

A Novel Surgical Treatment of Pediatric Fulminant *Clostridium difficile* Colitis

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Pediatric patients rarely present with severe, complicated *Clostridium difficile* colitis. The medical and surgical management of pediatric patients is primarily based on evidence from adult populations, in which standard therapy often includes subtotal colectomy and end ileostomy. New evidence in adults suggests that a diverting loop ileostomy and colonic lavage is an effective alternative for the management of refractory severe, complicated *C difficile* colitis. We report the case of a 15-year-old female patient who developed severe, complicated *C difficile* colitis. After failing medical management, she underwent a diverting loop ileostomy with antegrade colonic lavage and recovered uneventfully. There is limited literature on the medical management of *C difficile*-associated disease in pediatric patients and even less information on the medical or surgical management of severe, complicated *C difficile* colitis in pediatrics. Diverting loop ileostomy and colonic lavage should be considered as an alternative to subtotal colectomy and end ileostomy in a pediatric patient with severe, complicated *C difficile* colitis.

Pediatric patients are much less likely to be infected by *Clostridium difficile* than the general population in the United States. The incidence of *C difficile*-associated disease (CDAD) in pediatric patients is estimated to be 24.2 per 100 000 people, whereas the overall incidence of CDAD is 147.2 per 100 000 people.¹ The risk of developing CDAD is significantly higher in pediatric patients with inflammatory bowel disease (IBD)² and may be associated with increased morbidity and mortality.³

Currently, the medical management of pediatric patients with CDAD is based on evidence from adults.³ There is no reliable way to predict which patients will fail medical management and require surgery.⁴ In adult patients who develop severe, complicated CDAD, the surgical management is typically a subtotal

colectomy with end ileostomy.⁴ This procedure is known to have a high incidence of morbidity and has long-term consequences in the pediatric population. A new form of surgical treatment, diverting loop ileostomy and antegrade colonic lavage, has been studied and found to be safe and effective in adult patients.⁵ We report the case of a pediatric patient who failed medical management of severe, complicated CDAD and received a diverting loop ileostomy and colonic lavage while preserving the colon. Informed consent was obtained for publication.

CASE PRESENTATION

A 15-year-old White girl presented to the emergency department (ED) with one week of abdominal pain, diarrhea, and palpitations. She had a past medical history of autoimmune thyroiditis and gastritis. She was not

abstract

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Ms Hanson and Dr Wagner conceptualized and designed the study, acquired the data, interpreted the data, drafted the initial manuscript, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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on any medications and had no recent antibiotic therapy.

In the ED she was tachycardic, tachypneic, and tender in all 4 quadrants. Her white blood cell count (WBC) and C-reactive protein were elevated to 15.7 cells/mm³ and 33.8 mg/L, respectively. A computed tomography scan revealed pancolonic bowel wall thickening, hyperemia, and ascites (Fig 1). She was given supportive treatment with intravenous fluids, and pain control and stool cultures were sent. On her first hospital day (HD 1), she remained tachycardic, tachypneic, and diffusely tender and developed hematochezia. Stool cultures were positive for *C difficile*, and she was started on oral vancomycin. On HD 2, the patient had worsening abdominal distension and pain. She was transferred to the ICU where she was given additional intravenous fluids, metronidazole, and cefepime. On HD 3, the patient developed rectal prolapse with visible pseudomembranes (Fig 2). Her WBC was elevated to 34.6; she was thrombocytopenic and hypoalbuminemic (Table 1). Her daily abdominal radiographs revealed the progression of ascites (Fig 3). She was then diagnosed with severe, complicated *C difficile* pancolitis on the basis of criteria established by Neal



FIGURE 1 Computed tomography scan from the ED revealing pancolonic bowel wall thickening, hyperemia, and ascites.



FIGURE 2 Rectal prolapse and visible pseudomembranes that the patient developed on HD 3.

et al⁵ (Table 2). A surgical consultation was obtained. After discussion of the options for operative management with the patient and her parents, it was decided to pursue a diverting loop ileostomy with antegrade colonic lavage in an attempt to preserve the patient's colon, with the understanding that subsequent colectomy may be necessary if the patient did not improve.

