Updates in Small Bowel Imaging and Endoscopy

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The field of gastroenterology has had an abundance of technological advances in recent years, especially in the field of endoscopy. These advances are helpful to clinicians approaching gastrointestinal blood loss, especially in the small bowel. The authors report a case of a man who presented to the emergency department with obscure gastrointestinal blood loss. Results of an esophagogastroduodenoscopy and a colonoscopy suggested the source of the blood loss was within the small bowel. On an outpatient basis, the patient underwent video capsule endoscopy, which revealed scattered distal duodenal arteriovenous malformations. He then underwent oral double balloon endoscopy with ablation of the arteriovenous malformations, with no further bleeding or drop in hemoglobin. The authors review advances in small bowel imaging and endoscopy, including video capsule endoscopy, double balloon endoscopy, and computed tomography enterography. A comprehensive data review was conducted by searching the National Library of Medicine’s PubMed database to identify recent published literature in the fields of radiology and gastroenterology. The authors apply these findings to the workup and diagnosis of obscure gastrointestinal blood loss.

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Clinical Case
A 57-year-old man presented to the emergency department with complaints of weakness, fatigue, dizziness, and intermittent melanic stools and hematochezia. He had persistent melena and hematochezia for roughly 2 weeks, which he described as painless bleeding with intermittent, nonspecific abdominal cramping. The patient’s vital signs were within normal limits. Results of pertinent laboratory studies in the emergency room revealed hemoglobin of 7.7 g/dL, mean corpuscular volume of 72 µm³, and a blood platelet count of 553 × 10³ µL. His prothrombin time, partial thromboplastin time, and international normalized ratio were within normal limits. The patient was not taking any medications and denied use of nonsteroidal anti-inflammatory drugs. He also denied undergoing any surgeries in the past. His family history was unremarkable.

The patient was admitted to the hospital and underwent aggressive resuscitation through the administration of intravenous fluids and the transfusion of 2 units of packed red blood cells. After a purgative bowel preparation that night, the patient underwent an esophagogastroduodenoscopy and colonoscopy the next day. The esophagogastroduodenoscopy revealed mild gastritis; the source of bleeding was not identified. The colonoscopy revealed scattered mild colonic diverticula. No signs of active bleeding were present until arrival in the emergency room, in which there appeared to be old blood. The terminal ileum was intubated for 25 cm during colonoscopic examination, which revealed fresh blood 10 cm past the ileocecal valve in the ileum. However, no source for the blood was identified. The finding of fresh blood within the terminal ileum but not in the colon was clinically significant because it suggested the source of the blood loss was within the small bowel.

The patient’s hemoglobin levels remained stable during his hospitalization and he was discharged 2 days later. On an outpatient basis, he underwent video capsule endoscopy (VCE), which revealed scattered distal duodenal arteriovenous malformations. The patient underwent oral double balloon enteroscopy (DBE) 10 days after discharge with ablation of the arteriovenous malformations. At 1 month follow-up, the patient had no further bleeding or drop in hemoglobin.

Review
The presented case highlights several technologies used in the workup and diagnosis of obscure gastrointestinal blood loss. While endoscopy once provided just a simple visualization of the rectum, it has evolved to provide a full examination of the colon, esophagus, stomach, and portions of the duodenum with the ability for polypectomy and endoscopic hemostasis for both upper and lower gastrointestinal bleeding. Recent advances in gastrointestinal endoscopy and imaging have allowed clinicians to not only examine the small bowel, but to also provide interventional therapeutics if necessary.

loss. The field of gastroenterology has had an abundance of technological advances in recent years, especially in the field of endoscopy. We discuss the role of 2 technologies described in the present case—VCE and DBE—as well as computed tomography enterography (CTE) in the workup and diagnosis of obscure gastrointestinal blood loss.

