Fatal Clostridium difficile Enteritis as a Delayed Complication of Loop Ileostomy for Fulminant C difficile Colitis

Summer N. Rochester, DO; Robert Farrar, MD; R. Jared Sanders, MD; Megan K. Straughan, MD; and Meghann L. Kaiser, MD

From the Department of Surgery, Greenville Health System, Greenville, SC (S.N.R., R.J.S., M.K.S., M.L.K.), and Department of Pathology, Greenville Health System, Greenville, SC (R.F.)

Abstract

The recent introduction of loop ileostomy with colonic lavage represents a powerful surgical intervention for fulminant Clostridium difficile colitis, but is not without potential hazards. We present a case of fatal recurrent C difficile small bowel enteritis, a heretofore unreported potential complication of ileostomy reversal. A review of the literature suggests potential mechanisms and means to prevent this devastating outcome.

Clostridium difficile is an opportunistic pathogen that multiplies when more benign intestinal flora is lacking and produces a damaging, intensely inflammatory toxin capable of transmural permeation.1 C difficile colitis (CDC) has rapidly increased in incidence over recent decades and is now the most common cause of nosocomial diarrhea.2 It complicates the hospital stays of an increasingly frail geriatric population, frequently resulting in septic shock, organ dysfunction, and even death, despite maximal medical management. Thus surgical therapy remains the mainstay of salvage intervention. However, after failing various pharmaceuticals, many patients have deteriorated into multi-system organ dysfunction, rendering them less than ideal candidates for the conventional operation: an extensive, highly morbid total abdominal colectomy with permanent end-ileostomy. In 2011, Neal and colleagues at the University of Pittsburgh presented a less drastic alternative: minimally invasive creation of a loop ileostomy to allow for antegrade large-volume polyethylene glycol (PEG) and vancomycin enemas, accompanied by systemic intravenous metronidazole.3 Patients in that study undergoing this gentler option exhibited less than half the mortality of those receiving colectomy in short-term follow-up. As a result, for many general surgeons, temporary laparoscopic loop ileostomy with colonic lavage has become the preferred first option in a staged salvage approach to refractory CDC, reserving colectomy only for those that fail. We ourselves have found success creating many such loop ileostomies for fulminant CDC; however, we have since encountered a devastating potential complication of reversing these stomas: recurrent C difficile invading the small bowel, otherwise known as Clostridium difficile enteritis (CDE), an infection associated with overwhelming sepsis and a mortality of 30%.4

Case Description

GC was an 81-year-old Caucasian man with a history of coronary artery disease, dyslipidemia, and gastroesophageal reflux, for which he took multiple medications, including proton pump inhibitors. He was in otherwise good health and highly functioning, living at home with his spouse. He presented to his primary care physician complaining of unilateral facial tenderness and swelling, was given a diagnosis of parotiditis, and completed an empiric course of clindamycin. His symptoms, however, did not resolve, and further work-up ultimately revealed a malignant parotid tumor, likely metastatic melanoma.

In the interim, the patient developed diarrhea that persisted despite a 3-week course of oral ciprofloxacin and metronidazole at home, necessitating hospital admission for dehydration with acute kidney injury. Highly sensitive polymerase chain reaction (PCR) testing (Xpert C difficile/
Epi, Cepheid Inc, Sunnyvale, Calif.) revealed a particularly virulent B1/NAP/027 strain of C difficile. He was initially treated with systemic intravenous metronidazole as well as vancomycin per oral and rectum. Nonetheless, his condition continued to deteriorate, and surgical consultation was sought. The computed tomography (CT) scan obtained was suggestive of severe CDC (Fig. 1). After lengthy discussion, taking into account the patient’s advanced age, comorbidities, and worsening clinical status, the patient elected to proceed with emergent loop ileostomy on hospital day 3. The colon was closely inspected laparoscopically and found to be boggy and congested but otherwise viable. We accordingly proceeded with laparoscopic creation of loop ileostomy within a few centimeters of the ileocecal valve, allowing for easy cannulation, through which large-volume PEG and a 10-day course of vancomycin colonic flushes were administered, along with systemic intravenous metronidazole. Despite a complicated 30-day hospital course, the patient did exhibit complete clinical resolution of CDC and was discharged to a skilled nursing facility. Infectious disease consultants advised he be maintained on a regimen of enteric cholestyramine, to bind and inactivate C difficile toxin, and Saccharomyces boulardii probiotic supplements, to maintain healthy colonic flora. Repeat PCR testing of rectal output revealed no further evidence of C difficile.

