesion on UGI endoscopy. A prospective observational study of 62 patients also found that the sensitivity and specificity of an NGA for predicting active bleeding at the time of endoscopy were 79% and 55%, respectively [5].

There are several reasons to explain this finding. One explanation is that duodenal bleeding may be present, yet the blood may not have refluxed back into the stomach at the time the nasogastric aspiration was performed. Close to 50% of patients with recent bleeding from duodenal lesions, such as ulcers, do not have a bloody NGA [6]. In addition, UGI bleeding can be intermittent, despite the presence of a high-risk lesion, thereby producing a normal NGA while active bleeding is seen at the time of endoscopy. Although we generally do not rely on the results of nasogastric aspiration to decide whether UGI endoscopy is necessary, it continues to be widely used in clinical practice, despite a lack of adequate evidence that it affects the outcome of patients with UGI bleeding.

Upper gastrointestinal endoscopy is the diagnostic procedure of choice when acute and subacute UGI bleeding is believed to be present [7]. Prior to UGI endoscopy, the patient should be hemodynamically stable. Risks versus benefits of the procedure must be considered in all patients. In a study comparing endoscopy in patients who have had a recent myocardial infarction (MI) with age-

matched controls, patients with an MI within the past 30 days had a higher rate of complications (7.5% vs 1.5%), including fatal arrhythmia, near respiratory arrest, hypoxemia and hypotension. However, the same study also showed that the subset of acute MI patients who were very ill, with a high APACHE II score (> 16), are the ones who suffer complications most often (20% vs 2%).

For seriously ill cancer patients with multiple comorbid conditions, the rationale for UGI endoscopy must be carefully considered. Contraindications to UGI endoscopy in cancer patients are the same as those in patients without cancer with one notable addition: the neutropenic patient. In patients with absolute neutrophil counts below 500/mm^3, endoscopy should be avoided unless the benefit, such as coagulation of a bleeding vessel, outweighs the potential risk.

It frequently helps to lavage the stomach prior to endoscopy to remove blood and clots, which when present, often prevent adequate visualization of the musoca in the stomach and duodenum and also may limit adequate endoscopic treatment of the identified bleeding lesion. Gastric lavage can be performed with an Ewald tube. Erythromycin, used for its promotility properties, may be given in a single intravenous dose prior to endoscopy. In randomized trials, this approach has been shown to improve endoscopic visibility significantly, shorten endoscopy time, and reduce the need for a "second-look" procedure [8, 9]. Unfortunately, many patients may still require a second UGI endoscopy despite these steps.

Results of endoscopy can be used in combination with clinical characteristics of the bleeding and the patient to risk stratify patients with UGI bleeding. In one case series, criteria were defined to select patients with UGI bleeding for outpatient care [10]. Absolute contraindications to outpatient care included an endoscopic finding of arterial bleeding, an adherent clot, a visible vessel (Figure 3), varices, and portal hypertensive gastropathy. Relative contraindications to outpatient management included lack of adequate support at home, debilitation, serious concomitant illness, orthostasis, severe liver disease, anticoagulation therapy or coagulopathy, and severe anemia. Of 176 patients who fulfilled these criteria, only 2 required subsequent hospitalization for recurrent bleeding.

In a separate randomized study, patients who underwent early endoscopy in the emergency department had a significantly shorter length of hospital stay and lower cost of care than those patients who underwent endoscopy within the first 2 days [11]. Forty-six percent of patients were able to be discharged from the emergency department, and none had an adverse outcome. As much as these recent studies have impacted practice patterns for UGI bleeding in the general population, it may be difficult to extrapolate these findings for patients with cancer. Indeed, debilitated patients with serious comorbidities, such as advanced cancer, were excluded from entry into the outpatient care in the study previously noted, even when the endoscopically identified lesion was a "low-risk" lesion [10].

Figure 3 Non-bleeding Visible Vessel
Endoscopic photograph of a "visible vessel" in a duodenal ulcer.

