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The Risk of Colonic Strictures with Colitis Following Hemolytic Uremic Syndrome: A Case Report of a Toddler

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Abstract: Gastrointestinal manifestations of hemolytic uremic syndrome (HUS) are rare in pediatrics, but can have significant impact on the course of the disease. While various infectious etiologies are associated with HUS, Enterohemorrhagic *Escherichia coli* (EHEC) has been a focus of interest in its role in post-diarrheal HUS. We report a previously healthy 3-year-old boy who presented with bloody diarrhea, was found to be EHEC positive, and developed gastrointestinal complications of HUS including chronic colitis and strictures. The case illustrates that, though rare, HUS can have long-term gastrointestinal effects.

Key Words: EHEC, infectious diarrhea, HUS, hemolytic uremic syndrome, colitis, strictures

INTRODUCTION

Hemolytic uremic syndrome (HUS) arises from damage to the blood vessels in the kidneys from toxins produced by specific bacteria such as *Shigella dysenteriae* type 1, *Streptococcus pneumonia*, and most commonly *Enterohemorrhagic Escherichia coli* (EHEC) (1). The reported annual incidence of HUS from EHEC is 2–3 per 100 000 children less than 5 years old (2).

EHEC produces Shiga toxin and causes self-limited bloody diarrhea in most infected patients. However, a small group of EHEC-infected patients develops HUS, which consists of acute renal failure, hemolytic anemia, and thrombocytopenia. The course can be further complicated with seizures and neurological deficits such as paresis, coma, and cerebral edema (1,3). Factors such as the use of antimotility agents, antibiotics, age under 5 years, and female gender are hypothesized to increase the risk of HUS after infection with EHEC (1).

Gastrointestinal complications of HUS such as necrosis of the colon or ileum, hemorrhagic colitis, pancreatitis, transient diabetes, hepatic cytolysis and cholestasis, peritonitis, and prolapse of rectum are rare (4). Gastrointestinal involvement can extend to life-threatening conditions such as toxic megacolon and transmural necrosis of the colon with perforation and consequent strictures (4). Death has been reported in multiple case reports in children who suffered from gastrointestinal involvement requiring surgical interventions (5).

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CASE REPORT

A previously healthy 3-year-old boy was brought to the emergency room with bloody diarrhea and was found to have EHEC in the stool gastrointestinal pathogen panel. His creatinine on admission was 2.7 mg/dL (normal less than 0.47 mg/dL) and he quickly became anuric requiring continuous renal replacement therapy. He was then transitioned to intermittent hemodialysis for 11 days. His course was complicated by respiratory failure, convulsions, and aphasia. He was started on eculizumab (monoclonal antibody against complement component 5) treatment for concerns of atypical HUS. His course was further complicated by severe ileus, bilious output from a gastric sump, and total parenteral nutrition dependence for 2 weeks. Computerized tomography of the abdomen revealed pan-colitis. He eventually started tolerating enteral feeds and was discharged home in 6 weeks with close outpatient follow-up.

Two months after his initial presentation, he was readmitted to the hospital with progressive feeding intolerance manifested by abdominal distension, intermittent nonbloody and nonbilious emesis, diarrhea, and fussiness with enteral feeds. Symptoms appeared to improve when feeds were held. Abdominal radiograph showed moderately dilated loops of small bowel and colon with air-fluid levels, concerning partial obstruction due to stricture. Contrast enema revealed transverse colon and sigmoid/descending colon strictures (Fig. 1). Magnetic resonance enterography performed showed no evidence of small bowel disease. He underwent stricture resection and required ascending, transverse, and descending colectomy with loop ileostomy while maintaining the ileocecal valve. Histology revealed extensive mucosal ulceration, granulation tissue formation, patchy inflammation, and serosal adhesion (Fig. 2). Vascular injury was evident by the sharp demarcation between viable and ulcerated colon.

Two months later, he had a scheduled uneventful ileostomy takedown procedure. Shortly after he was readmitted with abdominal distension and vomiting and found to have small bowel obstruction due to adhesions which required surgical lysis. Six months later, he had another admission with increased stool volume and abdominal pain. Given concern for ongoing ischemic injury or vascular insult, a magnetic resonance imaging/angiography of the abdomen was performed, showing evidence of inflammation of the rectosigmoid and ascending colon and gaseous distension of the cecum and ascending colon and no mesenteric venous thrombus (Fig. 3). Infectious etiologies were ruled out; however, fecal calprotectin was elevated (573 μg/g), consistent with ongoing inflammation. The calprotectin peaked at 632 μg/g in a few days. Family elected to defer endoscopy due to significant medical trauma the patient had experienced. He started a strict bowel regimen with polyethylene glycol. His calprotectin decreased to 75 μg/g and 36 μg/g after 3 and 6 months, respectively. On follow-up, he has been doing well and has had adequate weight gain since his last hospitalization.

