

Carol Rees Parrish, MS, RDN, Series Editor

Ileostomy and *C. difficile* Infection



Gabriella C. Squeo



Sook C. Hoang

***Clostridioides difficile* is a common cause of infectious colitis, and a less recognized cause of enteritis. There have been several reported cases of *C. difficile* enteritis in patients who have an end ileostomy after a total colectomy. Like colitis caused by *C. difficile*, *C. difficile* enteritis can have a wide range of clinical manifestations, ranging from diarrhea to septic shock, although the most common presenting symptom is increased ileostomy output. Risk factors include recent antibiotic use, proton pump inhibitor use, inflammatory bowel disease, and immunosuppression. Diagnosis and treatment are the same as for *C. difficile* colitis, as diagnosis is confirmed with stool toxin assays and first line treatment is oral vancomycin. *C. difficile* enteritis is a rare disease that can have a fatal outcome, and thus providers must have a high index of suspicion to reduce morbidity and mortality.**

INTRODUCTION

C*lostridioides difficile* (CD) is a Gram-positive, spore-forming, toxin-producing bacillus, that is the most common etiology of nosocomial infectious diarrhea, and antibiotic-associated diarrhea.¹ The incidence of *C. difficile* has been increasing rapidly since the early 2000s, in part due to the highly virulent NAP1/BI/027 strain.² Lower clinical cure rates, increased recurrence rates, more severe disease, and higher 14-day mortality rates have been seen in patients infected with this strain.³

C. difficile infection (CDI) is well known to affect the colon, resulting in a large range of clinical outcomes, ranging from relatively asymptomatic diarrhea, to toxic megacolon and fulminant colitis which can result in hemodynamic instability,

end-organ failure and death. Less appreciated is its role as a cause of small bowel enteritis in patients who have undergone a total colectomy with an end ileostomy or ileal pouch-anal anastomosis. As CDI enteritis is rare, much of our knowledge of the disease comes from case reports, with approximately 60 cases reported in the literature to date.^{2,4-22}

CDI enteritis is associated with increased hospital length of stay (LOS) and health care costs, poor patient quality of life, and high mortality rate approaching 30%.^{2,4} This high mortality rate is likely due to delay in diagnosis given the rarity of the illness. Unfortunately, many patients are diagnosed only at the time of autopsy where pseudomembranes are identified within the small intestine.¹⁰ Luckily, with increased recognition of the disease and early diagnosis, prognosis is improving. Here, we aim to summarize the current evidence regarding CDI enteritis, specifically in the

(continued on page 54)

Gabriella C. Squeo, MD Resident Physician, Department of Surgery Sook C. Hoang, MD Assistant Professor, Department of Surgery Division of Colon and Rectal Surgery, University of Virginia Health System, Charlottesville, VA

(continued from page 52)

subset of patients who have had a total colectomy and an end ileostomy, and increase awareness of this underdiagnosed, yet potentially fatal disease.

Risk Factors and Pathogenesis

Risk factors for CDI enteritis include recent antibiotic and proton pump inhibitor (PPI) use, ICU or prolonged hospital stay, increasing age, immunosuppression, history of gastrointestinal surgery of the colon, and inflammatory bowel disease (IBD).^{4,14} Approximately 70% of patients have been found to have antibiotic usage in the 4 weeks prior to presentation, and approximately 35% have been found to have a medical condition that might lead to an immunocompromised state.^{2,9} Similar to colonic CDI, patients with a history of IBD are also at an increased risk of developing CDI enteritis. Approximately 40-50% of patients with CDI enteritis have a history of IBD.^{2,9} The abnormal gut mucosal immune response in IBD patients may play a role in increasing susceptibility to gastrointestinal infection amongst these patients.¹⁴

The pathogenesis of CDI enteritis in patients with an end ileostomy is unclear; however, several hypotheses have been suggested. There appears to be an increase in susceptibility to disease as a result of the histologic and microbiologic similarity between the small bowel and colon that may develop after a total colectomy. A competent ileocecal valve has been suggested to inhibit small bowel colonization with colonic bacterial flora. With removal of the colon and ileocecal valve, the small bowel flora changes such that the neoterminal ileum is characterized by colonic-type fecal flora, thereby making it more susceptible to overgrowth with CD.^{4,14} Patients with a history of CDI colitis are more susceptible to developing CDI enteritis, especially in the early postoperative phase, as a result of bacterial migration from the colon to the small bowel.¹⁴ Patients also develop colonic-type metaplasia and partial villous atrophy of the terminal end of the ileostomy as a result of alterations in fecal flow, thereby increasing its similarity to the colonic environment.^{2,4,8}