UGI endoscopy is the diagnostic modality of choice for acute UGI bleeding, as it has a high sensitivity and specificity for identifying and locating the bleeding cause [6]. Not all causes of UGI bleeding require endoscopic therapy. However, identification of the cause of bleeding allows therapy to be individualized. For example, patients found to have erosive esophagitis are most often treated medically with acid suppression, as are patients with diffuse gastritis. Both of these entities are more likely to cause significant bleeding in the setting of coagulopathy or thrombocytopenia, commonly seen in patients with cancer.

PEPTIC ULCER DISEASE

UGI endoscopy not only offers the opportunity to diagnose the cause of bleeding accurately, but it

A peer viewpoint on this article by Dr. Lawrence R. Coia appears on page 111.

also can provide a means to therapeutic intervention to stop active bleeding or reduce the risk of rebleeding. This approach has been well studied and described when peptic ulcer disease is the cause of UGI bleeding. Major endoscopic predictors of persistent or recurrent bleeding include active bleeding during endoscopy (90% recurrence), presence of a visible vessel in the ulcer base (50% recurrence), or the presence of an adherent clot (25% recurrence) [12]. If the ulcer is clean based, there is a low risk of recurrent bleeding (5% recurrence). Clean-based ulcers should not be treated endoscopically.

The benefit of endoscopic therapy over medical therapy alone has been demonstrated for peptic ulcer bleeding when there is active bleeding or a visible vessel is present. A variety of techniques have been used to control bleeding, including thermal coagulation, injection therapy, and, recently, endoscopically placed hemostatic clips. These methods also can be easily combined. High rebleeding rates have been seen when endoscopic injection therapy is used alone [13]. Injection of 1:10,000 dilution of epinephrine causes hemostasis by a combination of local tamponade and vasoconstriction of the culprit bleeding vessel. A transient tamponade effect may be seen with the injection of saline alone; this can be effective in achieving hemostasis, but the risk of rebleeding is high. Most endoscopists now opt for coaptive coagulation of the vessel either alone or in combination with an epinephrine injection to gain control of the bleeding site so that the coagulation probe can be more easily directed to the bleeding vessel.

The application of hemoclips for a bleeding lesion is an important addition to the endoscopist's armamentarium. These clips work by compressing and ligating the bleeding vessel. Typically, clips will spontaneously dislodge within about 8 weeks of their application. A randomized trial of endoscopic heater-probe treatment, used for thermal coagulation of the bleeding vessel, versus application of hemoclips showed comparable rates of hemostasis but favorable rates of rebleeding when hemoclips were used (21% vs 2%) [14]. However, in this study, the rate of rebleeding in the heater-probe group was higher than that in other studies evaluating rebleeding rates in thermally treated patients. Hemoclips continue to gain acceptance as an effective alternative and adjunct to injection therapy, electrocautery, and thermal coagulation.

Controversy still remains over the treatment of an adherent clot during UGI endoscopy. Lower rebleeding rates have been demonstrated when epinephrine was injected through the clot, followed by removal of the clot and endoscopic coagulation of the underlying bleeding vessel. In a randomized controlled trial of 32 patients, the rate of rebleeding with medical therapy was 35%, whereas it was 0% in endoscopically treated patients [15]. In another randomized controlled trial of 56 patients, the rate of rebleeding with medical versus endoscopic treatment was 34% versus 5%, respectively [16]. It seems clear that when an adherent clot is present, endoscopic treatment will likely reduce the rate of recurrent bleeding.

For many years, medical therapy with acid suppression has been used alone for low-risk lesions or in conjunction with endoscopic therapy for high-risk lesions. Although extensively studied, data to support the use of H_2 receptor blockers in this setting are not strong and suggest little, if any, benefit [17]. More recently, high-dose acid suppression with proton-pump inhibitors (PPIs) has been shown to reduce rebleeding of high-risk patients with peptic ulcer. This reduction is thought to be due to the ability of high-dose PPIs to maintain the gastric pH above 6.0, which helps to protect clots from the destabilizing effects of gastric acid.

