Journal of HOSPITAL MEDICINE www.journalofhospitalmedicine.com

CLINICAL CARE CONUNDRUMS

Taking the Detour

The approach to clinical conundrums by an expert clinician is revealed through the presentation of an actual patient's case in an approach typical of a morning report. Similarly to patient care, sequential pieces of information are provided to the clinician, who is unfamiliar with the case. The focus is on the thought processes of both the clinical team caring for the patient and the discussant.

This icon represents the patient's case. Each paragraph that follows represents the discussant's thoughts.

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A 60-year-old woman presented to a community hospital's emergency department with 4 days of right-sided abdominal pain and multiple episodes of "black stools." She reported nausea without vomiting. She denied lightheadedness, chest pain, or shortness of breath. She also denied difficulty in swallowing, weight loss, jaundice, or other bleeding.

The first priority when assessing a patient with gastrointestinal (GI) bleeding is to ensure hemodynamic stability. Next, it is important to carefully characterize the stools to help narrow the differential diagnosis. As blood is a cathartic, frequent, loose, and black stools suggest vigorous bleeding. It is essential to establish that the stools are actually black, as some patients will mistake dark brown stools for melena. Using a visual aid like a black pen or shoes as a point of reference can help the patient differentiate between dark stool and melena. It is also important to obtain a thorough medication history because iron supplements or bismuth-containing remedies can turn stool black. The use of any antiplatelet agents or anticoagulants should also be noted. The right-sided abdominal pain should be characterized by establishing the frequency, severity, and association with eating, movement, and position. For this patient's presentation, increased pain with eating would rapidly heighten concern for mesenteric ischemia.

The patient reported having 1 to 2 semiformed, tarry, black bowel movements per day. The night prior to admission she had passed some bright red blood along with the melena. The abdominal pain had increased gradually over 4 days, was dull, constant, did not radiate, and there were no evident aggravating or relieving factors. She rated the pain as 4 out of 10 in intensity, worst in her right upper quadrant.

Her past medical history was notable for recurrent deep venous thromboses and pulmonary emboli that had occurred even while on oral anticoagulation. Inferior vena cava (IVC) filters had twice been placed many years prior; anticoagulation had been subsequently discontinued. Additionally, she was known to have chronic superior vena cava (SVC) occlusion, presumably related to hypercoagulability. Previous evaluation had identified only hyperhomocysteinemia as a risk factor for recurrent thromboses. Other medical problems included hemorrhoids, gastroesophageal reflux disease, and asthma. Her only surgical history was an abdominal hysterectomy and bilateral oophorectomy many years ago for nonmalignant disease. Home medications were omeprazole, ranitidine, albuterol, and fluticasone-salmeterol. She denied using nonsteroidal anti-inflammatory drugs, aspirin, or any dietary supplements. She denied smoking, alcohol, or recreational drug use.

Because melena is confirmed, an upper GI tract bleeding source is most likely. The more recent appearance of bright red blood is concerning for acceleration of bleeding, or may point to a distal small bowel or right colonic source. Given the history of thromboembolic disease and likely underlying hypercoagulability, vascular occlusion is a leading possibility. Thus, mesenteric arterial insufficiency or mesenteric venous thrombosis should be considered, even though the patient does not report the characteristic postprandial exacerbation of pain. Ischemic colitis due to arterial insufficiency typically presents with severe, acute pain, with or without hematochezia. This syndrome is typically manifested in vascular watershed areas such as the splenic flexure, but can also affect the right colon. Mesenteric venous thrombosis is a rare condition that most often occurs in patients with hypercoagulability. Patients present with variable degrees of abdominal pain and often with GI bleeding. Finally, portal venous thrombosis may be seen alongside thromboses of other mesenteric veins or may occur independently. Portal hypertension due to portal vein thrombosis can result in esophageal and/or gastric varices. Although variceal bleeding classically presents with dramatic hematemesis, the absence of hematemesis does not rule out a variceal bleed in this patient.

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Additional Supporting Information may be found in the online version of this article.

Received: January 28, 2015; **Revised:** June 18, 2015; **Accepted:** June 22, 2015
2015 Society of Hospital Medicine DOI 10.1002/jhm.2424
Published online in Wiley Online Library (Wileyonlinelibrary.com).