Symptoms and Diagnosis

Patients with CDI enteritis may present with nonspecific symptoms. The most common

presenting symptom amongst case reports is increased ileostomy output, which may lead to dehydration or acute kidney injury.¹⁴ Diagnosis is often missed in those with an ileostomy, as watery diarrhea is expected, especially in the immediate postoperative period. Additionally, increased ileostomy output could have several other causes, including infection and partial obstruction, etc. Other symptoms include ileus, fever, abdominal or pelvic pain, and abdominal cramping. Depending on the severity of disease and degree of dehydration, some patients may present with hemodynamic instability, including tachycardia and hypotension.^{4,6,10} However, many patients are non-toxic with normal vital signs, and may or may not be febrile.^{5,8} Physical exam findings can include diffuse tenderness without signs of peritonitis.^{2,4,6} Laboratory and imaging studies may aid in the diagnosis of CDI enteritis. Patients will often have leukocytosis. In severe cases, patients may have evidence of acute kidney injury and electrolyte derangements as a result of dehydration.^{12,18} A computed tomography (CT) scan can show findings of distended, fluid-filled small bowel in the presence of mesenteric fat stranding and free intraabdominal fluid suggestive of enteritis.¹⁹ Although this is also nonspecific, the combination of laboratory derangements, CT scan findings and patient's symptoms should raise one's clinical index of suspicion and aid in the diagnosis of CDI enteritis.

CDI enteritis should be considered in any patient with an ileostomy presenting with the aforementioned symptoms, especially if they have a history of recent antibiotic use, IBD, or immunosuppression. Diagnosis is confirmed by the presence of CD toxin in a stool sample by polymerase chain reaction (PCR) or enzyme immunoassay.¹

Management

Management of CDI enteritis parallels that of CDI colitis, and is dictated by disease severity. The first line treatment for mild/moderate disease is a 10-day course of oral vancomycin or fidaxomicin. Metronidazole is a second-line agent but should be avoided in patients with associated IBD due to poor absorption. Recurrence may be treated with

(continued on page 56)

(continued from page 54)

a second course of oral vancomycin. For a second recurrence, one should consider fidaxomicin, pulse tapered regimen of vancomycin, or rifaximin regimen following PO vancomycin.⁴ Additional recurrences may necessitate consideration of a fecal microbiota transplant administered via upper endoscopy or ileoscopy through the stoma itself.^{4,24} As with CDI colitis, severe cases should be treated with antibiotics, supportive care and early consideration for surgical intervention.⁴

***C. Difficile* in Patients with Ileal Pouch-Anal Anastomosis**

Total colectomy with ileal pouch-anal anastomosis (IPAA), commonly referred to as a “J-pouch,” is the operation of choice for many patients with treatment-refractory ulcerative colitis, as it may cure the patient’s disease without necessitating a permanent ileostomy. Pouchitis, or inflammation of the ileal pouch, is the most common complication after IPAA, with cumulative incidence approaching 45% at 5 years.²³ It can be caused by infection, recurrence of IBD, and irritation to the pouch mucosa. CDI of the ileal pouch has been recognized as a possible cause of pouchitis. Approximately 10% of symptomatic patients seen at a tertiary referral center for pouch dysfunction are diagnosed with CDI of the pouch.²⁴

Unlike CDI enteritis, postoperative antibiotic exposure and use of immunosuppressive agents or PPIs do not appear to be associated with CDI pouchitis.²⁴ Rather, risk factors include male gender, recent hospitalization, and pre-surgery antibiotic usage.²⁴⁻²⁶ Patients with an ileal pouch are susceptible to CDI due to similarities of the pouch with the colon at both physiological and structural levels.²⁴ Fecal stasis within the pouch promotes gut microbial dysbiosis and colonic metaplasia of the ileal mucosa, which may predispose to CDI infection and colonization.²³

Patients commonly present with abdominal or pelvic pain and increased stool frequency.^{23,27,28} Diagnosis is confirmed with stool toxin assays, and endoscopic visualization by pouchoscopy may be of value.²⁴ CDI should be considered in ileal pouch patients particularly if there is a change to their usual symptomology and if the episode of pouchitis appears to be refractory to antibiotic management.²⁴

Table 1. Summary of *Clostridioides difficile* Enteritis Identification and Management

Risk Factors
<ul style="list-style-type: none"> • Recent antibiotic use • Proton pump inhibitor use • ICU or prolonged hospital stay • Increased age • History of colon surgery • Inflammatory bowel disease
Symptoms
<ul style="list-style-type: none"> • Increased ileostomy output/diarrhea • Ileus • Fever • Abdominal/pelvic pain/cramping
Diagnosis
<ul style="list-style-type: none"> • + stool toxin assay • CT scan findings (nonspecific findings) <ul style="list-style-type: none"> ○ Ascites/free fluid ○ Distended, fluid-filled small bowel ○ Mesenteric fat stranding
Treatment
<ul style="list-style-type: none"> • First line –PO vancomycin x 10 days • Severe cases may require operative intervention
Key Points and Provider Recommendations
<ul style="list-style-type: none"> • <i>Clostridioides difficile</i> infection is not a disease that is isolated to the colon, and frequency of small bowel enteritis is increasing. • <i>Clostridioides difficile</i> enteritis can be fatal, and providers must have a high index of suspicion as to not delay diagnosis and treatment. • Consider testing for <i>Clostridioides difficile</i> in any patient presenting with increased ileostomy output, especially if patient has other associated symptoms, CT findings, or risk factors. • First line of treatment is a 10-day course of vancomycin. • Consider testing for <i>Clostridioides difficile</i> in ileal pouch patients with change in normal symptom pattern or chronic antibiotic-refractory pouchitis.

