Colonic Necrosis and Perforation Secondary to *Escherichia coli* O157:H7 Gastroenteritis in an Adult Patient without Hemolytic Uremic Syndrome

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During a multistate outbreak of *Escherichia coli* O157:H7 diarrhea, we encountered a woman who had hemorrhagic colitis complicated by ischemic colitis with perforation. To our knowledge, this has not previously been described in adult patients. Because of the insensitivity of the commonly used diagnostic methods, this condition may be underrecognized.

*Escherichia coli* O157:H7 has been recognized as a frequent cause of gastroenteritis [1]. Illness occurs most often in young children [1]. This bacterium produces a verotoxin with powerful cytotoxic properties [2]. Many cases of infection are linked with consumption of undercooked ground beef. The hallmark of the disease is cramping abdominal pain accompanied by diarrhea that may become bloody (hemorrhagic colitis). Spontaneous recovery without receipt of specific therapy is typical [1]. In its most severe form, hemorrhagic colitis is followed by hemolytic uremic syndrome (HUS), with the triad of conditions of hemolytic anemia, thrombocytopenia, and renal failure [2]. An estimated 5%–10% of cases progress to HUS [1]. It has been speculated that extensive colonic mucosal damage caused by the verotoxin allows the toxin to enter the systemic circulation and to cause diffuse endothelial injury, cell death, and thrombotic microangiopathy [2]. Thus, colon involvement is generally more profound in patients manifesting HUS [2]. These patients often present with severe abdominal pain mimicking an acute surgical abdomen [2, 3]. Serious complications of colon involvement have been reported to occur only in children with HUS. These include massive lower gastrointestinal tract bleeding, toxic megacolon, rectal prolapse, intussusception, stricture, colon necrosis, and perforation [2–4].

Perforation or necrosis of the colon in pediatric patients with HUS is rare. There are only 4 reported cases of colon necrosis that required colectomy, and there are only 4 case reports of colon perforation [2–5]. There have been ≥6 outbreaks of *E. coli* O157:H7 colitis in elderly adults who reside in nursing homes [6, 7]. High attack rates as well as striking morbidity and mortality have been reported among these patients. Mortality was largely due to the development of HUS that resulted in acute renal failure and pulmonary edema. However, no cases of colonic necrosis and perforation were noted even in these debilitated adults. We report what is, to our knowledge, the first case of colonic necrosis and perforation due to *E. coli* O157:H7 in an adult patient without manifestations of HUS.

**Case report.** A 48-year-old woman presented to her medical clinic in Dakota County, Minnesota, on 4 December 2000 complaining of severe bilateral lower quadrant pain and abdominal bloating. On 20 November 2000, she had eaten a meal that included ground beef. The ground beef had been purchased at a local grocery store on 19 November during a period when the ground beef sold at this chain of grocery stores was subsequently shown to have been contaminated with *E. coli* O157:H7. On 23 November, the patient became ill, with sudden onset of nausea, vomiting, diarrhea, and fever. Diarrheal stools occurred 4 or 5 times daily. The patient had only a night-light on in her bathroom and could not confirm whether the diarrhea was bloody. On the day before presentation, she began to experience left lower quadrant pain and mild bloating, which worsened during the evening and then spread to the right lower quadrant.

The patient’s medical history was significant for hypertension, gastroesophageal reflux disease, bipolar affective disorder, and primary thrombocytopenia, which was discovered during a routine blood test in 1997. There were no prior episodes of abnormal bleeding or clotting. The patient’s platelet count was well controlled (range, 200,000–600,000 platelets/mm<sup>3</sup>) by anagrelide therapy (0.5 mg q.d.). Physical examination revealed that her temperature was 36.7°C, her pulse was 100 beats/min, and her blood pressure was 120/90 mm Hg. Her abdomen was quiet, distended, and tympanitic, with left lower quadrant tenderness without rebound. Radiography performed in the clinic revealed an ileus pattern and free subdiaphragmatic air. The patient was hospitalized at 6:30 p.m. on 4 December 2000 Laboratory studies revealed the following values: hemoglobin, 11.8 g/dL; WBC count, 19,200 cells/mm<sup>3</sup>; platelet count, 511,000...
platelets/mm$^3$; morphology without schistocytes; serum sodium, 119 mM; serum potassium, 2.7 mM; blood urea nitrogen, 35 mg/dL; serum creatinine, 1.2 mg/dL; bilirubin, 0.5 mg/dL; international normalized ratio, 2.3 IU; and fibrinogen, 543 mg/dL. Imipenem-cilastatin (500 mg every 6 h) was administered, and the serum electrolyte level was corrected.

