ILLUSTRATIVE CASE

# Blood and Guts: A Case of Early Childhood Crohn's Disease

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A 3-year-old Latino boy was transferred to a tertiary children's hospital after presenting with poor oral intake, several days of nonbloody/nonbilious emesis, and blood-streaked diarrhea. He was afebrile with normal vital signs; height was at the 15th percentile and weight at the sixth percentile; and BMI was 14.5 at the eighth percentile. He was a tired-appearing and pale toddler who was crying but consolable. He had dry lips with hyperactive bowel sounds but with a nontender and nondistended abdomen. He had bilateral pitting edema to his ankles and periorbital edema.

He was previously diagnosed as an outpatient with iron-deficiency anemia. His bloody diarrhea was thought to be secondary to milk-protein enterocolitis due to both its onset being around the time his diet was diversified between 6 and 12 months of age and to the finding of hypoalbuminemia. He was on an elimination diet of milk products plus supplementation with an extensively hydrolyzed whey protein formula. He had an esophagogastroduodenoscopy and colonoscopy done 6 weeks before this hospitalization demonstrating friable, edematous, and nodular colonic mucosa, with no duodenal villi blunting or colonic cryptitis, granulomas, or dysplasia on biopsy. These results were inconclusive but suggested a degree of inflammation.

Laboratory tests showed a white blood cell count of 25 000 cells/$\mu$L with 31% bands and a hemoglobin of 9.9 g/dL with a mean corpuscular volume of 77 fL. His sodium was 127 mEq/L, potassium of 2.1 mEq/L, albumin of 2.7 g/dL, total protein of 5.3 g/dL, aspartate transaminase of 22 U/L, alanine transaminase of 20 U/L, total bilirubin of 0.4 mg/dL, and C-reactive protein of 4.9 mg/dL. Infectious stool studies sent on admission were negative, including norovirus and adenovirus polymerase chain reaction, routine culture and stain for ova and parasite, rotavirus DAA, and *Clostridium difficile* molecular assay. His diet was changed to an amino acid–based elemental formula due to concern of exacerbation of suspected milk protein allergy, but he continued to have grossly bloody loose stools, requiring continued fluid support and three 10-mL/kg packed red blood cell transfusions.

Because of persistent bloody and loose stools despite antimicrobial and nutritive interventions, flexible sigmoidoscopy was performed 2 weeks after admission, which demonstrated grossly erythematous and friable mucosa in the sigmoid and rectum (Fig 1). Colonic biopsy demonstrated mild active cryptitis, occasional crypt abscesses, and crypt architectural distortion, suggesting inflammatory bowel diseases (IBD) (Fig 2). A presumptive diagnosis of Crohn disease (CD) was made after a subsequent colonoscopy demonstrated inflammation around the terminal ileum and Prometheus IBD sgi (serology-genetics-inflammation) panel (Societe des Produits Nestle, Switzerland) results were indicative of CD.

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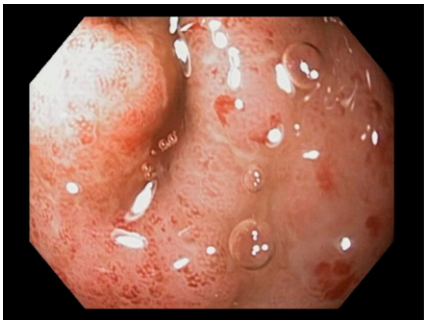

**FIGURE 1** Image obtained from flexible sigmoidoscopy showing an erythematous and friable rectum.

## Question *What Is the Epidemiology of CD, and How Is This Disease Typically Diagnosed and Managed?*

### Discussion

CD is part of the spectrum of IBDs, which also includes ulcerative colitis.[1] The incidence and prevalence of IBD has increased in the pediatric age range with current studies estimating an incidence of 4.5 per 100 000 population for CD and 2.14 per 100 000 for ulcerative colitis. This represents a 5% to 7.6% annual rise between the years 1994 and 2005.[2] The mean age for diagnosis of IBD in the United States is 12.5 years with <5% of new diagnoses made in children under age 5 years.[3] The fastest rates of rise in new diagnosis have also been in the younger age groups, including those <4 years.[2] The patient's ultimate diagnosis of CD was delayed in part because of his young age and the relative rarity of this diagnosis in his age group. The etiologies of inflammatory bowel disease are unclear but thought to be a combination of a genetic predisposition and environmental insults to the gastrointestinal tract and altered gut flora.[4]

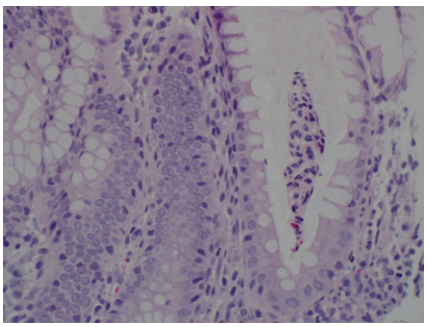

**FIGURE 2** Tissue biopsy of the colon obtained during the flexible sigmoidoscopy demonstrates crypt abscesses at 400× magnification.

The diagnosis of CD involves a combination of clinical, radiologic, and pathologic findings. Diffuse, crampy abdominal pain; diarrhea; and weight loss are the classic symptoms of CD and can be accompanied by nonbloody, melanotic, or grossly bloody stools.[5,6] Findings on physical examination can include poor growth, abdominal tenderness, and perianal lesions. Endoscopy remains the preferred method for diagnosis. The classic endoscopic description of CD includes areas of inflamed mucosa interspersed among unaffected patches, as well as linear ulcerations with adjacent edema. The rectum is generally unaffected. Noncaseating granulomas are typically seen on biopsy.[1] The goals of treatment may be different depending on whether CD is active and flaring or under control. Traditionally corticosteroids are used for the induction of remission, and salicylates including mesalamine and sulfasalazine are used for maintenance therapy. Immunomodulatory biologic agents, such as mercaptopurine, azathioprine, and infliximab, have demonstrated adjunctive benefits, allowing for reduction in steroid dosages and maintenance of remission after inductive therapy. Adjunctive therapies also include exclusive elemental or polymeric enteral formulas. Surgical management, generally involving bowel resection, remains an option for disease unresponsive to medical management.