DISCUSSION

HUS can have significant gastrointestinal manifestations in the pediatric population with long-term effects. Vascular injury due to the toxin from EHEC and similar pathogens are thought to be the cause of bowel ischemia leading to complications such as strictures; however, the exact pathophysiology is undefined (6). Although rare,

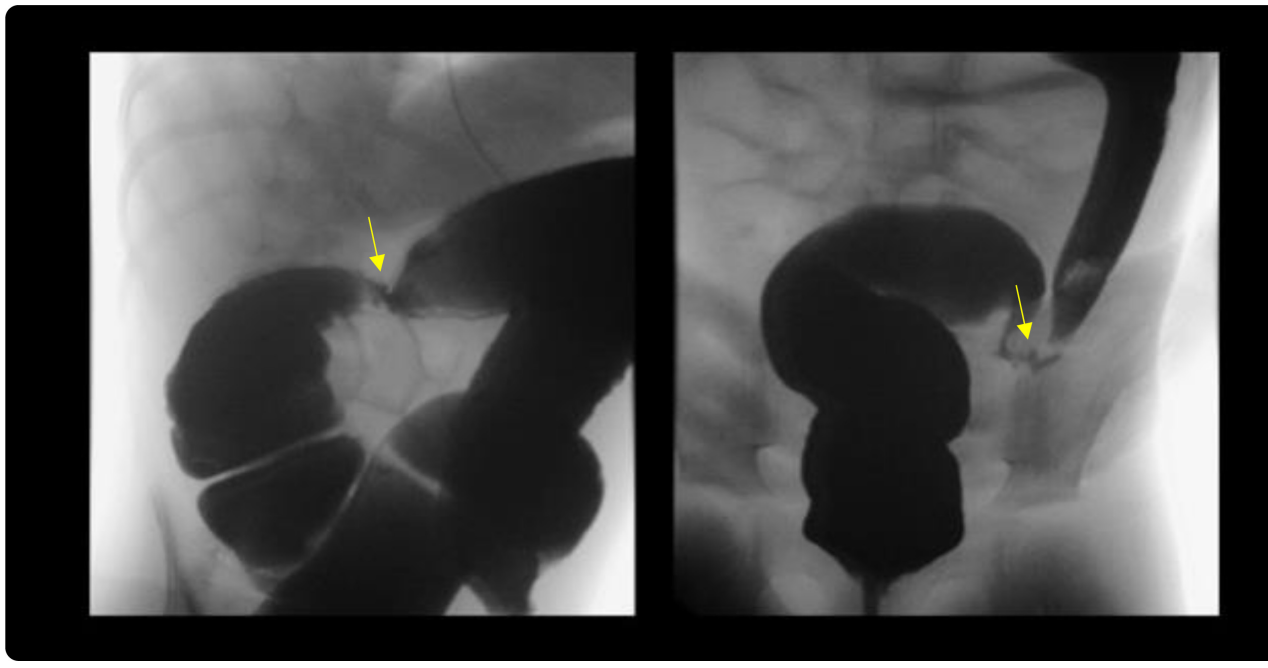

FIGURE 1. Transverse colon and sigmoid/descending colon strictures on fluoroscopic contrast enema.

