



Case report

Infection due to Shiga toxin-producing enterohemorrhagic *Escherichia coli* (EHEC) presenting as ischemic colitis



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ABSTRACT

Infections due to Shiga toxin-producing enterohemorrhagic *Escherichia coli* (EHEC) are often mild and self-limiting, but more severe cases can develop into hemolytic uremic syndrome (HUS) and hemorrhagic colitis. This case report documents a sporadic case of ischemic colitis likely triggered by EHEC but without manifestations of hemolytic uremic syndrome. From our literature review, we identified only one other case of an EHEC infection presenting as ischemic colitis in the absence of HUS. To our knowledge, this is the first case presentation of EHEC-induced ischemic colitis which did not lead to significant morbidity.

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Introduction

Escherichia coli infections can have a wide variety of clinical presentations ranging from a self-limiting diarrheal illness to more severe infections causing hemorrhagic colitis or hemolytic uremic syndrome (HUS) [1,2]. Patients classically present with abdominal pain and bloody diarrhea that typically resolve with supportive care. The illness can progress to catastrophic complications including HUS, although this is more common in pediatric patients [3]. These severe complications are often due to Shiga toxin-producing enterohemorrhagic *Escherichia coli* (EHEC), with serotype O157:H7 being the most common cause of HUS worldwide. [3]

We report a case of EHEC presenting as ischemic colitis without HUS, that improved without needing surgical intervention. This occurred in the setting of a national outbreak of *E. coli* O157:H7 in the United States.

Case report

A 32 year old female with no relevant medical history presented to the urgent care clinic with 1 day of diffuse abdominal pain and non-bloody diarrhea. She reported eating a salad from a national supermarket chain, which was later recalled due to bacterial contamination. Recent travel included a trip to the Sierra Nevada

Mountains, but she denied ingesting water from lakes or streams. She denied having fevers, chills, out-of-state travel, or recent antibacterial use. In the clinic, she was afebrile with a normal white blood cell (WBC) count. She was given IV fluids and sent home that day.

The following day, she presented to the urgent care clinic again with worsening abdominal pain and several episodes of now bloody diarrhea. She remained afebrile but was tachycardic to the 130 s with an elevated WBC count of 20.3. She was transferred to the emergency department. The patient denied any personal or family history of inflammatory bowel disease or colon cancer. Her outpatient medications included a hormonal vaginal ring for contraception. She denied any non-steroidal anti-inflammatory drug (NSAID) use. She reported using e-cigarettes daily for the last 6 years and smoking marijuana occasionally. She denied heavy alcohol use.

On physical exam, she was afebrile, with a pulse of 105 bpm and blood pressure of 110/67 mmHg. Abdominal exam revealed hypoactive bowel sounds and diffuse tenderness without guarding. Laboratory tests revealed a WBC count of 18,000 cells/mcL, hemoglobin 13.5 g/dL, sodium 129 mEq/L, bicarbonate 19 mEq/L, and creatinine 0.66 mg/dL. Liver function tests showed a total bilirubin 1.6 mg/dL and normal aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase. CT of the abdomen and pelvis with contrast showed diffuse wall thickening of the colon suspicious for colitis. Following admission, the patient was made nothing by mouth and started on ciprofloxacin and metronidazole.

On day 2 of hospitalization, the patient underwent a sigmoidoscopy which showed severe colitis spanning 15 cm to

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40 cm from normal appearing rectum (Figs. 1 and 2). The colonic mucosa appeared dusky with contiguous erythema, friability, granularity, and edema causing luminal narrowing (Figs. 3–5). The endoscopic appearance was noted to be atypical of inflammatory bowel disease and more suggestive of ischemia. Beyond 40 cm, there were non-contiguous segments of similar colitis up to the transverse colon. Mucosal biopsies obtained during sigmoidoscopy showed acute colitis of the transverse, descending, and sigmoid colon with changes consistent with ischemic injury (Figs. 6 and 7). The patient was followed closely by General Surgery due to concern that she might need a total colectomy with ileostomy, given the extent and distribution of disease.