### Case Continuation

During this patient's hospitalization, a peripherally inserted central catheter (PICC) was placed in the right basilic vein for total parenteral nutrition and fluid replacement. Ten days after placement of the PICC right-sided facial and upper extremity swelling was noted. An ultrasound demonstrated a partial nonocclusive thrombosis of the right internal jugular vein, and follow-up ultrasound demonstrated extension of the deep venous thrombus, extending from the right internal jugular vein and involving the subclavian, axillary, and basilic vein. The PICC was removed; however, anticoagulation was deferred because of ongoing bloody stools.

## Question *Are Patients With CD Predisposed to Coagulopathies?*

### Discussion

Thrombotic events (TE) are established complications of IBD in adults, and there is growing evidence of this same relationship in children.[7] In a retrospective cohort study analyzing data from 7 448 292 discharges across 5 nonconsecutive years, the relative risk of a TE in a hospitalized child or adolescent with IBD was 2.36.[8] The etiology of the increased risk of TE in IBD is unclear, although it may be due to increased inflammation leading to a combination of both a prothrombotic and a hypercoagulable state. The decision to initiate prophylaxis of venous thrombosis in children with IBD remains an area of debate. The American College of Chest Physicians recommends pharmacologic prophylaxis, whereas the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition does not recommend prophylactic measures given the lack of evidence of efficacy.[8]

### Case Continuation

The patient had no abdominal pain until ~20 days into his admission when he had 1 day of pain with defecation including an episode of drawing his legs to his chest. The pain self-resolved, and abdominal examination showed no tenderness or palpable mass. Abdominal ultrasound showed a targetoid rounded mass extending from the right lower quadrant to the right midabdomen with circumferential vascular flow, consistent with intussusception. He successfully underwent an urgent barium enema reduction of the intussusception.

## Question *Are Patients With CD at Higher Risk of Developing Intussusception?*

### Discussion

Intussusception is a relatively common cause of bowel obstruction in children between 3 months to 3 years old.[9] The most common form of intussusception is ileocolic, occurring in 80% to 95% of all

pediatric cases. Only 1.5% to 12% of cases have an identifiable pathologic lead point, such as Meckel diverticula, intestinal polyps, and mesenteric nodes, and the frequency of nonidiopathic intussusception increases with age.[10]

The typical presentation includes a recent history of a viral illness, vomiting, and diarrhea. The classic triad of intermittent abdominal pain, red currant jelly stool, and a palpable abdominal mass actually occurs in only 7.5% to 40% of cases.[11,12] Sonography is necessary for diagnosis and has a high sensitivity of 98% to 100% and specificity of 88% to 100%[13]; if positive, it should prompt immediate hydrostatic or pneumatic reduction or, if critically ill, immediate surgical reduction.[14] A delay in diagnosis may result in arterial obstruction, bowel necrosis, and bowel perforation.[9]

In the patient, the presentation for intussusception was atypical in that there was no recent vomiting and no palpable abdominal mass. His abdominal pain was brief and sharp rather than colicky and intermittent. Furthermore, he was already having bloody stools from his CD. The patient had 2 possible lead points visualized on sonography: one at the terminal ileum and cecum and 1 at the splenic flexure. Given the suspicion of lead points and the unclear duration of symptoms, surgical intervention may have been necessary; however, surgical reduction was deferred because he was hemodynamically stable with no signs of peritonitis or bowel perforation. The use of a barium enema to reduce intussusceptions has been rarely reported in the setting of acute inflammatory bowel disease, and this case illustrates that it can be a safe and effective intervention even in patients with acute CD flares. Because 80% of intussusception occurs before age 2 years and one-third of children older than 2 years have a pathologic lead point, it is most likely that his intussusception is secondary to CD.[9,15]

### Case Resolution

Oral mesalamine was begun after the endoscopy concerning for IBD, but subsequently discontinued because of worsening bloody stools. Intravenous methylprednisolone resulted in rapid improvement in his stool volume and blood. He was transitioned to an oral corticosteroid regimen and was able to tolerate a regular diet. With the resolution of his bloody stools, fondaparinux therapy for his deep venous thrombus was started. He was discharged from the hospital on both oral corticosteroids and fondaparinux with close gastroenterology and hematology follow-up.

## CONCLUSIONS

This case demonstrates a child with an unusually young age of presentation for IBD whose hospital course highlights the diverse complications seen in CD including hypercoagulability and intussusception. The development of his venous thrombus in the setting of his active and profuse hematochezia raises important factors to address when considering initiation of anticoagulation therapy. The atypical presentation of his intussusception complicated by his concurrent symptoms from CD raises the need to consider common pediatric abdominal emergencies in the setting of an ongoing evaluation for a chronic process. This case further describes successful barium enema reduction in a child with CD and outlines the challenges to consider when choosing between barium enema reduction and surgical reduction of intussusception secondary to CD. Emerging data suggest that IBD diagnosed in children this young is a separate disease entity with a unique phenotype and genotype, currently referred to as very early-onset IBD.[16] This new disease subset is being actively researched given the concern that patients with very early-onset IBD will have a more severe symptom profile and should eventually be considered in this patient.

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