**Video Capsule Endoscopy**

Video capsule endoscopy is a novel technology that allows physicians to see the small bowel by means of a wireless video capsule that is ingested by patients with a sip of water. The cylindrical capsule is 11 mm in diameter and 26 mm in length with a white light–emitting diode. Before ingesting the capsule, patients undergo a preparation, which can vary from a clear liquid diet the day before the test to small doses of a purgative bowel preparation. Patients are generally instructed to ingest nothing else by mouth from midnight the day of the test to test completion. Data are limited regarding patient preparation with VCE, but a small meta-analysis showed that purgative bowel preparation improves small bowel visualization, quality, and diagnostic yield.

Contraindications to VCE include the following: suspected gastrointestinal obstruction (even if partial), cardiac pacemakers or other implanted devices, any suspected or proven swallowing disorder, and pregnancy. Retained capsules within the small bowel as well as incidental VCE of the bronchial tree have been reported in the community of gastroenterology.

As the capsule transverses the small bowel, it captures 2 frames per second. This technology allows the gastroenterologist to view the small bowel in a natural state. While use of an endoscope with air insufflation can affect the pressure receptors in the small intestinal wall, causing lesions to be missed, VCE allows the gastroenterologist to view the small bowel undisturbed. The wireless video capsule sends the information to a recorder carried on the patient’s hip. After roughly 8 hours, the data from the recorder is downloaded for the gastroenterologist to view.

Capsule endoscopy has a wide array of diagnostic capabilities including celiac disease, inflammatory bowel disease (primarily Crohn’s disease), small bowel ulcers, and arteriovenous malformations. In a recent study, Tukey et al demonstrated that VCE has a sensitivity of 77% and specificity of 89% in diagnosing suspected Crohn’s disease. Mehdizadeh et al, using retrospective data, found that physicians were able to identify small bowel lesions using VCE technology in approximately half of patients with symptomatic Crohn’s disease, with no reports of capsule retention in their study population. Patients with obstructive symptoms such as postprandial nausea, vomiting, abdominal distension, and history of bowel obstruction were excluded from that study.

In clinical practice, the aforementioned symptoms, as well as any suspicion that the patient may have an obstructive process, excludes VCE.

As demonstrated by Mehdizadeh et al, VCE is helpful in locating lesions. Physicians can use data from the recorder, including time frames and anatomic landmarks, to identify anatomic regions such as the distal duodenum, jejunum, and ileum. Identifying the location of a lesion is helpful for clinicians because it can guide the route of endoscopic intervention, if needed.

The role of capsule endoscopy is still emerging. Studies investigating the use of VCE in the diagnosis of esophageal varices and in the screening of colon cancer have been performed, though these methods are not widely used in clinical practice or endorsed by any professional societies at this time. Incidental findings, such as arteriovenous malformations that are not seen at the time of esophagogastroduodenoscopy or colonoscopy examinations, can be seen on results of VCE.

**Double Balloon Enteroscopy**

Double balloon enteroscopy is an endoscopic procedure that has had its greatest development in Asia, primarily Japan. This procedure first became available in the United States in 2004 and is generally performed in tertiary care endoscopy centers. With DBE, endoscopists use an endoscope with an inflatable balloon and a soft overtube with a second inflatable balloon. Using this “double balloon” mechanism, endoscopists are able to “tether” the small bowel as it is advanced along the endoscope. This mechanism allows endoscopists to view a greater amount of the small bowel. Depending on the location of the suspected lesion, DBE can be performed antegrade (orally) or retrograde (rectally).

In addition to providing direct visualization of lesions, such as arteriovenous malformations, ulcers, or masses, DBE can also help clinicians obtain biopsies by means of the endoscope working channel. Biopsies of suspicious lesions or mucosa can help clinicians diagnose malignant lesions, celiac sprue, or inflammatory bowel disease. The diagnostic yield of DBE is high for patients in which clinicians have a high index of clinical suspicion for small bowel tumors. In one study, small bowel tumors were found in 144 of 1035 patients who underwent DBE for a suspected small bowel tumor.

The role of DBE in occult gastrointestinal blood loss has been recently studied on a larger clinical scale. Tanaka et al realized that a diagnostic yield difference was present in patients with overt-ongoing gastrointestinal bleeding, overt-previous bleeding, or occult gastrointestinal blood loss. As clinically suspected, a higher diagnostic yield with overt-ongoing bleeding was present. However, DBE is still useful in the other categories of gastrointestinal bleeding.

