Diagnostic and Therapeutic Dilemma of Obscure Gastrointestinal Bleeding

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Obscure gastrointestinal bleeding constitutes approximately five percent of all gastrointestinal bleeding cases. Patients with this condition are often difficult to diagnose and frequently undergo extensive GI testing. This is no news item to all gastrointestinal specialists. The following cases highlight several different presentation scenarios, the long road to correct diagnosis, and some important lessons learned from some of the more problematic situations.

Case #1: Mystery solved with side-viewing endoscope

A 73-year-old male with end-stage renal disease and leukemia presented with chronic passage of melena for four months. The bleeding accelerated, requiring two to three units of blood transfusions daily for nearly a month. Repeated routine endoscopies were unremarkable. A capsule endoscopy identified multiple angiodysplastic lesions in the small intestine. The patient’s cardiac, renal and hematologic conditions made him a poor candidate for exploratory surgery.

The patient was referred to Cedars-Sinai for further testing. An oral double balloon enteroscopy showed a few small jejunal angiodysplastic lesions, a small distal duodenal nodule and a duodenal diverticulum. Cauterization of the nodule and angiodysplastic lesions did not halt the bleeding. A colonoscopy and ileoscopy were performed and showed blood coming down from the small intestine. A push enteroscopy identified some blood in the duodenum and jejunum. A strong suspicion of a proximal bleeding source prompted further duodenal investigation that had not been done before. On a duodenoscopy with a side-viewing endoscope, a tiny bleeding spot was identified in the posterior proximal descending duodenum. Clips placement and BICAP cauteration stopped the bleeding without further incidence.

Figure 1: Endoscopic ultrasound confirmed a splenic artery aneurysm in patient with episodic hematochezia. Large red arrow indicates splenic artery aneurysm; small yellow arrows, the pancreatic duct.

Figure 2: A circumferential ulcerated stricture found in the distal jejunum. Biopsy indicated lymphoma.

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It’s vitally important to pay attention to the clinical presentation. The chronic melena suggested an upper GI source of bleeding, but the three proximal small bowel problems caused confusion in correctly identifying the bleeding lesion. Repeated treatments were unsuccessful and suggested that something else was going on. When blood was noted in the proximal duodenum, we began to suspect a lesion not readily identifiable with standard endoscopic tools. The most useful instrument in this case was a side-viewing endoscope.

Case #2: ERCP and EUS may be a part of the work up

A 46-year-old male presented with episodic hematochezia every few days for six weeks, requiring transfusion of 60 units of blood. He also suffered from hypotension and severe generalized abdominal pain during the bleeding episodes. Numerous upper and lower endoscopies were unremarkable. Two capsule endoscopies and an operative total enteroscopy were negative. Two mesenteric angiograms and two abdominal CT studies were also negative, as was a push enteroscopy. Severe episodic epigastric pain raised the possibility of hemosuccus pancreaticus. Finally, an endoscopic retrograde cholangiopancreatography (ERCP) showed a polypoid lesion in the mid-pancreatic duct. An endoscopic ultrasound confirmed a splenic artery aneurysm (fig. 1). A mid-pancreatic resection was performed and the bleeding stopped.

Episodic hypotension and hematochezia are suggestive of large-volume bleeding. But severe epigastric pain is uncommon in bleeding from a gastroduodenal tract source. A pancreatic or biliary source should be considered in this type of obscure bleeding.

Case #3: Close review of previous capsule study helps in making correct diagnosis

A 73-year-old male presented with a six-month history of intermittent passage of melena, requiring six units of blood transfusions. His routine endoscopic examinations were negative. A capsule endoscopy showed fresh blood in the small bowel, but no definite lesion was seen.

The patient was referred to Cedars-Sinai for a double balloon endoscopy. However, upon review of the original capsule enteroscopy CD-ROM, we identified a suspicious mid jejunal lesion behind the floating fresh blood. As a result, we performed a single balloon enteroscopy and identified a small, fresh jejunal erosion with blood oozing from it. We were uncertain if it was a scope-induced trauma or a bleeding ulcer. However, the lesion did not match what was shown on the capsule endoscopy. Therefore, the scope was passed much further down the distal jejunum where a circumferential ulcerated stricture was confirmed (fig. 2). The biopsy was consistent with a lymphoma.

This is a clear-cut situation of a small bowel bleeding source. However, we would have stopped the enteroscopy had we not first examined the capsule study that had been done prior to referral to our institution.

Reviewing a capsule endoscopy record is a new experience for many seasoned endoscopists, so not all the findings are always correctly interpreted. It is often necessary for endoscopists to consult with experts in the field to confirm their findings and interpretations. It is also important for those performing double or single balloon enteroscopy to review previously recorded capsule studies whenever possible.