On physical examination, the patient had a temperature of 37.1°C with a pulse of 90 beats per minute and blood pressure of 161/97 mm Hg. Orthostatics were not performed. No blood was seen on nasal and oropharyngeal exam. Respiratory and cardiovascular exams were normal. On abdominal exam, there was tenderness to palpation of the right upper quadrant without rebound or guarding. The spleen and the liver were not palpable. There was a lower midline incisional scar. Rectal exam revealed nonbleeding hemorrhoids and heme-positive stool without gross blood. Bilateral lower extremities had trace pitting edema, hyperpigmentation, and superficial venous varicosities. On skin exam, there were distended subcutaneous veins radiating outward from around the umbilicus as well as prominent subcutaneous venous collaterals over the chest and lateral abdomen.

The collateral veins over the chest and lateral abdomen are consistent with central venous obstruction from the patient's known SVC thrombus. However, the presence of paraumbilical venous collaterals (caput medusa) is highly suggestive of portal hypertension. This evidence, in addition to the known central venous occlusion and history of thromboembolic disease, raises the suspicion for mesenteric thrombosis as a cause of her bleeding and pain. The first diagnostic procedure should be an esophagogastroduodenoscopy (EGD) to identify and potentially treat the source of bleeding, whether it is portal hypertension related (portal gastropathy, variceal bleed) or from a more common cause (peptic ulcer disease, stress gastritis). If the EGD is not diagnostic, the next step should be to obtain computed tomography (CT) of the abdomen and pelvis with intravenous (IV) and oral contrast. In many patients with GI bleed, a colonoscopy would typically be performed as the next diagnostic study after EGD. However, in this patient, a CT scan is likely to be of higher yield because it could help assess the mesenteric and portal vessels for patency and characterize the appearance of the small intestine and colon. Depending on the findings of the CT, additional dedicated vascular diagnostics might be needed.

Hemoglobin was 8.5 g/dL (12.4 g/dL 6 weeks prior) with a normal mean corpuscular volume and red cell distribution. The white cell count was normal, and the platelet count was 142,000/mm^3. The blood urea nitrogen was 27 mg/dL, with a creatinine of 1.1 mg/dL. Routine chemistries, liver enzymes, bilirubin, and coagulation parameters were normal. Ferritin was 15 ng/mL (normal: 15–200 ng/mL).

The patient was admitted to the intensive care unit. An EGD revealed a hiatal hernia and grade II nonbleeding esophageal varices with normal=appearing stomach and duodenum. The varices did not have stigmata of a recent bleed and were not ligated. The patient continued to bleed and received 2 U of packed red blood cells (RBCs), as her hemoglobin had decreased to 7.3 g/dL. On hospital day 3, a colonoscopy was done that showed blood clots in the ascending colon but was otherwise normal. The patient had ongoing abdominal pain, melena, and hematochezia, and continued to require blood transfusions every other day.

Esophageal varices were confirmed on EGD. However, no high-risk stigmata were seen. Findings that suggest either recent bleeding or are risk factors for subsequent bleeding include large size of the varices, "nipple sign" referring to a protruding vessel from an underlying varix, or red wale sign, referring to a longitudinal red streak on a varix. The lack of evidence for an esophageal, gastric, or duodenal bleeding source correlates with lack of clinical signs of upper GI tract hemorrhage such as hematemesis or coffee ground emesis. Because the colonoscopy also did not identify a bleeding source, the bleeding remains unexplained. The absence of significant abnormalities in liver function or liver inflammation labs suggests that the patient does not have advanced cirrhosis and supports the suspicion of a vascular cause of the portal hypertension. At this point, it would be most useful to obtain a CT scan of the abdomen and pelvis.

The patient continued to bleed, requiring a total of 7 U of packed RBCs over 7 days. On hospital day 4, a repeat EGD showed nonbleeding varices with a red wale sign that were banded. Despite this, the hemoglobin continued to drop. A technetium-tagged RBC study showed a small area of subumbilical activity, which appeared to indicate transverse colonic or small bowel bleeding (Figure 1). A subsequent mesenteric angiogram failed to show active bleeding.