A randomized study of 240 patients compared 72 hours of intravenous use of the PPI omeprazole (Prilosec) versus placebo after endoscopic treatment of active bleeding or non-bleeding visible vessels [18]. The trial was terminated early due to the significantly lower rate of rebleeding in patients who received omeprazole (6.7% vs 22.5%). In the United States, the only intravenous PPI available is pantoprazole (Protonix). It is given in an 80-mg bolus dose followed by 8 mg/h. High doses of oral omeprazole (40 mg twice daily) have decreased the rate of continued or recurrent bleeding, transfusions, and surgery compared with placebo for patients with high-risk peptic ulcers not treated with endoscopic therapy [19]. High-dose PPIs are not necessary to reduce the rate of rebleeding when a low-risk ulcer is identified.

MALLORY-WEISS TEARS

Mallory-Weiss tears occur in the distal esophagus at the gastroesophageal junction, often after bouts of vomiting or retching, especially in patients with a preexisting hiatal hernia [20]. The nausea and vomiting suffered by many cancer patients as a result of treatment are a common cause of UGI bleeding in this population. Most Mallory-Weiss

tears heal spontaneously, and recurrent bleeding is rare in the absence of portal hypertension or coagulopathy [21]. Endoscopic therapy is necessary only in a minority of patients.

ESOPHAGEAL VARICES

If esophageal varices are identified as the cause of UGI bleeding, endoscopic therapy should be used. Approximately 50% of patients with esophageal varices eventually experience bleeding, and more than 70% of these patients will have recurrent hemorrhage. The most reliable predictor of future hemorrhage is variceal size, with larger varices more likely to bleed secondary to increased wall stress [22].

When variceal bleeding is suspected, medical therapy with octreotide (Sandostatin) may be initiated prior to endoscopy. Octreotide, an analog of somatostatin, indirectly causes splanchnic vasoconstriction and decreases portal pressure. Octreotide has been found to be more effective for controlling bleeding than has vasopressin, an older, less-selective vasoconstricting agent with many significant and potentially dangerous side effects [23]. Once initiated, octreotide infusions (50-μg bolus followed by 50 μg/h) are continued for 5 days. Despite its widespread use, octreotide has not been shown to reduce mortality from esophageal variceal hemorrhage [24].

In addition, patients not already on a beta-blocker such as propranolol are often started on one to further reduce portal pressure. Beta-blockers are commonly started once the patient is hemodynamically stable and after hemostasis has been achieved with endoscopic therapy.

Endoscopic therapy is often the definitive treatment of actively bleeding esophageal varices. It is performed by injection of a sclerosing agent into and around the varices or by variceal band ligation. Variceal band ligation is at least as effective as is sclerotherapy for acute control of bleeding, and some clinical trials suggest an advantage for band ligation, with hemostasis rates generally > 80% [25]. In addition, ligation may reduce the rebleeding and mortality rates compared with sclerotherapy [26].

THE ROLE OF ANGIOGRAPHY

Most cases of UGI bleeding either will stop on their own or can be controlled endoscopically. Occasionally, the source of UGI bleeding cannot be identified on UGI endoscopy, or bleeding may not be controlled endoscopically. If bleeding is brisk enough (typically > 1.0 mL/min), angiography may be used both to aid in diagnosing the location of the bleeding and to provide angiographic intervention to control the bleeding source.

In certain situations, angiography and intervention may be better suited to control UGI bleeding than is endoscopic intervention. For example, diffuse hemorrhagic gastritis cannot be treated effectively endoscopically, because the area of stomach mucosa involved is too large to cauterize or inject with epinephrine. Angiography allows intra-arterial infusion of vasopressin into the left gastric or celiac arteries, thereby stopping bleeding from a diffuse mucosal surface area within the stomach.

Vasopressin causes vasoconstriction via its direct effect on the smooth muscle in the vessel wall. Infusion of vasopressin causes a rapid reduction in blood flow, which allows clotting to take place. In a series of 194 patients with gastric bleeding, vasopressin controlled bleeding in 73% of patients, and rebleeding occurred in 18% [27]. If initial infusions control bleeding, they are continued in the intensive care unit for 24 to 36 hours and then are tapered over 12 to 24 hours [28].