Case #4: Patience leads to discovery of Dieulafoy lesion

An 84-year-old man was transferred to Cedars-Sinai because of persistent fresh blood per rectum and transfusion dependency. All of his prior GI testing had been negative, including two colonoscopies that showed blood in the colon as far back as the cecum. There was even some blood tinged fluid in the terminal ileum. A capsule endoscopy done before the transfer was negative.

We repeated the capsule study as soon as the patient arrived, and the small intestine was again seen to be free of any blood or lesions. We then performed a colonoscopy with a continuous water flush up the blood-filled colon. Every centimeter of the colon was washed and cleaned before scope advancement. After scoping for nearly 50 centimeters, blood was seen oozing from a seemingly normal mucosal surface in the proximal descending colon. The oozing spot was thought to be a Dieulafoy lesion and it was cauterized with a single endoscopic clip (fig. 3-4). The bleeding stopped and the patient was discharged.

A small amount of blood in the terminal ileum is not confirmatory evidence for small bowel bleeding because of the potential for reflux of colonic contents through the ileocecal valve. The first capsule endoscopy raised the possibility that it was a colonic bleeding all along, but up to one third of small bowel lesions may be missed on a single capsule study. Therefore, a repeat examination may be appropriate in some situations. As illustrated in this case, both capsule studies were negative and this confirmed our suspicion that the patient was bleeding from his colon. Dieulafoy lesions are not commonly associated with colonic bleeding, but it can occur. If the colon is covered with blood in spite of a good prep, it’s essential to be patient – carefully cleaning every inch of the bowel as the instrument is advanced. In this case, our careful examination paid off and the source of bleeding was eventually found.

Case #5: Hemicolectomy is often not the answer

An 82-year-old female presented with hematochezia while on anticoagulation therapy. She continued to pass fresh blood per rectum after stopping the medication. All of her GI testing was negative, including her mesenteric angiogram and capsule endoscopy. Two bleeding scans showed a possible right colonic source, and she underwent a right hemicolectomy. She bled again one week after the surgery, and was subsequently transferred to Cedars-Sinai.

Figure 3: Careful examination – cleaning every inch of the colon as the instrument was advanced – led to the discovery of this small Dieulafoy lesion with active bleeding (circled).

Figure 4: Dieulafoy lesion cauterized with a single endoscopic clip, which stopped the bleeding.
We performed a repeat capsule study that was negative except for some ulcers at the anastomotic site. A colonoscopy was performed, and two small oozing spots at the anastomosis were cauterized. No further bleeding was noted — but the patient was not started back on her anticoagulation therapy.

The source of the patient’s bleeding is still uncertain. While it might have been from the right colon, nuclear bleeding scans should not be relied upon to direct surgical resection. Far too often, a hemicolectomy is performed only to have bleeding recur soon after the operation because the wrong part of the GI tract is removed. If the colon is seriously suspected, colonoscopies should be repeated until the source is positively identified. This case illustrates how some obscure GI bleeding cases may not be solved during one hospitalization. This patient quite possibly will return with further bleeding, and will require a repeated work up at that time.

Summary

Each case presented above illustrates the following key points about diagnosing obscure gastrointestinal bleeding:

■ There is no set standard for performing a GI workup. Published algorithms are merely examples of how cases might be approached.

■ It is essential to pay attention to the clinical presentation.

■ Patience is paramount. It is often necessary to repeat procedures over and over again to find the source of the bleeding.

■ All resources should be utilized. As noted above, a side-viewing endoscopy should be done if an obscure duodenal source is suspected.

■ A hemicolectomy should not be performed based on the findings of nuclear bleeding scans.

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Cyclic Vomiting Syndrome: Recognition Gives Hope

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From time to time, a clinical syndrome is recognized and described and, as a result, patients who suffer from the syndrome benefit in many ways. One such example has resulted from the clinical observations of David Fleisher, MD. While working in the Department of Pediatrics at Cedars-Sinai in the 1980s, Dr. Fleisher brought to our awareness a little-known clinical observation going back to 1882. Though first recognized in the pediatric population, Dr. Fleisher went on to describe it in adults as well.

Cyclic vomiting syndrome (CVS) is defined as stereotypic episodes of incapacitating nausea and vomiting lasting hours to days and separated by symptom-free intervals, which typically last weeks or months.

Patients with the syndrome are often seen in the emergency room setting but are seldom recognized to have CVS. They are treated symptomatically for an acute vomiting illness and sent on their way. Often the patient or a family member eventually finds the syndrome described on the Internet, and in my experience, the benefits of this recognition are significant. Understanding that the syndrome is well described reduces uncertainty and alleviates the patient’s sense of being out of control. As a result, anxiety is immediately reduced. This reduction in anticipatory anxiety can be key to avoiding coalescence of episodes, where one episode flows into another. Once properly diagnosed, a caring physician can effectively address symptom relief and offer approaches to avoiding episodes. This in turn reduces the severe sense of vulnerability CVS patients experience.