A red wale sign confers a higher risk of bleeding from esophageal varices. However, this finding can be subjective, and the endoscopist must individualize the decision for banding based on the size and appearance of the varices. It was reasonable to proceed with banding this time because the varices were large, had a red wale sign, and there was otherwise unexplained ongoing bleeding. Because her hemoglobin continued to drop after the banding and a tagged RBC study best localized the bleeding to the small intestine or transverse colon, it is unlikely that the varices are the primary source of bleeding. It is not surprising that the mesenteric angiogram did not show a source of bleeding, because this study requires active bleeding at a sufficient rate to radiographically identify the source.

The leading diagnosis remains an as yet uncharacterized small bowel bleeding source related to mesenteric thrombotic disease. Cross-sectional imaging with IV contrast to identify significant vascular occlusion should be the next diagnostic step. Capsule endoscopy would be a more expensive and time-consuming option, and although this could reveal the source of bleeding, it might not characterize the underlying vascular nature of the problem.

Due to persistent abdominal pain, a CT without intravenous contrast was done on hospital day 10. This showed extensive collateral vessels along the chest and abdominal wall with a distended azygos vein. The study was otherwise unrevealing. Her bloody stools cleared, so she was discharged with a plan for capsule endoscopy and outpatient follow-up with her gastroenterologist. On the day of discharge (hospital day 11), hemoglobin was 7.5 g/dL and she received an eighth unit of packed RBCs. Overt bleeding was absent.

As an outpatient, intermittent hematochezia and melena recurred. The capsule endoscopy showed active bleeding approximately 45 minutes after the capsule exited the stomach. The lesion was not precisely located or characterized, but was believed to be in the distal small bowel.