She remained on bowel rest and started on total parenteral nutrition. Antimicrobials were changed to ceftriaxone. However, the patient continued to have fevers and was transitioned to piperacillin-tazobactam. On hospital day 4, the bacterial GI panel stool test came back positive for the Shiga toxin gene. The panel also tested for *Salmonella*, *Shigella*, *Enteroinvasive E. coli (EIEC)*, and *Campylobacter*, all of which were not detected. The bacterial GI panel does not test for the O157:H7 antigen, however if positive for Shiga toxin, it will reflexively test for stool cultures for *E. coli* O157:

H7, which are cultured on MacConkey-Sorbitol agar. Of note, the patient's stool culture for *E. coli* O157:H7 showed no growth.

Infectious Disease was consulted on hospital day 4 who recommended discontinuing antimicrobials to avoid the development of HUS. On hospital day 5, the patient was able to tolerate clear liquids. She was eventually discharged home on day 7.

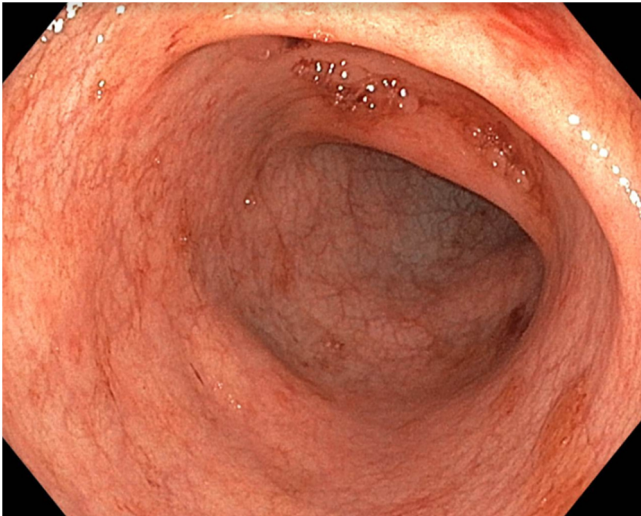


Fig. 1. Sigmoidoscopy (rectum).

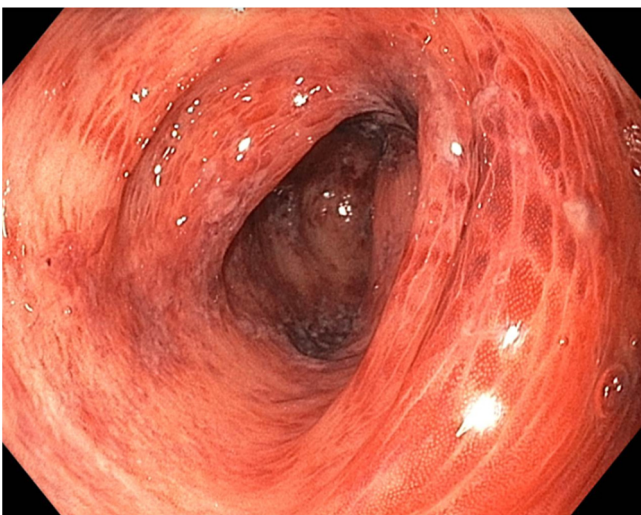


Fig. 2. Sigmoidoscopy (sigmoid colon).

