IBD in a 2-year-old

Jacob Rotter, MD
Cohen Children's Medical Center
Queens, New York

The case

A 2-year-old boy presented in the emergency department with bloody stools for 13 days. He was having approximately 5 to 8 loosely formed stools daily, and more than half of those were bloody. He also had intermittent, diffuse abdominal pain. He had a similar episode several months prior to his current presentation which resolved after eliminating dairy from his diet. However, he now additionally presents with a 5-pound weight loss over the past 2 weeks, and was refusing food secondary to abdominal pain associated with eating.

Other than the previous episode of bloody stool, he had no significant past medical history. He was born at full term with a relatively uncomplicated birth history and has been developing appropriately. He has 3 otherwise healthy siblings, though his family history is notable for a maternal aunt and maternal cousin with Crohn's disease (CD). There is no immediate family history of inflammatory bowel disease(IBD). His review of systems was significant for fatigue, weight loss, and decreased appetite. His physical exam was significant for tachycardia without fever; was found to have conjunctival injection; and had no oral ulcers or lesions. His abdomen was soft, nontender, nondistended with voluntary guarding. He had no masses or organomegaly. He also had no perianal skin tags, fissures, or fistulae.

The differential for bloody diarrhea in this age group is very broad. One of the more common causes for bloody diarrhea in this age group is infectious, specifically bacterial, enteritis. These children are typically greater than 2 years of age and contract the illness via fecal-oral transmission after exposure to poultry or contaminated meat. These children typically present with high fevers, tenesmus, severe abdominal pain, and grossly bloody or mucoid stool. Bacterial enteritis is typically diagnosed with a stool culture or gastroinstestinal (GI) polymerase chain reaction (PCR). One specific infectious etiology to highlight further is cytomegalovirus (CMV) colitis. CMV colitis can often mimic primary GI disorders such as IBD or intussusception. Children with CMV colitis often present with nonspecific symptoms, such as this patient, and often are indistinguishable from IBD until biopsy or serology is done.

There are a tremendous number of primary gastrointestinal disorders to consider in a patient like this case. Primary fistulae/fissures are a common source of rectal bleeding that can lead to GI discomfort. These can be caused by other disorders such as IBD or constipation, but are less likely in our patient given his reassuring perianal exam. An important diagnosis to consider given his age and presentation is intussusception. Although this diagnosis cannot be definitively ruled out based on his history and exam alone, it is less likely given that his abdominal pain does not appear to be episodic in nature. Intussusception also typically presents with vomiting as a primary symptom, and though not always present, our patient does not have an abdominal mass on exam. Another consideration given his age is Meckel's diverticulum. This diagnosis classically follows the "rule of 2s" (2% of the population, 2:1 male to female ratio, presents within 2 feet of the ileocecal valve, and is typically 2 inches in length). However, the primary symptom of Meckel's is painless lower gastrointestinal bleeding, and is thus less likely in our case. Given his family history and symptomology, IBD is a critical etiology to evaluate. Although he is a very young age to present with IBD, there is a subset of patients that can present this early.

Another domain to consider are the vasculitides and other vascular disorders. Hemolytic uremic syndrome is classically defined as the triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury (AKI), which requires laboratory testing to evaluate. The scale of AKI can range from microscopic proteinuria to severe renal failure. Immunoglobulin A vasculitis, or Henloch-Schonlein purpura, typically presents with a normal platelet count, arthritis or arthralgias, abdominal pain, and renal disease. This presentation can be variable, though our patient only currently meets 1 of these 5 criteria. Although aterio-venous malformations (AVMs) or hemangiomas can also result in lower GI bleeding, AVMs or hemangiomas of the rectum or colon are rare.

A final group of diagnoses to consider are those that may mimic lower GI bleeding. Ingestion of substances like red food dye, rifampin, ampicillin, or red liquids such as Kool-Aid may appear similar to hematochezia, especially with high-sugar drinks with high osmotic loads that result in fast transit times. Of note, substances with peroxidase activity such as rare red meat, horseradish, turnips, and cherries may result in a falsely positive fecal occult blood test (FOBT). Finally, it is important to ask about vitamin C intake, as ascorbic acid is a strong reducing agent that can block the oxidative guaiac reaction, causing a falsely negative FOBT.