A few hours later, she was taken to the operating room and underwent a diverting loop ileostomy with antegrade colonic lavage through a pezzar gastrostomy tube in the distal limb of the loop ileostomy. The colonic lavage was done intraoperatively, with 4 L of polyethylene glycol (PEG) and vancomycin 500 mg in 500 mL normal saline. A biopsy was also taken from the terminal ileum to evaluate for underlying IBD. The patient tolerated the procedure well.

Her postoperative treatment course followed the recommendations of

Neal et al,⁵ which included antegrade vancomycin enemas 500 mg in 90 mL normal saline every 6 hours through the distal limb of the loop ileostomy and intravenous metronidazole for 10 days. On postoperative day (POD) 1, the patient had a dramatic improvement in her status, with her tachycardia, tachypnea, and abdominal pain improved. Her cefepime and oral vancomycin were discontinued, and she was transferred out of the ICU. She was discharged on POD 9, after completing her course of intravenous metronidazole. Her significant rectal prolapse and labial edema also delayed her discharge.

At her 1-week follow-up in clinic, the patient was doing well, and her labial edema and rectal prolapse resolved. The biopsy of the terminal ileum revealed attenuative villi, with reactive epithelium and acute inflammation. Three months later, she underwent colonoscopy, upper endoscopy, and ileoscopy, with biopsies that revealed chronic cecitis, chronic colitis continuous from the ascending colon to the sigmoid colon, and mild crypt architectural distortion in the rectum consistent with ulcerative colitis (Figs 4 and 5). She was initially treated with mesalamine but was changed to sulfasalazine because of associated pain. Her ileostomy was reversed 4 months after her initial operation.

DISCUSSION

C difficile is an anaerobic, Gram-positive, spore-forming, toxin-

TABLE 1 Patient's Inflammatory Marker Values Throughout Admission

Time	WBC	Hemoglobin	Platelets	ESR	C-Reactive Protein	Lactic Acid
ED	15.7	16.5	290	7	33.8	—
HD 3	29.8	16.3	88	8	35.8	25
HD 4	34.6	16.4	87	—	—	18
POD 1	38.4	12.8	75	—	—	11
POD 2	31.5	13.8	63	—	—	—
POD 3	22.9	14.4	49	—	—	—
POD 4	17.8	13.8	54	—	—	—
POD 5	13.8	13.6	82	—	—	—

—, not applicable.

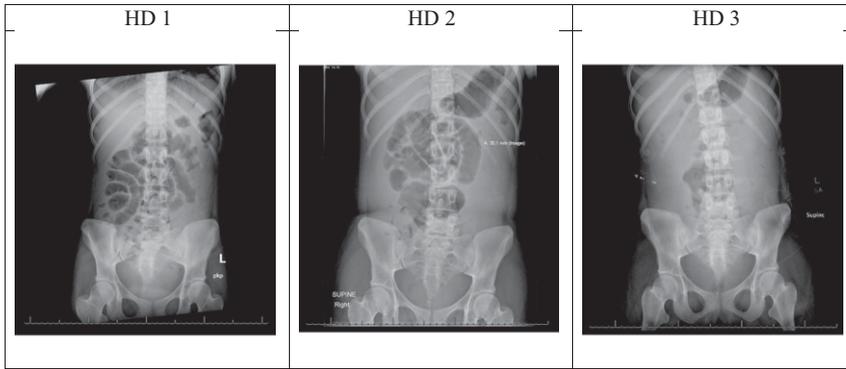


FIGURE 3

Abdominal radiographs from HDs 1 to 3, revealing dilated loops of bowel and increasing ascites.

producing bacillus. Its colonization route is fecal-oral, and infections often present in the context of a disruption of the intestinal microbiome, such as antibiotics. The exotoxins produced by *C difficile* attack the intestinal epithelial cells, causing tissue damage and diarrhea.⁶ The incidence and severity of CDAD has been increasing, and there is more antimicrobial resistance.⁷ Risk factors for CDAD include hospitalization, antibiotic use, gastric acid suppression, and medical comorbidities, such as IBD, cystic fibrosis, and Hirschsprung disease.⁸ There is regional variation in the incidence of IBD in pediatric patients. The incidence is up to 32.6 per 100 000 in some areas.⁹