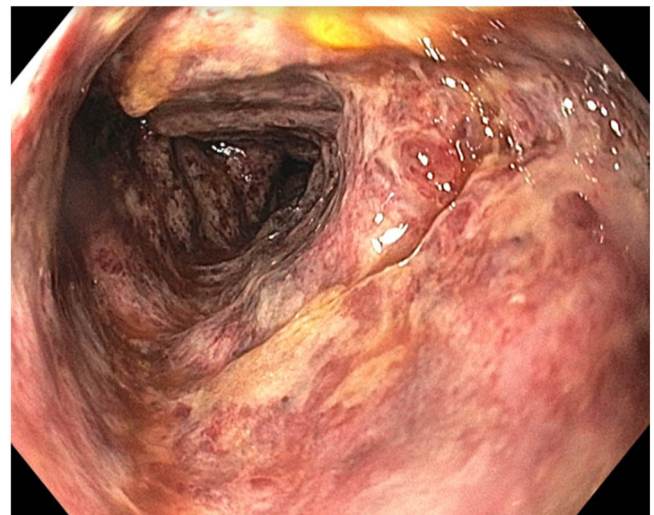
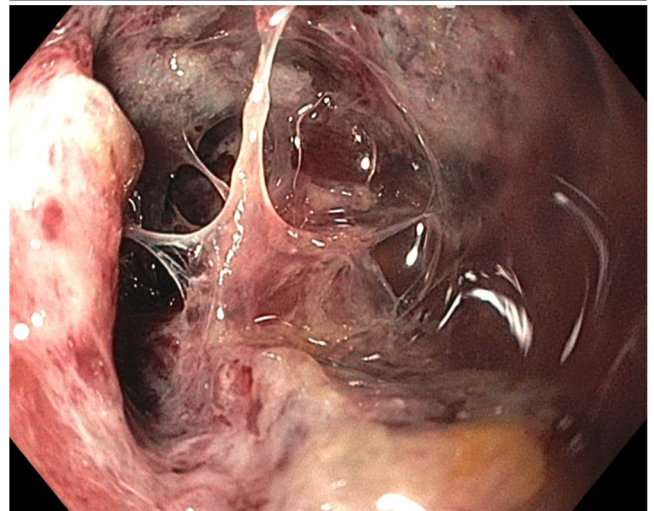
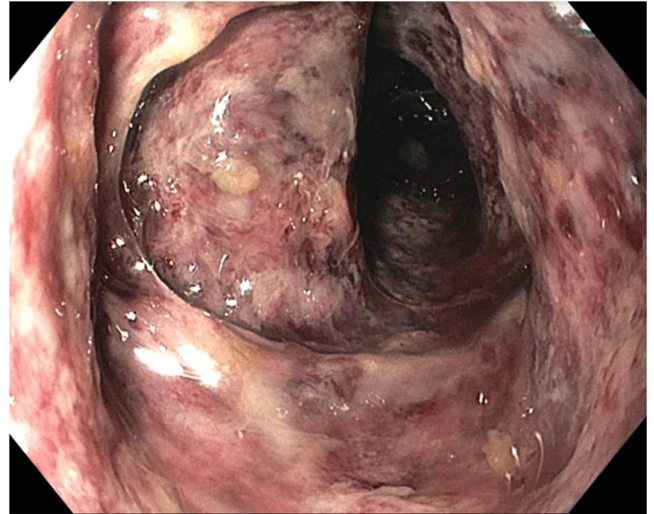


Fig. 3. Sigmoidoscopy (descending colon).

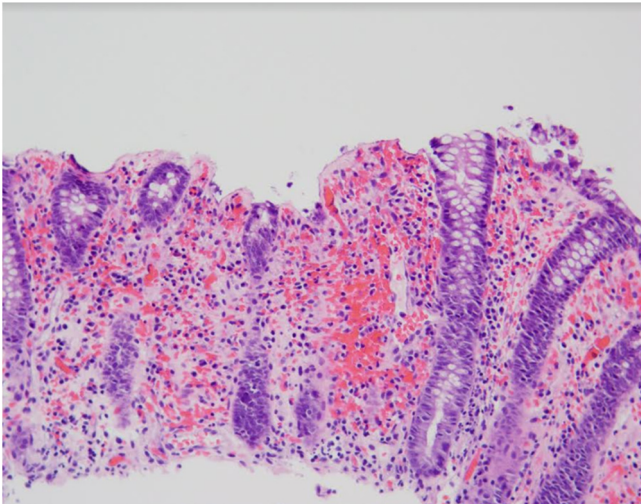


Fig. 6. Biopsy of the transverse colon with evidence of ischemic injury characterized by loss of surface epithelium, lamina propria hemorrhage, scattered neutrophils, and mucin depleted crypts with a regenerative appearance.