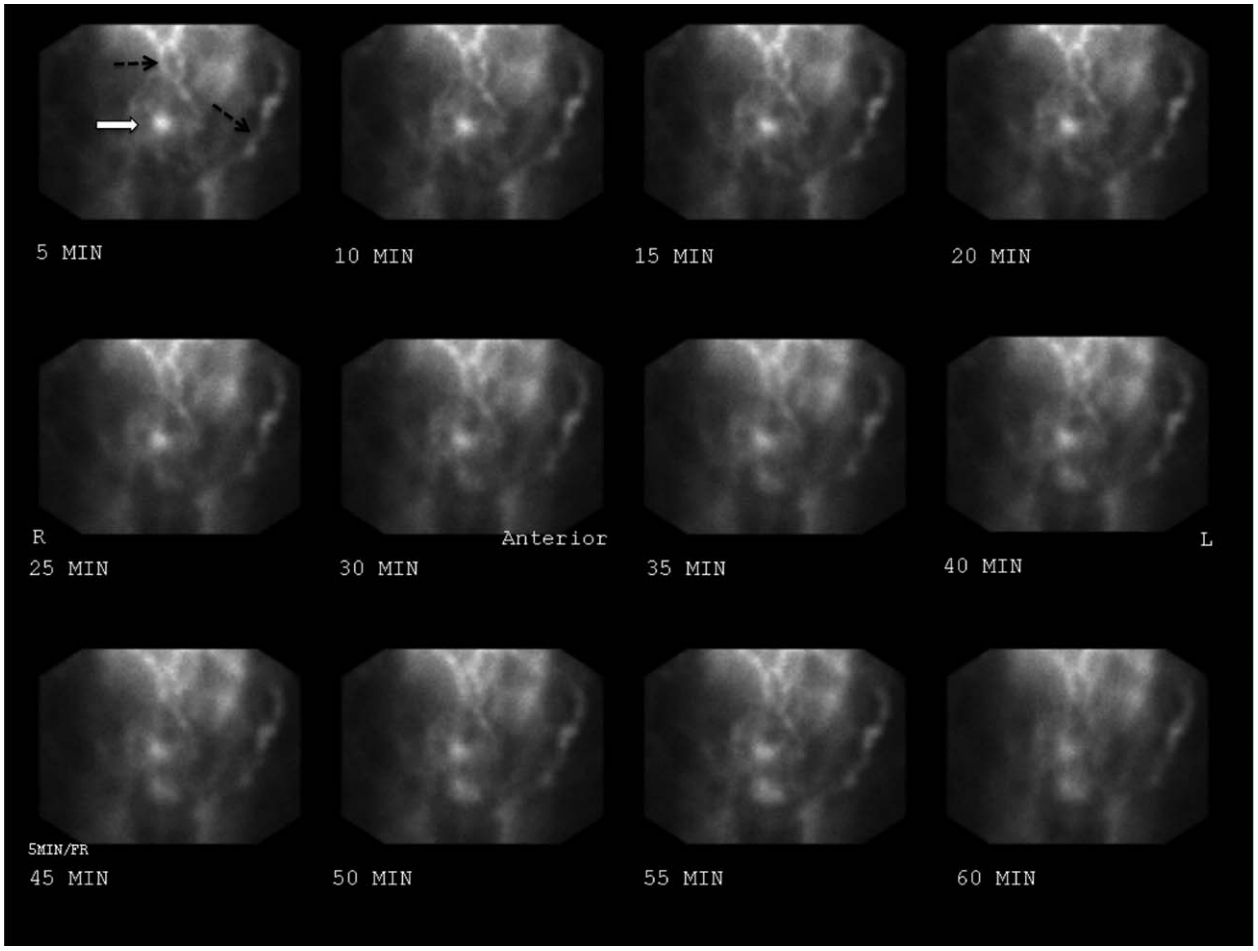

FIG. 1. Tagged red blood cell (RBC) scan. A focus of activity is centrally located in the lower half of the midabdomen below the umbilicus (white solid arrow) at 5 minutes following the intravenous administration of 27.4 mCi of Tc-99m–labeled RBCs that fades over time. There are prominent vascular patterns around and within the abdomen (black dotted arrow).

The capsule finding supports the growing body of evidence implicating a small bowel source of bleeding. Furthermore, the ongoing but slow rate of blood loss makes a venous bleed more likely than an arterial bleed. A CT scan was performed prior to capsule study, but this was done without intravenous contrast. The brief description of the CT findings emphasizes the subcutaneous venous changes; a contraindication to IV contrast is not mentioned. Certainly IV contrast would have been very helpful to characterize the mesenteric arterial and venous vasculature. If there is no contraindication, a repeat CT scan with IV contrast should be performed. If there is a contraindication to IV contrast, it would be beneficial to revisit the noncontrast study with the specific purpose of searching for clues suggesting mesenteric or portal thrombosis. If the source still remains unclear, the next steps should be to perform push enteroscopy to assess the small intestine from the luminal side and magnetic resonance angiogram with venous phase imaging (or CT venogram if there is no contraindication to contrast) to evaluate the venous circulation.

The patient was readmitted 9 days after discharge with persistent melena and hematochezia. Her hemoglobin was 7.2 g/dL. Given the lack of a diagnosis, the patient was transferred to a tertiary care hospital, where a second colonoscopy and mesenteric angiogram were negative for bleeding. Small bowel enteroscopy showed no source of bleeding up to 60 cm past the pylorus. A third colonoscopy was performed due to recurrent bleeding; this showed a large amount of dark blood and clots throughout the entire colon including the cecum (Figure 2). After copious irrigation, the underlying mucosa was seen to be normal. At this point, a CT angiogram with both venous and arterial phases was done due to the high suspicion for a distal jejunal bleeding source. The CT angiogram showed numerous venous collaterals encasing a loop of mid–small bowel demonstrating progressive submucosal venous enhancement. In addition, a venous collateral ran down the right side of the sternum to the infraumbilical area and drained through the encasing collaterals into the portal venous system (Figure 3). The CT scan also revealed IVC obstruction below the distal IVC filter and an enlarged portal vein measuring 18 mm (normal <12 mm).

The CT angiogram provides much-needed clarity. The continued bleeding is likely due to ectopic varices in the small bowel. The venous phase of the CT angiogram shows thrombosis of key venous structures and evidence of a dilated portal vein (indicating portal hypertension) leading to ectopic varices in the abdominal wall and jejunum. Given the prior studies that suggest a small bowel source of bleeding, jejunal varices are the most likely cause of recurrent GI bleeding in this patient.