Double balloon enteroscopy also has an emerging therapeutic role in gastroenterology. An argon plasma cautery catheter can be placed through the channel of the endoscope to ablate arteriovenous malformations. For example, if a distal duodenal or proximal jejunal lesion such as an arteriovenous malformation is identified using VCE, the arteriovenous malformation may be accessible with oral DBE and treated with
argen plasma cauter. If a distal ileal lesion is found, DBE may be an option vi the retrograde approach. In addition, DBE has recently been studi for its therapeutic role in Crohn’s disease; successful dilation of symptomatc strictures in Crohn’s disease have been reported in a small patient population.11

The DBE procedure is generally used in clinical practice as an adjunct to VCE. For example, in some instances, fresh blood may be seen on VCE, and the source cannot be identified. In these cases, patients are usually recommended for DBE. Because VCE, comparatively, is a noninvasive test, most gastroenterologists prefer to review VCE results before recommending DBE. Video capsule endoscopy can miss lesions that can be seen on DBE, with VCE, the camera does not always capture pictures of the lesion because of position, possibly because the lesion is behind bowel wall folds. In a small case series by Postgate et al.,12 DBE located the cause of bleeding in 2 of 5 patients with persistent occult gastrointestinal bleeding after VCE was unsuccessful. Though this is a small sample size, it reinforces the use of DBE in the workup of obscure gastrointestinal blood loss. Of 15 patients, Ross et al.13 detected 4 cases of primary small bowel adenocarcinoma missed by VCE.

With all endoscopic procedures, risks and benefits should be discussed with the patient. In addition to the risks of endoscopy, such as bleeding, infection, and perforation, pancreatitis is now a known complication of DBE. Gerson et al.14 noted that the risk of pancreatitis in the patient population studied was 0.2%. Perforation with DBE was also higher in patients with surgically altered anatomy.13 This trend is not surprising, as DBE does place a substantial amount of strain on the bowel and mesentery during the procedure. The simple mechanical strain may contribute to the rise in amylase as well as pancreatitis. However, in some instances, DBE is ideal for altered surgical anatomy, which should not exclude a patient from DBE. In cases of Roux-en-Y anastomosis, DBE is ideal to investigate possible lesions in the afferent loop.15 Double balloon enteroscopy should be performed by an advanced or experienced endoscopist who has had training in DBE in a center that can provide supportive care for patients who have complications.

**Computed Tomography Enterography**

Computed tomography enterography is a radiologic approach that examines the small bowel in a more detailed fashion than routine computed tomography scanning. The CTE method uses the oral intake of large volumes of neutral contrast agents and rapid intravenous administration of iodinated contrast to improve visualization of the small bowel wall and its mural features.16 Unlike VCE, which only looks at the luminal surface of the bowel, CTE shows the radiologist and gastroenterologist not only the mucosal surface, but also the mural features of the bowel wall, which can be extremely helpful in cases of Crohn’s disease or malignancy. While CTE is most commonly known for its role in the evaluation of small bowel Crohn’s disease, it has expanded to also have roles in the diagnosis of obscure gastrointestinal bleeding and in the detection of small bowel tumors. In regard to Crohn’s disease, the American College of Radiology Appropriateness Criteria rates CTE as the most appropriate radiologic method in the evaluation of initial presentation or known Crohn’s disease with acute exacerbation or suspected complications.17 In cases of Crohn’s disease with possible strictures in which VCE is contraindicated, CTE may be the test of choice.

