58-Year-Old Woman With Melena

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A 58-year-old woman presented to the emergency department with a 3-day history of passing dark, tarry stools. Her medical history was notable for symptomatic hemophilia A carrier state, gastroesophageal reflux disease, internal hemorrhoids, papillary thyroid cancer treated with radioactive iodine for nodal metastasis with secondary hypothyroidism, and obesity with a recent intentional 22.5-kg weight loss. She reported a 3-day history of passing black, tarry stools, averaging 3 stools per day. She did not have light-headedness on standing, any previous episodes, abdominal pain, vomiting, hematochezia, hematemesis, or history of liver or renal disease or alcohol abuse. She was not taking nonsteroidal anti-inflammatory drugs, iron, bismuth subsalicylate, or antiplatelet or anticoagulant medications.

Her family history was notable for adenomatous colonic polyposis (at age 17 years, her son was diagnosed as having adenomatous colonic polyps that necessitated a subtotal colectomy). The patient’s last colonoscopy was 4 years before the current presentation and was negative for masses or polyps.

On presentation, she had sinus tachycardia at 110 beats/min with a blood pressure of 111/51 mm Hg. Examination findings were remarkable for conjunctival pallor and positive results on a fecal occult blood test with melenic stool noted on rectal examination. Examination revealed no abdominal tenderness or stigmata of chronic liver disease.

Laboratory testing revealed the following notable results (reference ranges provided parenthetically): hemoglobin, 5.5 g/dL (12.0-15.5 g/dL); platelets, 179 × 10^9/L (150-450 × 10^9/L); international normalized ratio, 1.0 (0.8-1.2); activated partial thromboplastin time, 27 seconds (28-38 seconds); factor VIII activity, 86% (55%-200%); sodium, 139 mmol/L (135-145 mmol/L); potassium, 4.2 mmol/L (3.6-5.2 mmol/L); serum urea nitrogen, 28 mg/dL (6-21 mg/dL); and creatinine, 0.7 mg/dL (0.6-1.1 mg/dL).

1. Which one of the following factors is most predictive of bleeding from an upper gastrointestinal (GI) tract source?
   a. Blood or the appearance of coffee grounds detected during nasogastric lavage
   b. A ratio of serum urea nitrogen to serum creatinine greater than 30
   c. Melenic stool on examination
   d. Patient-reported history of melena
   e. Blood clots in the stool

A meta-analysis investigating factors predictive of upper GI tract bleeding found that blood or the appearance of coffee grounds detected during nasogastric lavage had a likelihood ratio (LR) of 9.6.1 Performing nasogastric lavage in patients with suspected acute upper GI tract bleeding is controversial, partly because it has failed to document superior clinical outcomes.2 In general, patients should only undergo nasogastric lavage if particulate matter, fresh blood, or clots need to be removed from the stomach to facilitate endoscopy. A ratio of serum urea nitrogen to serum creatinine greater than 30 has an even lower LR of 7.5. Because of the combination of blood absorption from the small bowel and a degree of decreased renal perfusion, patients with acute upper GI tract bleeding typically have an increased serum urea nitrogen to creatinine ratio. The higher the ratio, the more likely that the bleeding is from an upper GI tract source.3 Melenic stool on examination has the highest LR at 25. Patient-reported history of melena has a substantially lower LR of 5.1 to 5.9. Contrary to the aforementioned factors, the presence of blood clots in the stool makes an upper GI tract source less likely, with an LR of 0.05.

Upper GI tract bleeding is defined as bleeding from a site proximal to the ligament of Treitz. However, it is important to acknowledge that in 90% of patients melena originates proximal to the ligament of Treitz, but in 10% it can originate from the distal small bowel or right side of the colon.4

Our patient had a self-reported history of melena, melenic stool was found on examination,
and her serum urea nitrogen to serum creatinine ratio was 40. These factors are strongly suggestive of an upper GI tract bleeding source. Intravenous access was secured in the form of 2 large-bore intravenous lines, and aggressive fluid resuscitation with 0.9% normal saline was initiated, supplemented with packed red blood cell transfusion. An intravenous bolus of pantoprazole was administered followed by an infusion. The hematology service was consulted and recommended assessing her factor VIII level and administering 4500 U of recombinant factor VIII. She remained hemodynamically stable throughout her time in the emergency department before being transferred to the GI hospital service for further evaluation and management.