Angiography also allows the opportunity to inject particulate matter into the bleeding artery, thereby embolizing it. It can be performed after vasopressin infusion; however, vasopressin should not be infused after embolization, because it may cause vasoconstriction of the collateral blood supply, resulting in intestinal ischemia [29]. Embolization can be performed with a variety of agents, including a gelatin sponge (Gelfoam). Success rates for control of UGI bleeding with vasopressin or embolization generally range from 60% to 75% and vary with the type of lesion [30–32]. The choice between vasopressin and embolization should be individualized for each patient, but institutional and angiographer expertise also plays an important role in the decision.

Lower Gastrointestinal Bleeding

Lower gastrointestinal (LGI) bleeding is usually suspected when a patient presents with hematochezia, the passage of bright-red blood, clots, or maroon stools per rectum. However, stool color is not always predictive of the bleeding location [33]. As noted previously, patients with massive UGI bleeding may present with hematochezia and are often hemodynamically unstable. Conversely, bleeding from the small bowel or right colon may produce melena or black stools, which are com-

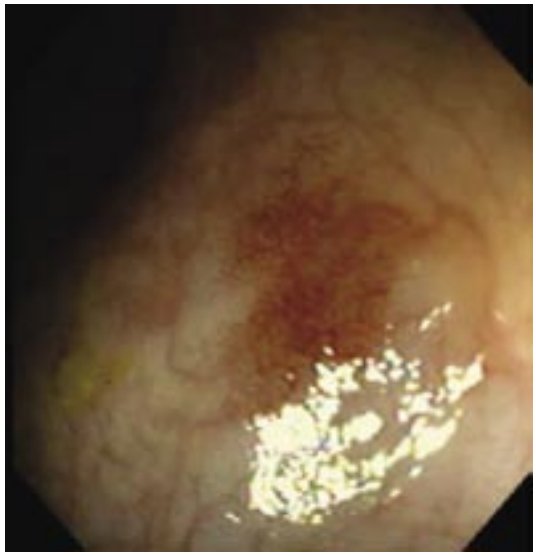

Figure 4 Angiodysplasia

A non-bleeding angiodysplasia found in the cecum on colonoscopy.

monly attributed to UGI bleeding. As with UGI bleeding, subacute and chronic LGI bleeding may present with brown stools that are chemically positive for occult blood.

The initial assessment for LGI bleeding is the same as for UGI bleeding. Massive blood loss in patients with comorbid medical conditions requires hospital admission for evaluation. Slower chronic or subacute bleeding may be evaluated semi-electively on an outpatient basis. Hemodynamic assessment and prompt resuscitation are always the first steps in treating patients with a presumed large-volume blood loss.

CAUSES

Colonic diverticulosis is the most frequent cause of massive colonic bleeding, accounting for approximately 70% of these episodes [34]. Diverticulosis is a common asymptomatic finding in elderly patients. The presence of diverticulosis increases with age. The incidence of bleeding from diverticulosis ranges from 10% to 30%, with massive hemorrhage occurring in about 5% [35]. It is fortunate that in 95% of patients, the bleeding stops spontaneously.

Angiodysplasia (Figure 4) is also frequently diagnosed in patients with LGI hemorrhage. The characteristic lesions are frequently found in the right colon or distal small bowel, although various reports claim up to 20% of lesions are found in the transverse or left colon [36]. The patient with angiodysplasia is usually elderly. There may be an association between angiodysplasia and valvular heart disease and end-stage renal disease. Hemorrhage from angiodysplasia may be intermittent and chronic, with iron-deficiency anemia as the major presenting problem. Some series report that up to half of the patients present with major hemorrhage [37].

Cancer of the large bowel (Figure 5), particularly of the rectum, will often cause rectal bleeding. The bleeding is almost always submassive and does not cause hemodynamic instability. Cancers involving the right colon are more likely to produce melanotic stools or occult bleeding with the gradual development of iron-deficiency anemia. Adenomas of the left colon may present with bright-red rectal bleeding, and adenomas of the right colon can produce anemia. The large bowel may be directly invaded by other tumors, such as gynecologic, bladder, and prostate cancers. Less commonly, cancer may metastasize to the colon. Depending on the location involved, tumor involvement of the colon can cause a spectrum of LGI bleeding, from occult bleeding to frank hematochezia.