Like all diagnostic testing, CTE does have some limitations. For example, CTE can, at times, cause suboptimal jejunal distension in a minority of patients. In these situations, computed tomography enteroscopy or magnetic resonance enterography may be preferred when jejunal pathology is suspected.18 An additional limiting factor is the radiation associated with computed tomography scanning. For instance, if a younger patient with difficult-to-control Crohn’s disease is undergoing frequent imaging, magnetic resonance enterography may be preferred to minimize cumulative radiation dose.18

Computed tomography enterography has an evolving role in the diagnosis of obscure gastrointestinal blood loss. Huprich et al.19 evaluated the role of triple-phase CTE in the outpatient setting. In their study population, 10 of 22 CTE examinations revealed gastrointestinal blood loss. Of these 10 patients, 4 had negative VCE results. In cases of arteriovenous malformations, radiologists may notice an early filling vein during the arterial phase, which may be a clue to the nearby location of the lesion in the small bowel. As mentioned previously, the possible location of the lesion is important for the gastroenterologist to know because this information will help to determine if any possible endoscopic intervention can be performed. Small bowel tumors can be challenging to diagnose for both the gastroenterologist and primary care physician in light of nonspecific symptoms. At times, obscure gastrointestinal blood loss is the only clinical sign that may lead to the diagnosis of small bowel tumors. Though no large published studies on the efficacy of CTE for evaluating small bowel tumors are available,16 it is still used as a diagnostic tool in clinical practice.

Pilleul et al.20 using computed tomography enteroscopy, which is similar to CTE, revealed 55 of 164 patients had gastrointestinal blood loss. The overall sensitivity and specificity in identifying patients with small bowel lesions were 84.7% and 96.9%, respectively. Not only can CTE show a focal intraluminal mass, it may also be able to distinguish the mass and thus help direct treatment. A pedunculated or predominantly exenteric mass suggests a gastrointestinal stromal tumor.21 An exenteric mass combined with adjacent lymphadenopathy or aneurismatic ulceration suggests lymphoma as the primary consideration.21 Carcinoid tumors arise from neuroendocrine precursors in the mucosa or small bowel wall and may manifest as avidly enhancing polyps, or as enhancing carpet lesions mimicking the wall thickening of Crohn’s disease.21 In our experience, CTE has slowly replaced the small bowel follow-through examination as the test of choice for small bowel lesions.
Comment

In a patient with obscure gastrointestinal blood loss and an unremarkable medical history, such as the patient described in the present article, arteriovenous malformations, small bowel tumors, and even Crohn’s disease should be considered in the differential diagnosis, and any of the discussed small bowel imaging modalities (ie, VCE, DBE, CTE) may be used. If, during the inpatient stay, the patient has no further signs of overt bleeding after endoscopic workup, the patient’s hemoglobin and hematocrit levels remain stable, and the patient is able to tolerate a liquid diet, VCE is frequently recommended as an outpatient procedure. Depending on the VCE results, further workup may not be needed or the patient may proceed to DBE.

Patients with obscure gastrointestinal blood loss and negative VCE results represent a clinical challenge. In this situation, physicians should discuss options with patients and reach a consensus whether to monitor the patient for further bleeding or to pursue more invasive methods, such as DBE. In one study of 25 patients with obscure gastrointestinal blood loss, a negative VCE was associated with a low rate of recurrent bleeding in the long-term. If a patient with obscure gastrointestinal blood loss and a negative VCE continues to have blood loss during hospitalization, then the situation becomes challenging for the gastroenterologist as well as the primary care team. One factor that makes the clinical situation challenging is that, while VCE is available in most areas in the inpatient setting, it is not widely available in the inpatient setting because of cost and insurance reimbursement. At these times, physicians may want to consider CTE or more conventional studies such as tagged red blood cell scans and mesenteric angiography to help with the diagnosis.

Conclusion

A patient with this clinical presentation is seen often by gastroenterologists in the inpatient and outpatient settings. Obscure gastrointestinal blood loss is sometimes the only clinical sign that may lead to the diagnosis of small bowel tumors, which can be challenging to diagnose because of nonspecific symptoms. Diagnostic tools such as VCE, DBE, and CTE can help clinicians approach gastrointestinal blood loss, especially when the suspected source is the small bowel. Future advances in small bowel imaging are on the horizon, including robotic and manually controlled VCE. Further workup of patients with obscure gastrointestinal blood loss must be coordinated with the primary care team, the radiologist, and the patient.

References