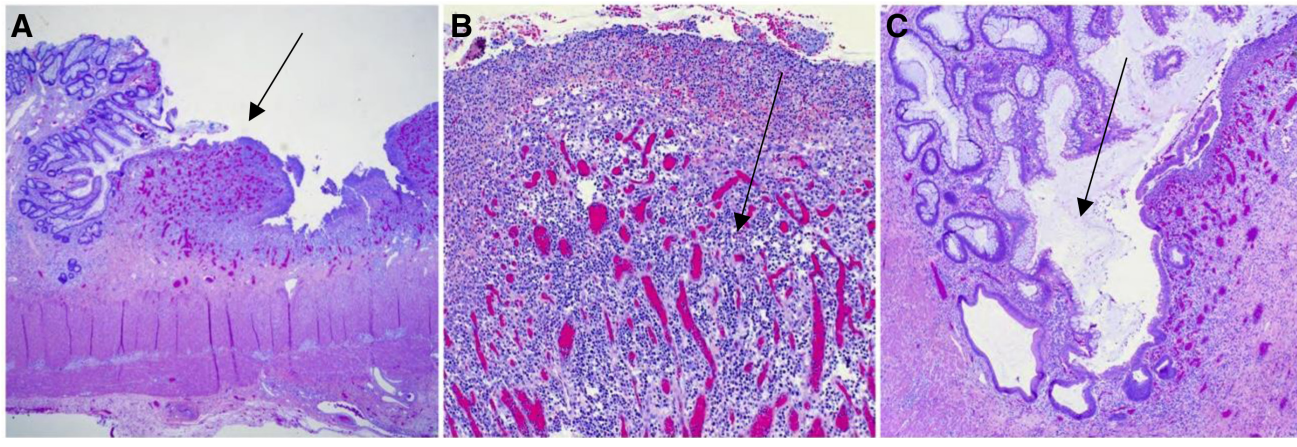

FIGURE 2. Microscopic examination of the colectomy demonstrated extensive mucosal ulceration which was sharply demarcated from adjacent viable mucosa **(A)**, consistent with a vascular pattern of injury. The ulcer beds were composed of granulation tissue accompanied by submucosal chronic inflammation **(B)**. Viable mucosa at the interface with ulcerated mucosa showed crypt branching and dilatation **(C)**.

HUS can result in chronic colitis and colonic strictures that can present as feeding intolerance and require surgical interventions. It is important therefore to have a high index of suspicion for such complications and obtain contrast enema if patients present with such symptoms after HUS. A prior case report of a 5-year-old female child described a stricture of the sigmoid colon and adhesive band from the stricture to the bladder requiring resection (6).

We believe that our patient's transient colonic inflammation was secondary to dysmotility caused by his severe course of HUS and vascular ischemic injury. Upon treatment with a strict bowel regimen, his symptoms and self-limited colitis resolved. Although some patients have been reported to have an inflammatory bowel disease-like presentation after severe HUS with involvement anywhere from esophagus to perianal area in the form of transmural necrosis and strictures (4,7), this is much less likely in our patient given his improvement without an inflammatory bowel disease-specific treatment regimen. Our patient will continue to be monitored with fecal calprotectin, and endoscopy will be considered to reassess the anastomotic area.

Patients who have experienced such severe inflammation post-HUS should be monitored closely by a pediatric gastroenterologist for the evolution of the disease process. While the treatment of EHEC HUS includes fluid and electrolyte management, other factors such as avoiding antidiarrheal agents and antibiotic therapy may help decrease the risk of severe gastrointestinal complications (7,8). Further research is needed to study mucosal and bowel wall integrity and motility after severe colonic HUS and how motility may affect microbial dysbiosis in these patients. Moreover, further studies are needed regarding

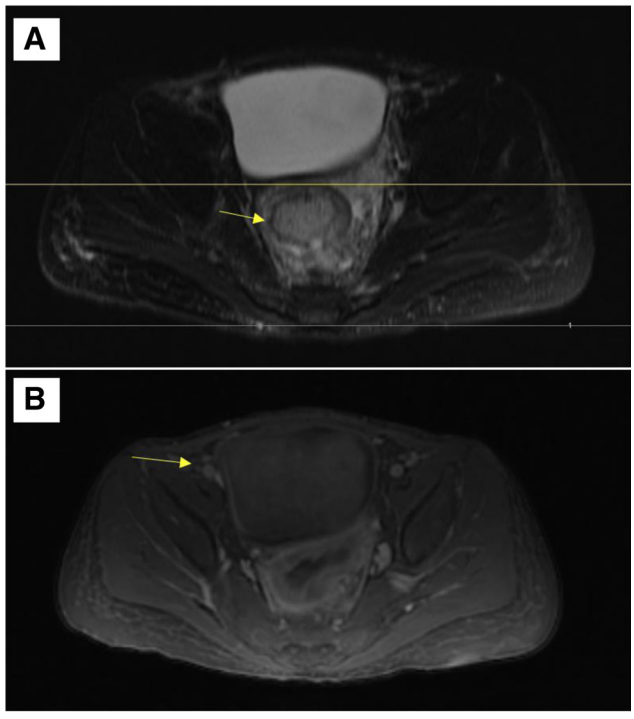

FIGURE 3. A) The T2 image shows nonspecific circumferential bowel wall thickening with intramural edema. **B)** Coronal T2 image showing gas distension of the cecum.

environmental, genetic, host immunity factors, and medication exposures that might play a role in gastrointestinal manifestations of HUS.

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