His initial laboratory data was significant for leukocytosis, anemia with a hemoglobin of 5.6, an elevated C-reactive protein (CRP), hyponatremia, hypokalemia, and hypoalbuminemia with a negative GI PCR, stool culture, and *Clostridioides difficile* toxin. He had an abdominal ultrasound that was negative for intussuception. He was initially admitted for a 7-day course requiring transfusions of blood, iron, and intravenous repletion of electrolytes. Given his initial labs, the primary team was suspicious for IBD, which is consistent with what is seen in the literature regarding newly diagnosed IBD.[1] He ultimately had an endoscopy that was consistent with IBD with diffuse inflammation from his rectum to the ascending colon.

IBD is typically comprised of 2 major disorders—ulcerative colitis (UC) and CD. The mean age of diagnosis is 10.3 years, and 15% of children are diagnosed before 6 years of age.[2] Family history is positive in approximately 29% of these patients, and isolated colonic disease, like our patient, is more common in children aged younger than 8 years rather than older children.[2] CD can present with perianal fistulae, abscesses, or skin tags. Imaging can often reveal small bowel involvement, and endoscopy typically shows ulceration or stenosis of the ileocecal valve, mucosal cobblestoning, and linear ulcerations.[3] The classic finding on pathology are noncaseating granulomas, which are evident in 25%-50% of CD patients.[3] Disease severity is classified with the Pediatric Crohn's Disease Activity Index (PCDAI) scoring system. PCDAI evaluates historical features (abdominal pain, stool frequency, activity level); physical exam features (weight, height, abdominal tenderness, perianal disease, extraintestinal manifestations); and laboratory features (hematocrit, albumin, erythrocyte sedimentation rate). UC typically has transmural, continuous inflammation that begins at the rectum and progresses proximally. Histopathologic features include submucosal inflammation, cryptitis, and crypt abscesses, and with chronic UC, architectural distortion, basal lymphoid aggregates, and left colonic Paneth cells can also be seen, which may represent a localized response to inflammatory changes or may also represent altered bacterial flora that can be seen in IBD.[3]

Very early-onset BID (VEO-IBD) is an important entity to consider given our patient's age. VEO-IBD presents at less than 6 years of age, and is more likely to have single-gene defects that alter global immune function or disturb the epithelium, and typically has a more severe

disease course than classical IBD. These patients typically have a family history of IBD or immunodeficiency, with male predominance, and present more frequently in consanguineous families.[4-6]

Our patient re-presented approximately a week after his discharge with similar symptoms, suggesting resistance to typical therapies. On hospital day 1, he began having left gaze preference with nystagmus. A computed tomography scan revealed a right temporoparietal infarct suggestive of a stroke, and was also subsequently found to have an inferior vena caval thrombus as well as a right common femoral deep vein thrombosis. Hypercoagulability in IBD can be thought of in a 3-pronged approach. IBD is known as a protein-losing enteropathy, as chronic and acute inflammation leads to GI tract erosion and protein loss, as well as poor absorption. Loss of antithrombin III and alpha-a1-antitrypsin results in less inhibition of the coagulation cascade.[7] Additionally, the anemia seen in IBD causes increased turbulent flow of blood, which can lead to increased endothelial activation. This, coupled with thrombocytosis seen in IBD, can lead to increased thrombi formation.[8] Finally, inflammatory mediators that are increased in IBD can lead to hypercoagulability. Elevated CRP has been associated with increased macrophage tissue factors which inhibit anticoagulant pathways and fibrinolytic activity. Chronic inflammation can cause endothelial damage and lead to an increase in pro-inflammatory cytokines.[9]

Our patient received several doses of infliximab but continued to have worsening Pediatric Ulcerative Colitis Activity Index scores. He ultimately required a subtotal colectomy with an end ileostomy. He was discharged on hospital day 32 and has been doing well outpatient. He is currently not on any anticoagulation and is currently in the 33rd body mass index percentile for his age.

When thinking about bloody diarrhea in the toddler age group, although infectious causes are typically the most common, it is vital to consider primary GI disorders such as IBD. This patient ultimately reflected many different manifestations of IBD, including that IBD as a protein-losing enteropathy. Although this can manifest as mere hypoalbuminemia, these patients should always be thought of as hypercoagulable patients, and prophylaxis should always be considered.

References

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