The patient underwent exploratory laparotomy. Loops of small bowel were found to be adherent to the hysterectomy scar. There were many venous collaterals from the abdominal wall to these loops of bowel, dilating the veins

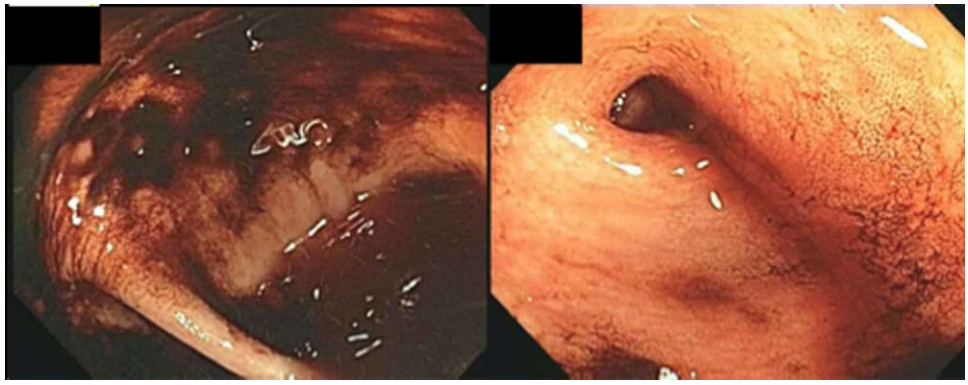

FIG. 2. Third colonoscopy showing a large amount of dark red blood and clots through the entire colon, including the cecum (left pane), which after copious irrigation revealed normal-appearing underlying mucosa (right pane).

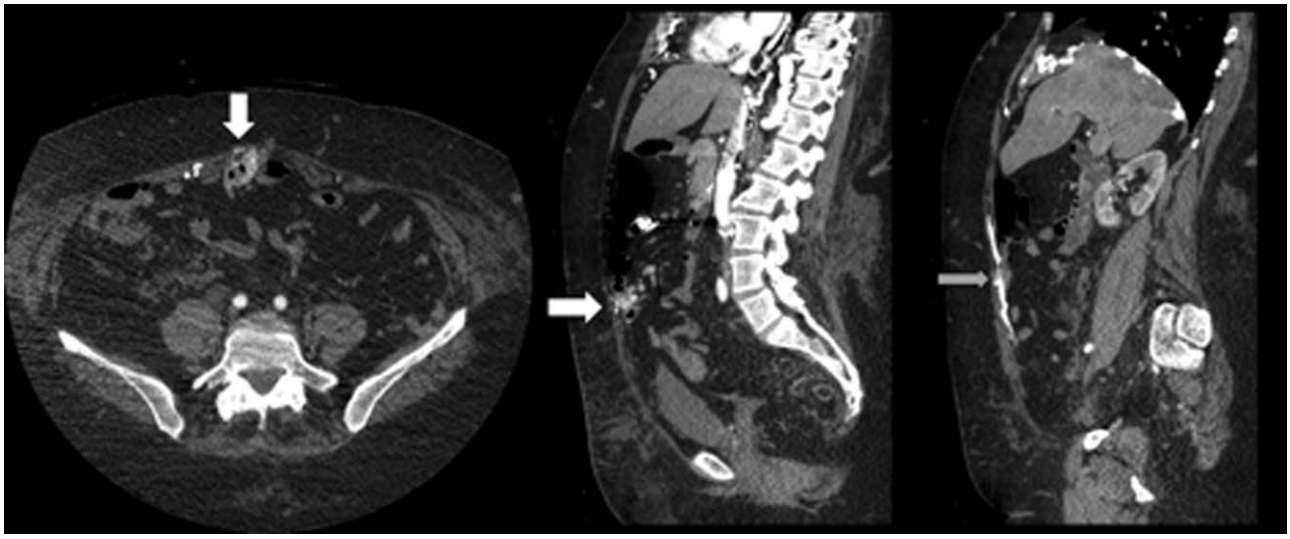

FIG. 3. Computed tomography with intravenous contrast, venous phase. There are prominent venous collaterals (white solid arrow) encasing a loop of small bowel, showing submucosal venous enhancement in axial (left pane) and sagittal view (center pane). There are extensive collaterals along the anterior abdominal wall that drains blood from the intrathoracic veins into the inferior vena cava (right pane, grey arrow), some of which drains into the collaterals encasing the loop of small bowel.

both in intestinal walls and those in the adjacent mesentery. After clamping these veins, the small bowel was detached from the abdominal wall. On unclamping, the collaterals bled with a high venous pressure. Because these systemic-portal shunts were responsible for the bleeding, the collaterals were sutured, stopping the bleeding. Thus, partial small bowel resection was not necessary. Postoperatively, her bleeding resolved completely and she maintained normal hemoglobin at 1-year follow-up.