2. Based on the patient’s clinical presentation, which one of the following hemoglobin parameters is the most appropriate transfusion threshold?
   a. Less than 10 g/dL
   b. Less than 11 g/dL
   c. Less than 9 g/dL
   d. Less than 7 g/dL
   e. Less than 8 g/dL

   Although blood transfusion remains an integral step in the management of acute upper GI tract bleeding, the most effective transfusion strategy has long been the source of debate. The risks of blood transfusions include transmission-transmitted pathogens (human immunodeficiency virus, hepatitis B virus, hepatitis C virus, cytomegalovirus, bacteria, parasites), allergic and immunologic reactions, transfusion-associated circulatory overload, transfusion-related acute lung injury, and electrolyte abnormalities. The decision to transfuse blood should not be taken lightly and must be individualized. Certainly, a more liberal approach such as a hemoglobin transfusion threshold of less than 10 g/dL or less than 11 g/dL has not been found to improve outcomes and should be avoided. Generally, one should avoid a hemoglobin transfusion threshold of less than 9 g/dL unless active cardiovascular symptoms are present (ie, signs of myocardial ischemia, active severe hemorrhage and orthostatic hypotension, or tachycardia unresponsive to fluid replacement). A recent randomized controlled trial revealed that patients with acute upper GI tract bleeding treated with a restrictive transfusion strategy (<7 g/dL) had significantly less rebleeding and adverse events than patients treated with a more liberal transfusion strategy (<9 g/dL). There was also a trend toward lower mortality in patients with peptic ulcer disease, although this wasn’t statistically significant. Our patient had no signs of active cardiovascular symptoms, and thus a transfusion threshold of less than 7 g/dL is most appropriate. This latest evidence has revealed that a threshold of less than 7 g/dL, as opposed to a threshold of less than 8 g/dL, in stable patients is effective and avoids the risks associated with blood transfusions. Importantly, the initial hemoglobin level in patients with acute upper GI tract bleeding will often be at the patient’s baseline because the patient is losing whole blood. Typically, the hemoglobin level will decrease after 24 hours as the blood is diluted by the influx of extravascular fluid into the vascular space and by fluid administered during resuscitation.

   Our patient received 2 U of packed red blood cell concentrate because of her hemoglobin level of 5.5 g/dL. She remained stable after appropriate resuscitation. However, she had signs of ongoing bleeding requiring more blood transfusions. Therefore, esophagastroduodenoscopy (EGD) was performed, which was unrevealing for a source of bleeding.

3. Which one of the following is the best next step in evaluating this patient’s GI tract bleeding?
   a. Observation
   b. Angiography
   c. Colonoscopy
   d. Wireless video capsule endoscopy
   e. Deep small-bowel enteroscopy

   Observation is not appropriate because our patient has signs of ongoing bleeding and has required further blood transfusions to sustain her hemoglobin level above 7 g/dL. Angiography is not typically indicated until GI tract bleeding ensues despite maximal medical and endoscopic therapy. In patients with melena and no abnormalities detected on upper EGD, the recommendation is to perform colonoscopy to rule out a right-sided colonic source of the bleeding. Therefore, colonoscopy is the most appropriate next step for our patient. A suspected bleeding source was identified in 5% of patients in a recent study of colonoscopies performed for the evaluation of...
melena following nondiagnostic upper endoscopy. Capsule endoscopy would be indicated in GI tract bleeding in a hemodynamically stable patient after a negative EGD result and colonoscopy or obscure GI tract bleeding. Our patient will have to undergo colonoscopy before obscure GI tract bleeding can be diagnosed. The main advantages of capsule endoscopy are that it is noninvasive, the entire length of the small bowel can be examined, and it can guide further deep small-bowel enteroscopy. However, it does not permit tissue sampling or therapeutic intervention. Furthermore, it is also contraindicated in patients with partial or intermittent small-bowel obstruction because of the risk of capsule retention. Deep small-bowel enteroscopy enables tissue sampling and therapeutic maneuvers. However, this procedure is invasive and is not appropriate at this early stage of the evaluation.

Our patient underwent colonoscopy, which did not reveal any active bleeding or gross lesions. She continued to have signs of persistent bleeding. The decision was made to further evaluate for a source of bleeding.

4. Based on patient’s age and presentation, which one of the following procedures will most likely yield the diagnosis?
   a. Push enteroscopy
   b. Radionuclide bleeding scan
   c. Meckel scan
   d. Wireless video capsule endoscopy
   e. Computed tomographic (CT) enterography with triple-phase protocol

In our 58-year-old patient, our leading differential diagnosis at this stage was a small-bowel tumor. Push enteroscopy involves peroral passage of a dedicated push enteroscope enabling up to 80 cm of jejunum distal to the ligament of Treitz to be evaluated. Studies have described the diagnostic yield of push enteroscopy in identifying bleeding lesions as ranging from 3% to 70%. However, noninvasive tests such as capsule endoscopy have largely superseded push enteroscopy at this stage of evaluation. A radionuclide bleeding scan (eg, technetium Tc 99m pertechnetate—labeled autologous red blood cells) detects bleeding that is occurring at a minimum rate of 0.1 to 0.5 mL/min. The real usefulness of a bleeding scan is to confirm that active bleeding is occurring before localization with angiography; it will not help with etiology. A Meckel scan consists of the intravenous administration of technetium Tc 99m pertechnetate, which has an affinity for gastric mucosa, followed by scintigraphy. A Meckel scan is particularly appropriate in children and young adults but not in middle-aged patients. Although the management algorithm for obscure GI tract bleeding would suggest capsule endoscopy as the appropriate next step, at our institution CT enterography has been found to be superior in detecting small-bowel tumors compared with capsule endoscopy. It is important to acknowledge that the reported study used a triple-phase CT enterography protocol, not the single-phase protocol that is the modality available at most medical centers. Furthermore, in the current patient there was concern about a partially obstructing tumor that could increase the risk of capsule retention.