The current standard for surgical management of severe, complicated

CDAD is subtotal colectomy, which has been traditionally used to remove accumulated toxins in addition to the *C difficile* organisms.⁴ However, CDAD is rarely associated with colonic necrosis; thus, there is no primary reason to remove the colon.^{4,10} Additionally, subtotal colectomy is associated with high morbidity and mortality.⁴ Recently, diverting loop ileostomy with colonic lavage has been suggested as an alternative to colectomy in the adult population.^{5,10}

In their 2011 study on diverting loop ileostomy and colonic lavage as surgical management of severe, complicated CDAD, Neal et al⁵ showed a statistically significant decrease in postoperative death when compared with colectomy in

TABLE 2 Proposed CDAD Severity Scoring System by Neal et al⁵

Criteria	Points
Immunosuppression and/or chronic medical condition ^a	1
Abdominal pain and/or distention ^a	1
Hypoalbuminemia (<3 g/dL) ^a	1
Fever >38.5°C	1
ICU admission ^a	1
CT scan with nonspecific findings of pancolitis, ascites, and/or bowel wall thickening ^a	2
White blood cell count >15 000 or < 1500 and/or band count >10% ^a	2
Creatinine 1.5-fold greater than baseline	2
Abdominal peritoneal signs ^a	3
Vasopressors required	5
Mechanical ventilation required attributed to CDAD	5
Disorientation, confusion, or decreased consciousness	5

Mild to moderate disease: 1–3 points; severe disease: 4–6 points; severe complicated disease: ≥7 points. Patient's score: 11.

^a Criteria met by patient.

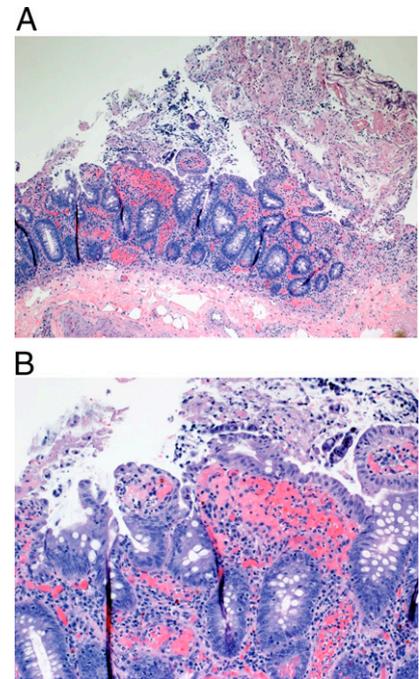


FIGURE 4

Terminal ileum. Endoscopic biopsy reveals active ileitis characterized by attenuation of villi and focal infiltration of crypt and surface epithelium by neutrophils, hematoxylin, and eosin staining. A, Original magnifications of 40× and B, Original magnifications of 100×.

84 adult patients with severe, complicated CDAD who met indications for operative management (Tables 2 and 3). A total of 8 of 42 patients treated with diverting ileostomy and colonic lavage died, whereas 21 of the 42 patients treated with subtotal colectomy died, which was statistically significant. The surviving patients were followed for 6 months, and 79% of the patients receiving diverting ileostomy and colonic lavage had their ileostomy reversed, as opposed to 19% of the patients treated with subtotal colectomy.⁵

Currently, the medical management of pediatric patients is based on the medical management of adult CDAD.⁸ Pediatric patients with mild CDAD are medically managed with oral metronidazole, whereas the