Radiation therapy is often employed as treatment of gynecologic and prostate cancers, and despite advances in radiation technology, it can still lead to radiation damage of the rectosigmoid and gastrointestinal bleeding. LGI bleeding is usually a late complication, typically presenting 8–12 months after the completion of therapy [38]. Usually occurring as a result of radiation proctitis, LGI bleeding is characterized by the presence of telangiectasias and mucosal friability in the rectum or distal sigmoid. Depending on the radiation field, other areas of the colon and small bowel may also be involved. Radiation proctitis typically will cause recurrent rectal bleeding, but it is almost never massive.

Diagnosis and Treatment of LGI Bleeding

When LGI bleeding is suspected, colonoscopy is the initial procedure of choice for both diagnosis and treatment [39]. Despite the fact that blood acts as an effective cathartic, bowel cleansing is still necessary to provide a thorough evaluation of the colonic mucosa. This step can be accomplished with 4 L of a polyethylene glycol solution given orally over several hours [40]. Bowel cleansing has not been shown to reactivate or to increase the rate of bleeding and is safe in this setting.

Despite adequate cleansing of the bowel, colonoscopy still may not identify the site of bleeding.

In many cases, bleeding often ceases by the time colonoscopy is performed. Blood and clots may obscure thorough examination of the colonic mucosa, and the precise bleeding site may not be identified. Other diagnostic procedures may be necessary, especially in patients with massive LGI bleeding. These studies include radionucleotide imaging and angiography. Barium studies of the colon play no role in the evaluation of acute LGI bleeding.

DIVERTICULAR BLEEDING

Diverticular bleeding may be treated endoscopically with epinephrine injection and electrocautery if the bleeding site can be identified. The largest study of urgent colonoscopy for the treatment of diverticular bleeding included 123 patients in two phases [41]. Colonoscopy was performed 6 to 12 hours after hospitalization or the onset of hematochezia. During the initial phase, 17 of 73 patients (23%) had definite signs of diverticular hemorrhage (active bleeding, a non-bleeding visible vessel, or an adherent clot). These patients were all treated conservatively but underwent hemicolectomy for continued or recurrent diverticular bleeding as necessary. Of 17 patients, 9 (53%) had additional bleeding after colonoscopy, and 6 required surgery.

In the second phase, those with active diverticular bleeding or stigmata of diverticular bleeding (visible vessels or adherent clots) were treated with an epinephrine injection (1:20,000 U) and/or cautery. Clots were removed in much the same fashion as in those patients with peptic ulcer bleeding described previously. Of 48 patients, 10 (21%) had definite signs of diverticular hemorrhage, all of whom were treated endoscopically, and none had recurrent bleeding or required surgery.

It is important to point out that this study was completed by a dedicated gastrointestinal bleeding endoscopy team. Its general applicability remains unclear because, in many community settings, such teams with adequate experience in these techniques typically do not exist. Nonetheless, the fact that no complications were encountered suggests that endoscopic treatment of diverticular bleeding holds promise and should be considered at the time of colonoscopy.

Nuclear imaging with technetium-labeled red blood cells or technetium sulfur colloid can be utilized to detect LGI bleeding occurring at a rate of at least 0.1 mL/min. It is more sensitive than angiography, which generally requires blood loss > 1 mL/min for a positive study. However, nuclear scanning localizes bleeding to a particular area of the abdomen rather than an area within the colon. As a result, surgeons should not depend on the localization of bleeding suggested by these scans. In one series studying the use of nuclear imaging for LGI bleeding, 8 of 52 patients underwent unwarranted surgical procedures as a result of inaccurate scanning results [42]. Colonoscopy is recommended prior to nuclear imaging for the evaluation of LGI bleeding because of its higher diagnostic yield and the inaccuracy of nuclear imaging [39]. Despite its continued use in clinical practice, there is little evidence that nuclear imaging reduces the morbidity and mortality of patients with LGI.