The patient was taken to the operating room at 10:00 a.m. on 5 December 2000. Exploratory laparotomy revealed gross fecal peritonitis. Multiple areas of the colon appeared frankly necrotic, with perforations visible in the descending and transverse colon and the cecum. There was no evident thrombosis of the mesenteric arteries or veins. Total abdominal colectomy, ileostomy, and Hartmann’s pouch procedure were performed after thorough debridement and irrigation. Pathologic examination of the colon confirmed the multiple perforations. Microscopic examination revealed extensive acute colitis with hemorrhagic and ischemic features, with extensive superficial necrosis of the mucosa and congested mucosal and submucosal blood vessels. There were deep ulcers scattered into the muscularis, occasional areas of full-thickness necrosis, and bowel wall rupture. The mesenteric vessels were without thrombosis or emboli. Culture of a stool sample obtained from the colectomy specimen revealed no enteric pathogens, including $E. coli$ O157:H7. Tests of stool samples for Shiga-like toxin were not performed.

After the operation, the patient was transferred to a tertiary care hospital in St. Paul, Minnesota, because of respiratory and hemodynamic instability. She was treated with intravenous piperacillin-tazobactam, fluconazole, and dopamine and gradually made a full recovery, and she was discharged from the hospital on 24 December 2000. Serologic testing for antibodies to $E. coli$ O157 lipopolysaccharide by EIA was performed at the Centers for Disease Control and Prevention (Atlanta, Georgia), as described by Barrett et al. [8]. Paired serum specimens obtained 22 days and 57 days after the onset of illness both showed an IgM titer of 1:160, but the IgG titer had increased from 1:320 to 1:2560, an 8-fold increase indicative of an acute infection [6].

Discussion. The present case significantly extends the clinical spectrum of colonic disease caused by $E. coli$ O157:H7 gastroenteritis. All previous reports of colon necrosis and colon perforation (8 cases total) involved children with concomitant HUS. The patient in the present case report was an adult and did not have HUS. Nevertheless, she had extensive colonic necrosis with multiple perforations and peritonitis. The diagnosis was considered because the patient was too young for ischemic colitis to be likely, had no mesenteric arterial or venous thrombosis noted at surgery, and presented in the midst of a multistate outbreak of $E. coli$ O157:H7 gastroenteritis associated with consumption of ground beef. The patient had consumed ground beef purchased from one of a chain of grocery stores implicated in the outbreak. Culture of a stool sample obtained from the patient’s colectomy specimen was negative. However, acute-phase and convalescent-phase serologic tests showed an 8-fold increase in IgG antibodies to $E. coli$ O157:H7, which confirms that this infection was the cause of the colon perforation.

This case was part of a large multistate outbreak of $E. coli$ O157:H7 infection due to contaminated ground beef from a single distributor [9]. Forty-two laboratory-confirmed cases were identified among Minnesota residents; of these cases, 40 were confirmed by culture for $E. coli$ O157:H7. All isolates were indistinguishable by PFGE subtyping. The outbreak strain of $E. coli$ O157 was cultured from 19 ground beef samples, including samples from 3 case households and 3 grocery stores [9].

The negative stool culture result is not surprising and does not detract from the diagnosis of $E. coli$ O157:H7 colitis. The culture sample was obtained 16 h after the initiation of intravenous antibiotic therapy, which could explain the negative finding. In addition, the stool sample was obtained 14 days after the onset of illness. The rate of recovery of $E. coli$ O157:H7 from the stool specimens of patients with HUS decreases dramatically, to only 30%, if the sample is obtained >7 days after the onset of diarrhea [10]. Finally, direct culture on sorbitol MacConkey agar, the method used for culturing this patient’s stool sample, is not as sensitive as methods that use enrichment techniques, such as immunomagnetic separation and/or addition of cefixime and tellurite to sorbitol MacConkey medium [11, 12]. Suboptimal culture techniques may also impair the recovery of $E. coli$ O157:H7.

Our patient had essential thrombocythemia discovered by serendipity 3 years before the onset of hemorrhagic colitis. However, she had no previous or subsequent thrombotic events, and her platelet level had been well controlled by treatment with anagrelide. Neither colonic ischemia nor necrosis are reported side effects of anagrelide use. Thus, the role her platelet disorder played in the genesis of her necrotizing, hemorrhagic colitis is unclear.

In conclusion, we report a case of $E. coli$ O157:H7 gastroenteritis that progressed to colon necrosis and colon perforation in an adult patient without HUS. This entity may be difficult to diagnose without serologic testing because of the low sensitivity of standard stool culture methods, especially after the first week of illness. The diagnosis was only entertained because the patient’s illness occurred in the midst of a large, multistate outbreak of $E. coli$ O157:H7 infection. Perhaps this entity occurs more commonly than is now appreciated but is underdiagnosed because of a low index of suspicion (outbreak-associated cases of $E. coli$ O157:H7 account for only ~20% of the total number of cases of $E. coli$ O157:H7 infection [13]), the insensitivity of
routine stool culture on sorbitol-MacConkey medium, and the infrequent use of serologic methods for diagnosis.

References