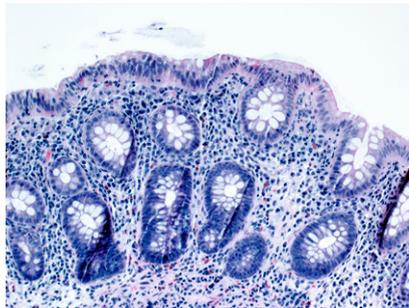


FIGURE 5 Descending colon. Endoscopic biopsy reveals features of focally active chronic colitis characterized by crypt architectural distortion, increased lymphoplasmacytic infiltration of the lamina propria, and occasional neutrophilic infiltration of crypt epithelium (hematoxylin and eosin staining; original magnification 100×).

treatment of more severe infections is varied but generally includes oral vancomycin.^{3,8} Fidaxomicin is a newer antibiotic option that can also be used for CDAD and is gaining traction, particularly in the treatment of recurrent CDAD.⁸ Fecal microbiota transplants have also been shown to be effective.⁸

In 1996, Liacouras and Piccoli successfully used whole-bowel irrigation with PEG in 2 pediatric patients with refractory CDAD.¹¹ Both patients had frequent recurrences of CDAD and failed treatment with vancomycin, metronidazole, bacitracin, rifampin, cholestyramine, and lactobacillus.

Neither patient met criteria for severe, complicated CDAD. After the PEG infusion, the patients were both treated with 3 weeks of vancomycin, and 1 patient was also treated with lactobacillus to assist gut microbiota recolonization. Both patients were asymptomatic within 3 days of treatment and did not experience CDAD recurrence.¹¹

Likewise, our pediatric patient, despite being critically ill and meeting the criteria for severe, complicated CDAD, responded quickly and recovered fully after colon-preserving loop ileostomy and antegrade irrigations. This appears to be the first report using this approach to treat a critically ill pediatric patient with severe, complicated CDAD. This novel approach in a pediatric patient allowed us to minimize the long-term consequences of CDAD by preserving her colon. Colonic preservation should be considered in this population because many patients with Crohn disease or ulcerative colitis do not progress to colectomy.¹² The use of biological agents to medically treat IBD has been found to reduce the number of patients requiring colectomies.¹³

In the future, clinicians may want to consider evaluation of the rectal function and defecation before ileostomy take down, given the risk

for peristalsis after a bacterial infection and operation. Because our patient had a brief course diverted, we did not think it was necessary in her case. Colonic motility and anorectal manometry may be considered in the assessment of proper function before ileostomy take down.

In conclusion, diverting loop ileostomy and antegrade colonic lavage in a pediatric patient was an effective and safe way to manage this patient's severe, complicated CDAD without requiring a colectomy. There are benefits for children to avoid total abdominal colectomy both in the short and long-term. Additionally, loop ileostomy with antegrade lavage is a simpler, less morbid operation on a critically ill patient. To our knowledge, this is the first reported case in the literature of this surgical approach in a critically ill pediatric patient with severe, complicated CDAD. More research should be done on the management of CDAD in pediatric patients, including the surgical management and the long-term outcomes.

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TABLE 3 Indications for Operative Management in Patients with Severe, Complicated CDAD as Identified by Neal et al 2011⁵

A Diagnosis of CDAD as Determined by History of Ongoing or Recent Diarrhea and 1 of the Following	Plus Any 1 of the Following Criteria
1. Positive toxin assay result ^a	1. Peritonitis ^a
2. Endoscopic findings ^a	2. Worsening abdominal distention and/or pain ^a
3. CT scan findings consistent with <i>C difficile</i> colitis (pancolitis +/- ascites) ^a	3. Sepsis ^a
	4. New onset ventilatory failure
	5. New or increasing vasopressor requirement
	6. Mental status changes
	7. Unexplained clinical deterioration
	8. Nonimproving or worsening white blood cell count >20 or <3 despite appropriate antibiotic therapy for 96 h
	9. Nonimproving and worsening bacteremia (>10%) despite appropriate antibiotic therapy for 96 h

^a Criteria met by patient.

ABBREVIATIONS

CDAD: *Clostridium difficile*-associated disease
ED: emergency department
HD: hospital day
IBD: inflammatory bowel disease
PEG: polyethylene glycol
POD: postoperative day
WBC: white blood cell count

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