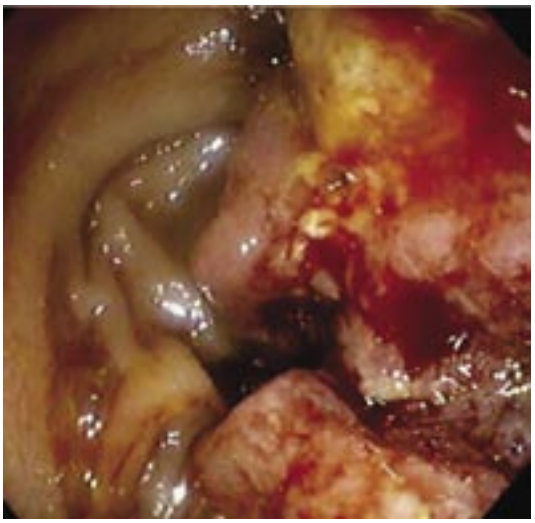

Figure 5 Rectosigmoid Cancer

Bleeding, partially obstructing rectosigmoid cancer as seen on colonoscopy.

When colonoscopy fails to identify the location of diverticular bleeding, or it cannot be controlled via colonoscopic intervention, angiography should be considered. Unlike nuclear imaging, angiographic localization of bleeding is accurate. However, because it requires higher rates of bleeding for a positive study, it is less sensitive. Transcatheter intra-arterial infusion of vasopressin or embolization can be utilized to control bleeding if the site is identified.

In a series of 50 patients with massive LGI bleeding, angiography localized the bleeding site in 72%, and selective vasopressin infusion stopped the bleeding in 91% [43]. Unfortunately, 50% of patients rebled once the infusion was discontin-

ued. Embolization can also be used in much the same way as for UGI bleeding but is associated with a risk of intestinal infarction of about 20%. Embolization of the most distal site possible should always be attempted to reduce this risk [44].

Despite these advances, the complication rate is higher for angiography than for colonoscopy. Colonoscopy is recommended before angiography not only because of the lower complication rate but because of the higher diagnostic yield, as well. Angiography can be considered when colonoscopy is not feasible or as an alternative to surgery in those with persistent bleeding [39].

For patients who continue to bleed, surgery may become necessary. For this reason, it is important to involve surgeons when patients present with massive LGI bleeding. Segmental colectomy is performed when the source of bleeding has been localized, either prior to surgery with colonoscopy or angiography or intraoperatively. Subtotal colectomy is reserved for patients in whom no bleeding site has been identified.

ANGIODYSPLASIA

For patients with acute LGI bleeding caused by angiodysplasia, the approach is similar to patients with diverticular bleeding. Colonoscopic interventions include endoscopic coagulation, injection sclerotherapy, and argon plasma coagulation. Angiography and embolization can also be employed.

Although actively bleeding angiodysplastic lesions should be treated, controversy exists concerning how to approach such lesions in a variety of other clinical circumstances. Incidentally discovered angiodysplastic lesions generally should not be treated. Lesions discovered during a work-up for occult bleeding are usually treated endoscopically if significant anemia does not respond to iron supplementation. A more difficult decision regarding treatment occurs when both diverticulosis and angiodysplasia are discovered on a colonoscopy performed for a work-up of LGI bleeding but there is no active bleeding. This scenario is relatively common, since both conditions exist in the same age group, and both stop bleeding spontaneously in the vast majority of cases.

RADIATION PROCTITIS

Patients who develop iron-deficiency anemia as a result of rectal bleeding from radiation proctitis should be treated with iron supplementation and stool softeners. If iron-deficiency anemia persists, endoscopic treatment of the radiation-induced rectal telangiectasias can be attempted, typically with argon plasma or bipolar coagulation [45]. However, recurrent bleeding is common. Medical therapy with sucralfate, 5-ASA (5-acetylsalicylic acid), or corticosteroid enemas have generally shown disappointing results but should be tried prior to endoscopic treatment [46].

Bleeding of the Small Intestine

When endoscopic evaluation fails to identify a source of acute, chronic, or occult gastrointestinal bleeding, the small bowel should be evaluated. Common causes of small bowel bleeding include angiodysplasia, tumors (primary or metastatic), and ulcers. Traditionally, evaluation of the small bowel started with a barium small bowel series or, preferably, enteroclysis of the small bowel. The diagnostic yield for identifying a small bowel lesion is low using these radiographic techniques, and, in one series, it was only 20% [47].