After undergoing radical parotidectomy, complicated by a superficial wound infection, the patient was treated with a course of cephalaxin and experienced no return of diarrhea or other gastrointestinal complaints. Multiple discussions were had with both patient and family throughout this period. The patient acknowledged that ileostomy reversal was not medically necessary; nevertheless, he felt the stoma adversely affected his quality of life and ardently desired reversal. Five months after initial ileostomy creation, and 1 month following his parotidectomy, the patient underwent elective ileostomy reversal. One gram of prophylactic cefoxitin was administered preoperatively, and a stapled anastomosis was created without incident. The patient was extubated immediately thereafter and transferred to a monitored floor bed. By postoperative day (POD) 2 the patient was tolerating an oral diet and ambulating without complaints. On POD3, however, he acutely decompensated into respiratory distress with frank peritonitis. Broad-spectrum antibiotics, including intravenous metronidazole, were initiated. CT (Fig. 2) was concerning for possible small and large bowel ischemia, and the patient returned to the operating room for emergent exploratory laparotomy. Once again, the colon was noted to be boggy and friable, as was the ileum. The anastomosis was intact without biliary staining, and the mesenteric vessels surveyed via Doppler transmitted strong signals throughout. With no other obvious explanation for the patient’s clinical findings, we elected to proceed with resection of the involved bowel, which entailed a total abdominal colectomy and partial distal small bowel entrectomy. The specimens grossly exhibited mucosal pseudomembranes with cobblestoning not only throughout the colon but also extending a significant distance proximally past our anastomoses and into the resected ileal portion (Fig. 3, Page 58). Formalin fixation prevented definitive testing for the C difficile toxin. However, vessels were noted to be patent, making primary ischemia an unlikely explanation. Multiple pathologists judged CDE the most likely pathology (Fig. 4, Page 58).

Intraoperatively the patient continued to deteriorate, and we elected to leave him in discontinuity with an open abdomen to expedite aggressive fluid resuscitation in the intensive care unit. Overnight, despite heroic efforts, including vancomycin per rectum and nasogastric tube, severe shock unre-
sponsive to fluids, pressors, and inotropes ensued. The family elected to withdraw support in accordance with the patient’s previously expressed wishes, and he expired shortly thereafter on POD4.

Discussion
CDE was once felt to be a rare entity with dismal prognosis, affecting primarily postcolectomy patients suffering from inflammatory bowel disease (IBD). Between 1980 and 2000, only 9 cases were reported in the literature. Subsequently, a relative multitude have erupted, many associated with neither IBD nor colectomy. This exponential rise is likely the product of heightened clinical suspicion, coupled with the prevalence of several factors now recognized to increase susceptibility, including advanced age, immunosuppression, recent antibiotic exposure, hospitalization, white race, gastric acid suppression, and the B1/NAP/027 strain of C difficile. Our patient exhibited many of these risk factors, but the last 2 may be particularly damaging. Clinically significant infection of the small bowel likely requires a greater burden of both pathogen and toxin. While a more neutral pH encouraged proliferation of the C difficile microorganism, the B1/NAP/027 genotype simultaneously enabled far greater toxin production.

A recent study found that ileostomy effluent collected from 16% of asymptomatic patients carried the C difficile toxin. A survey of jejunal specimens harvested at autopsy from patients without known gastrointestinal pathology likewise revealed a 3% rate of C difficile colonization. These findings suggest that, far from being the innocent bystander once thought, the small bowel may in fact represent a silent reservoir for recurrent C difficile infections. Ileostomy reversal and right hemicolectomy are especially linked to CDC, suggesting that breach of the ileocecal barrier may release the pathogen. Our case study supports this hypothesis. Following loop ileostomy and vancomycin enemas, our patient was asymptomatic and rectal specimen tested negative for persistent C difficile toxin, but an ileal sample was not obtained. Moreover, the patient received a maintenance regimen of toxin-binders and probiotics, which may have rendered small bowel colonization subclinical. Later, however, stapled anastomosis of a very distal ileostomy using a long, 75 mm cartridge likely extended across and thereby compromised his ileocecal valve. This insult, coupled with additional antibiotic exposure and the immunosuppression of malignancy with recent surgery allowed the pathogen to re-enter and flourish in the colon. Thus circumstances set the stage for a fulminant and ultimately fatal infection encompassing both large and small bowel. In the future, potential precautionary steps we are considering include 1) sampling ileostomy effluent to identify asymptomatic carriers, 2) performing hand-sewn end-to-end ileal anastomoses to preserve the integrity of the ileocecal valve, and 3) administering newer pharmaceuticals such as fidaxomicin that are associated with significantly lower recurrence rates than vancomycin.

Conclusion
The recent introduction of loop ileostomy with colonic lavage has improved short-term survival rates among patients with fulminant CDC. Nevertheless, increasingly virulent strains affecting an elderly, complicated patient population compel surgeons to suspect the small bowel as a potential source of ongoing colonization and CDE as a potentially fatal ultimate outcome. Research efforts are certainly warranted to determine what steps should be taken prior to and during ileostomy reversal to ensure our patients’ continued wellbeing.
RECURRANT FATAL C DIFFICILE AFTER ILEOSTOMY TAKEDOWN

References


Correspondence

Address to: Meghann L. Kaiser, MD Greenville Health System, Dept of Surgery 3rd Floor Support Tower 701 Grove Rd Greenville, SC 29605 (mkaiser@ghs.org)