To this end, CT enterography with oral and intravenous contrast using the triphase enterography protocol (arterial, enteric, and delayed phases) was performed. Computed tomographic enterography revealed a 1.3-cm hypervascular nodule in the proximal ileum that was highly characteristic of a carcinoid tumor. There was no evidence of metastatic disease, and the patient’s urinary 5-hydroxyindoleacetic acid level was within normal limits.

5. Which one of the following is the most appropriate management strategy for this patient?
   a. Radiation therapy
   b. Chemotherapy
   c. Octreotide
   d. Localized small-bowel resection
   e. Expectant management with symptom control

Radiation therapy or chemotherapy should be considered only if the carcinoid tumor has metastasized and when surgical excision is not suitable. Our patient has no evidence of metastasis on imaging, so these treatment options are not appropriate. Octreotide, a somatostatin analogue, is highly effective in reducing symptoms once metastasis has occurred. Our patient is asymptomatic so does not require symptomatic pharmacological treatment. Patients with nonmetastatic small-bowel carcinoid tumors should be treated with resection of the involved
segment and small-bowel mesentery. Expectant management is not an option when surgical resection is possible.

Our patient underwent a successful partial ileoectomy with resection of her carcinoid tumor and a primary end-to-end anastomosis. The pathology report confirmed the presence of a 1.4-cm, well-differentiated, G1 (low-grade) neuroendocrine tumor with margins free of tumor and a single lymph node negative for tumor, consistent with stage I disease. Studies performed by the American Joint Committee on Cancer found that patients with stage I small-bowel carcinoid tumors have a 95% 10-year survival rate, giving our patient an excellent prognosis.11 Evidently, her underlying hemophilia resulted in her carcinoid tumor presenting at an early stage, enabling curative resection. She had an uneventful postoperative course with cessation of her bleeding and stabilization of her hemoglobin level at 9.5 g/dL before discharge. On follow-up, our patient has not had recurrence of bleeding.

**DISCUSSION**

Obscure bleeding is defined as bleeding from the GI tract that persists or recurs without an obvious etiology after upper endoscopy and colonoscopy. Obscure bleeding may be either overt or occult and accounts for about 5% of GI tract bleeding events. Obscure occult GI tract bleeding occurs without visible evidence of hemorrhage (ie, melena or hematochezia). Our patient had overt obscure bleeding, presenting as melena. The source is in the small bowel in 75% of patients.12 The remainder of cases are due to missed lesions in either the upper or lower GI tract.

The etiology of obscure GI tract bleeding is best classified according to prevalence in particular age groups.8 In young adults (17-40 years), Crohn disease and Meckel diverticulum should be primary considerations. In middle-aged patients (41-65 years), small-bowel tumors, particularly GI tract stromal tumors, should be principally considered. In elderly patients (>65 years), vascular anomalies are the most common cause. Depending on the clinical scenario, other possible etiologies include nonspecific enteritis, Dieulafoy lesion, small-bowel ulcers, nonsteroidal anti-inflammatory drug enteropathy, hemobilia, aortoenteric fistula, celiac disease, and hemosuccus pancreaticus.

The American Gastroenterological Association recommends wireless video capsule endoscopy for the evaluation of obscure (occult or overt) GI tract bleeding in hemodynamically stable patients and consideration of angiography or even intraoperative enteroscopy in unstable patients.7 However, if available, triple-phase CT enterography should be considered in middle-aged patients because it is more likely to detect small-bowel tumors, the most common cause of obscure bleeding in this age group, than capsule endoscopy. If results are negative and the patient has ongoing bleeding, repeated upper endoscopy and colonoscopy is recommended before entertaining alternative investigative testing of the small bowel such as deep small-bowel enteroscopy, radionuclide scanning (Meckel scan, tagged red blood cell scan), CT enterography, or laparoscopy/laparotomy with intraoperative enteroscopy.

Carcinoid tumors are of neuroendocrine origin and derived from primitive stem cells in the gut wall, and they have a high potential for metastasis. Carcinoid tumors of the small intestine are most commonly found in the ileum within 60 cm of the ileocecal valve. Measurement of urinary 5-hydroxyindoleacetic acid levels can help in diagnosing carcinoid syndrome but may not help in detecting tumors at an early stage of development when they are potentially curable with resection. Appropriate imaging (such as CT or positron emission tomography) combined with biopsy via enteroscopy provides the definitive diagnosis. Patients with nonmetastatic tumors should be treated with resection of the involved segment and small-bowel mesentery. If metastasis has occurred and in cases in which surgical excision is not suitable, chemotherapy and somatostatin analogues are currently recommended.

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**REFERENCES**


**CORRECT ANSWERS:** 1. c. 2. d. 3. c. 4. e. 5. d