COMMENTARY

The axiom "common ailments are encountered most frequently" underpins the classical stepwise approach to GI bleeding. First, a focused history helps localize the source of bleeding to the upper or lower GI tract. Next, endoscopy is performed to identify and treat the cause of bleeding. Finally, advanced tests such as angiography and capsule endoscopy are performed if needed. For this patient, following the usual algorithm failed to make the diagnosis or stop the bleeding. Despite historical and examination features suggesting that her case fell outside of the common patterns of GI bleeding, this patient underwent 3 upper endoscopies, 3 colonoscopies, a capsule endoscopy, a technetium-tagged RBC study, 2 mesenteric angiograms, and a noncontrast CT scan before the study that was ultimately diagnostic was performed. The clinicians caring for this patient struggled to incorporate the atypical features of her history and presentation and failed to take an earlier detour from the usual algorithm. Instead, the same studies that had not previously led to the diagnosis were repeated multiple times.

Ectopic varices are enlarged portosystemic venous collaterals located anywhere outside the gastroesophageal region.[1] They occur in the setting of portal hypertension, surgical procedures involving abdominal viscera and vasculature, and venous occlusion. Ectopic varices account for 4% to 5% of all variceal bleeding episodes.[1] The most common sites include the anorectal junction (44%), duodenum (17%–33%), jejunum/ileum (5%–17%), colon (3.5%–14%), and sites of previous abdominal surgery.[2,3] Ectopic varices can cause either luminal or extraluminal (i.e., peritoneal) bleeding.[3] Luminal bleeding, seen in this case, is caused by venous protrusion into the submucosa. Ectopic varices present as a slow venous ooze, which explains this patient's ongoing requirement for recurrent blood transfusions.[4]

In this patient, submucosal ectopic varices developed as a result of a combination of known risk factors: portal hypertension in the setting of chronic venous occlusion from her

hypercoagulability and a history of abdominal surgery (hysterectomy). [5] The apposition of her abdominal wall structures (drained by the systemic veins) to the bowel (drained by the portal veins) resulted in adhesion formation, detour of venous flow, collateralization, and submucosal varix formation.[1,2,6]

The key diagnostic study for this patient was a CT angiogram, with both arterial and venous phases. The prior 2 mesenteric angiograms had been limited to the arterial phase, which had missed identifying the venous abnormalities altogether. This highlights an important lesson from this case: contrast-enhanced CT may have a higher yield in diagnosing ectopic varices compared to repeated endoscopies—especially when captured in the late venous phase—and should strongly be considered for unexplained bleeding in patients with stigmata of liver disease or portal hypertension.[7,8] Another clue for ectopic varices in a bleeding patient are nonbleeding esophageal or gastric varices, as was the case in this patient.[9]

The initial management of ectopic varices is similar to bleeding secondary to esophageal varices.[1] Definitive treatment includes endoscopic embolization or ligation, interventional radiological procedures such as portosystemic shunting or percutaneous embolization, and exploratory laparotomy to either resect the segment of bowel that is the source of bleeding or to decompress the collaterals surgically.[9] Although endoscopic ligation has been shown to have a lower rebleeding rate and mortality compared to endoscopic injection sclerotherapy in patients with esophageal varices, the data are too sparse in jejunal varices to recommend 1 treatment over another. Both have been used successfully either alone or in combination with each other, and can be useful alternatives for patients who are unable to undergo laparotomy.[9]

Diagnostic errors due to cognitive biases can be avoided by following diagnostic algorithms. However, over-reliance on algorithms can result in "vertical line failure," a form of cognitive bias in which the clinician subconsciously adheres to an inflexible diagnostic approach.[10] To overcome this bias, clinicians need to "think laterally" and consider alternative diagnoses when algorithms do not lead to expected outcomes. This case highlights the challenges of knowing when to break free of conventional approaches and the rewards of taking a well-chosen detour that leads to the diagnosis.

KEY POINTS

1. Recurrent, occult gastrointestinal bleeding should raise concern for a small bowel source, and clinicians may need to "take a detour" away from the usual workup to arrive at a diagnosis.
2. CT angiography of the abdomen and pelvis may miss venous sources of bleeding, unless a venous phase is specifically requested.
3. Ectopic varices can occur in patients with portal hypertension who have had a history of abdominal surgery; these patients can develop venous collaterals for decompression into the systemic circulation through the abdominal wall.

Disclosure: Nothing to report.

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