Though the cause of CVS is not precisely known, two hypotheses seem to account for almost all cases. The pathogenesis appears to start in the central nervous system, not the abdomen. It seems that nearly all patients follow a pattern consistent with either a migraine-equivalent disorder or a variant of panic disorder, and frequently respond to appropriate interventions. Interestingly, many patients have characteristics of both migraine and panic, and management needs to be addressed accordingly.

Although the diagnosis and management of CVS crosses over a number of subspecialties, it is generally accepted as being within the purview of the gastroenterologist with an interest and background in motility and functional gastrointestinal disorders.

Hundreds of patients with CVS have been identified, and an increasing recognition of this disorder has prompted efforts at a number of medical centers around the country to specifically address the diagnosis and management of these patients. Further information on this syndrome can be obtained at the website of the Cyclic Vomiting Syndrome Association. Details regarding clinical phases of the disorder and management issues are described in a recent report on the subject by Fleisher et al., published in 2005 in BMC Medicine and available online at biomedcentral.com.

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Figure 1: Schematic representation of the four phases of Cyclic Vomiting Syndrome and their therapeutic goals. From D R Fleisher, B Gornowicz, K Adams, R Burch and E Feldman, “Cyclic Vomiting Syndrome in 41 adults: the illness, the patients, and problems of management” in BMC Medicine 2005, 3:20.
Immunization Issues in Patients with IBD

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Patients with inflammatory bowel disease (IBD) are often treated with long-term immunosuppressive therapies. While such treatments are beneficial for controlling the primary disease, they can potentially place the patient at increased risk for acquiring various infections, some of which are preventable by available vaccines. Furthermore, infections such as pneumococcus, varicella, and hepatitis B (HBV) can be more severe or even fatal in the setting of immunosuppression.

Immunization uncommon

In a study completed at the Inflammatory Bowel Disease Center at Cedars-Sinai in 2006, 86 percent of respondents with IBD reported current or prior use of immunosuppressive medications, but only 45 percent recalled tetanus immunization within the past 10 years; only 28 percent reported regularly receiving flu shots; only nine percent reported having received pneumococcal vaccine; and 11 percent lacked a reliable history of chicken pox or varicella vaccination.

The study also revealed that 35 percent of patients had previously been transfused. While 44 percent of IBD patients had at least one risk factor for HBV, only a third of those at risk had been vaccinated against the infection. Furthermore, protective antibody titers against hepatitis B were sustained in only a third of patients previously vaccinated against HBV. One study participant was found to be actively infected with HBV, another was found to have a latent HBV infection. The results suggest that all patients with risk factors for viral hepatitis should therefore undergo HBV serologic screening prior to initiation of immunosuppressive therapy, particularly anti-TNF therapy which may cause reactivation and flare of HBV.

Proactive immunization

At Cedars-Sinai, we recommend assessing the immunization status of patients with IBD, and we suggest that, when possible, immunizations and booster shots be administered prior to initiation of immunosuppressive therapy. Studies in patients receiving vaccinations while on immunosuppressive therapy for a range of indications have demonstrated suboptimal serologic responses with waning protective antibody titers to a variety of vaccinations. Such observations have led to modification of recommendations for specific patient groups with low rates of seroconversion after pneumococcal and HBV vaccination. These recommendations include testing for serologic immunity after vaccination and more frequent dosing of vaccines. Consideration should also be given to checking for protective antibody titers to vaccines to determine if booster dosing may be beneficial.

Since many patients with IBD eventually require blood transfusion, we recommend that they receive the HBV vaccination as a preventative measure. While the rate of transmission of HBV is low, the vaccine could potentially prevent the patient from contracting Hepatitis B and the complications associated with it.

Reports of fatal varicella infection in patients with IBD and other chronic immune-mediated conditions on biologic and immune-suppressive therapy, including steroids, underscore the importance of immunity through immunization of patients without a reliable history of chickenpox. We believe that given the high but unpredictable likelihood of future immunosuppressive therapy, a strategy for immunization of all patients with newly diagnosed IBD is warranted.

Who oversees immunization?

The most common patient-provided reason for inadequate uptake of vaccinations is lack of awareness that they are indicated. Whose responsibility is it to ensure that patients with IBD receive appropriate immunizations? The gastroenterologist and the primary care physician may assume that the other is taking care of the task – while the patient is generally unaware of its necessity.

Increased awareness needed

Adults and children with IBD should be assessed for preventable illnesses, including influenza, pneumococcal disease, varicella, HBV, tetanus, hepatitis A, meningococcus and human papillomavirus. Despite existing recommendations, vaccination rates in high-risk adult populations with IBD and other chronic illnesses who have a reasonable likelihood of future immunosuppression are inadequate. While efforts are underway to better characterize the immunogenicity of immunizations in the setting of immunosuppressive medications, greater physician and patient awareness of recommended vaccination guidelines in order to minimize preventable morbidity and mortality in the IBD patient population is needed.

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