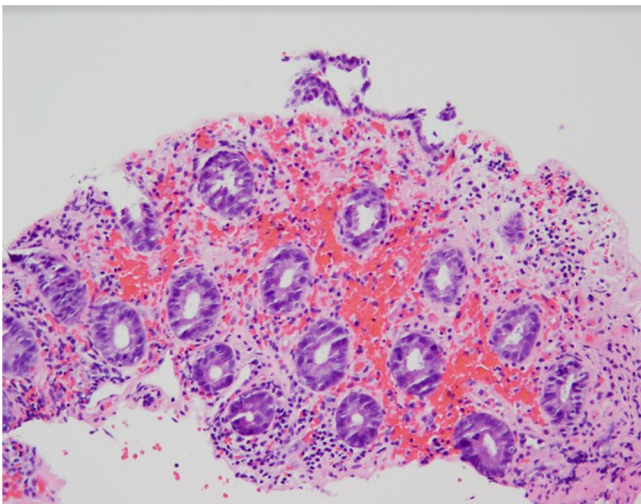


Fig. 7. Biopsy of the sigmoid colon with features of ischemic colitis including superficial mucosal necrosis, hemorrhage into the lamina propria, and regenerating crypts.

Discussion

This case of ischemic colitis by a Shiga-toxin producing organism demonstrates one of the most severe complications of this infection without manifestations of HUS. It occurred in the setting of a nationwide outbreak of *E. coli* O157:H7. The Centers for Disease Control and Prevention (CDC) reported that 43 people from 12 states were infected with the outbreak strain of Shiga toxin-producing *E. coli* O157:H7 over the span of 24 days [4]. Given the outbreak and history of consumption of contaminated product, we suspect that the present case was due to infection with *E. coli* O157:H7, despite the negative result on stool culture. The presence of Shiga toxin in our patient's stool was identified using the BD Max enteric bacterial panel (EBP). This EBP is a multiplex nucleic acid amplification assay designed to detect *Salmonella*, *Shigella*, and *Campylobacter* species, and Shiga-like toxin genes in stool specimens.

A study in 2013 found that the BD Max EBP exhibited 100% sensitivity at 10^5 CFU/mL for Shiga-like toxins, and was more

sensitive than routine stool culture, reliably detecting organisms at concentrations 1 to 3log10 lower [5].

The county Public Health Department also ran enzyme immunoassay (EIA) tests on the patient's stool which were negative for Shiga toxin. However, another study in 2015 compared the BD Max EBP to routine stool cultures and EIA. The authors found that compared to stool cultures, the BD Max EBP assay had a greater sensitivity and positive predictive agreement (PPA) [6]. They also found that stool samples which tested positive by BD Max EBP but negative by culture or EIA were still likely to be true-positive results. Negative cultures are likely due to loss of organism viability or insufficient number of organisms present to detect. Also, *E. coli* is the most common producer of Shiga toxin [7] in the U.S., so it is likely that this was the pathogen involved in our patient's illness.

Other diagnoses such as an underlying hypercoagulable disorder were considered given the severity of ischemia in an otherwise healthy young female. The patient reported a history of smoking and use of hormonal contraception but had no other risk factors for ischemia. Her imaging studies were reviewed with Radiology, who confirmed that the celiac artery and superior mesenteric artery were well visualized and showed no vascular obstruction.

This seems to have been a case of EHEC infection presenting as ischemic colitis in a young, healthy female, which occurred in the absence of HUS. Bowel ischemia is a severe complication associated with EHEC, but is rarely described in the literature [7]. On our review, we found only one other case of EHEC-associated colonic ischemia and necrosis, without evidence of HUS, described in an adult [8]. That particular case led to bowel perforation, an exploratory laparotomy, and prolonged hospitalization with subsequent improvement. To our knowledge, this is the first case in which the infection progressed to ischemic colitis without significant morbidity. It is unclear how often this manifestation of EHEC infection occurs. However, given the associated morbidity and mortality if not identified early in the course, it is a manifestation well worth considering early in the presentation.

Additionally, it is worth noting that the use of certain antimicrobials, specifically beta-lactam antimicrobials (penicillins or cephalosporins), fluoroquinolones, and metronidazole in patients with *E. coli* O157:H7 are linked with an increased risk of developing HUS [9–11]. This is important to note because our patient was initially started on ciprofloxacin and metronidazole, changed to ceftriaxone, then transitioned to piperacillin-tazobactam. Despite receiving ceftriaxone, ciprofloxacin, and metronidazole antimicrobials over the course of illness, our patient did not develop evidence of HUS.

In conclusion, while severe complications of EHEC are more widely associated with the pediatric population, this case sheds light on the importance of considering other manifestations of EHEC infections in adults outside of hemorrhagic colitis and HUS.

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