ENTEROSCOPY

Push enteroscopy can also be employed in such patients, with a higher diagnostic yield than the radiographic techniques previously noted. This technique involves passing a pediatric colonoscope or enteroscope as far as possible beyond the ligament of Treitz. This procedure allows visualization of the proximal to mid jejunum (about 60 cm). The diagnostic yield for obscure bleeding is approximately 40%, with angiodysplasia being the most common finding [48, 49]. Push enteroscopy also allows endoscopic treatment if an endoscopically treatable lesion, such as angiodysplasia, is seen [49].

CAPSULE ENDOSCOPY

Wireless video-capsule endoscopy was approved by the US Food and Drug Administration in 2000 (Given Imaging, Ltd., Yogneam, Israel). It provides diagnostic imaging of the entire small intestine. The indications for wireless capsule endoscopy continue to evolve. The most accepted indication is for the evaluation of obscure gastrointestinal bleeding.

The capsule is administered by mouth after an overnight fast. It takes two images per second, and a signal is transmitted to an external recorder, which the patient wears on a belt. The exam takes 8 hours to complete, and the images are downloaded, processed, and viewed using a computer workstation. The capsule is disposable and is excreted in the stool.

Capsule endoscopy appears to be superior to push enteroscopy in most reports, with diagnostic yields of 50%–70% [50, 51]. The diagnostic yield appears to be higher for patients with ongoing overt bleeding than for patients being evaluated for prior overt or occult bleeding [52]. Angiodysplasia remains the most common finding when video-capsule endoscopy is used, but, unlike push enteroscopy, no treatment can be applied.

One of the main risks with capsule endoscopy is capsule retention due to a small bowel stricture or mass. If the capsule becomes lodged behind such a lesion, it can be seen on a plain abdominal radiograph. The lesion, which prevents passage of the capsule, is usually the cause of the obscure bleeding. It is important to note that patients with a history of intra-abdominal malignancy, irradiation, or surgery are at particular risk for capsule retention. A barium small bowel series should be performed prior to capsule endoscopy to exclude an unforeseen, partially obstructing lesion. Even if the results of small bowel series are normal, careful consideration must be given before performing capsule endoscopy in such patients. Patients who are inoperable and those who refuse surgery would not be candidates for wireless video-capsule endoscopy.

Bleeding Gastrointestinal Tumors

Gastrointestinal tumors, direct local invasion by other malignancies, and metastatic disease to the gastrointestinal tract can all cause gastrointestinal bleeding. As noted previously, tumor bleeding is rarely massive and seldom causes hemodynamic instability. However, cancer patients may be on anticoagulation for deep venous thrombosis or pulmonary emboli or may be coagulopathic. In this setting, bleeding from tumors involving the gastrointestinal tract may be more brisk, necessitating frequent transfusions and ongoing hospitalization.

Attempts to control tumor bleeding using endoscopic methods, such as injection and cautery, are often not practical or useful. However, endoscopic treatment may slow or stop the bleeding temporarily, but recurrent tumor bleeding is likely, and endoscopic management rarely, if ever, impacts on overall survival. If gastrointestinal tumor bleeding is brisk, angiography and embolization can be considered, but such bleeding is rarely rapid enough for them to be successful. Depending on the location of the bleeding and the overall prognosis of the patient, palliative surgery may be an option. This approach is rarely practical, however, because of the morbidity of the surgical procedure. Palliative radiation therapy may also be considered as another alternative.

Summary

Gastrointestinal bleeding can be a serious problem in patients with cancer. The causes of both UGI and LGI bleeding in cancer patients are similar to those in patients without cancer. Diagnostic and management strategies also parallel those developed for benign causes of UGI and LGI bleeding. As the etiology of gastrointestinal bleeding in the cancer patient is often due to benign disease such as gastritis or diverticulosis, aggressive management should be considered in all patients with a reasonable performance status. The gastroenterologist plays a major role, and with the development of new endoscopic management techniques and drugs, fewer patients will require more invasive procedures for gastrointestinal bleeding.

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A peer viewpoint on this article by Dr. Lawrence R. Coia appears on page 111.

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