Testing for CDI should be considered in pouch patients presenting with fever, urgency, increased stool frequency, hematochezia, incontinence, and abdominal or pelvic pain.²³

Treatment for CDI pouchitis is the same as treatment for CDI colitis and enteritis, with oral vancomycin being the first line agent. Although exploratory, fecal microbiota transplantation may be useful in severe or antibiotic-refractory cases.²⁴ Overall, the prognosis is relatively good, and most patients are successfully treated with antibiotics; however more severe cases of CDI pouchitis have also been reported. There is one case reported in the literature that required pouch excision with conversion to ileostomy,²⁹ and one case of fulminant CDI resulting pseudomonas aeruginosa septicemia, intravascular coagulopathy, acute renal failure, hemorrhagic ascites, respiratory failure, and eventual death.³⁰

SUMMARY AND RECOMMENDATIONS

Although better known for causing colitis, *Clostridioides difficile* is a rare cause of enteritis, particularly in patients who have undergone a total colectomy. Physicians treating patients with end ileostomies and ileal pouch-anal anastomoses should have a high index of suspicion for *C. difficile* infection in any patient presenting with increased stool output, abdominal cramping, and/or fever, especially if they have a history of recent antibiotic use, PPI use, inflammatory bowel disease, or an immunosuppressed state. CDI enteritis can be a highly morbid and even fatal disease, and thus prompt recognition and initiation of treatment is imperative to improve outcomes. See Table 1 for a summary of identification and management of CDI enteritis. ■

References

- Dupont HL. Diagnosis and management of *Clostridium difficile* infection. *Clin Gastroenterol Hepatol*. 2013;11(10):1216-23.
- Dineen SP, Bailey SH, Pham TH, et al. *Clostridium difficile* enteritis: A report of two cases and systematic literature review. *World J Gastrointest Surg*. 2013;5(3):37-42.
- Marsh JW, Arora R, Schlackman JL, et al. Association of relapse of *Clostridium difficile* disease with BI/NAP1/027. *J Clin Microbiol*. 2012;50(12):4078-82.
- Aujla AK, Averbukh LD, Potashinsky A, et al. A Rare Case of *Clostridium difficile* Enteritis: A Common Bug in an Uncommon Place. *Cureus*. 2019;11(4):e4519.
- Casey MW, Spencer MP, Steele SR. *Clostridium difficile* enteritis after colectomy. *Am Surg*. 2009;75(12):1203-6.
- Freiler, JF, Durning SJ, Ender PT. *Clostridium difficile* small bowel enteritis occurring after total colectomy. *Clin Infect Dis*. 2001;33(8):1429-32.
- Gagandeep D, Ira S. *Clostridium difficile* enteritis 9 years after total proctocolectomy: a rare case report. *Am J Gastroenterol*. 2010;105(4):962-3.
- Khan MS, Levy D, Mann S. *Clostridium difficile* infection in the absence of a colon. *BMJ Case Rep*. 2010 Oct 21;2010:bcr0220102728.
- Kim JH, Muder RR. *Clostridium difficile* enteritis: a review and pooled analysis of the cases. *Anaerobe*. 2011;17(2):52-5.
- Kim KA, Wry P, Hughes E, et al. *Clostridium difficile* small-bowel enteritis after total proctocolectomy: a rare but fatal, easily missed diagnosis. Report of a case. *Dis Colon Rectum*. 2007;50(6):920-3.
- Kurtz LE, Yang SS, Bank S. *Clostridium difficile*-associated small bowel enteritis after total proctocolectomy in a Crohn's disease patient. *J Clin Gastroenterol*. 2010;44(1):76-7.
- Lundeen SJ, Otterson MF, Binion DG, et al. *Clostridium difficile* enteritis: an early postoperative complication in inflammatory bowel disease patients after colectomy. *J Gastrointest Surg*. 2007;11(2):138-42.
- Nasser H, Munie S, Shakaroun D, et al. *Clostridium difficile* Enteritis after Total Abdominal Colectomy for Ulcerative Colitis. *Case Rep Crit Care*. 2019;2987682.
- Navaneethan U, Giannella RA. Thinking beyond the colon-small bowel involvement in *clostridium difficile* infection. *Gut Pathog*. 2009;1(1):7.
- Peacock O, Speake W, Shaw A, et al. *Clostridium difficile* enteritis in a patient after total proctocolectomy. *BMJ Case Rep*. 2009;2009:bcr10.2008.1165.
- Seril DN, Shen B. *Clostridium difficile* infection in the postcolectomy patient. *Inflamm Bowel Dis*. 2014;20(12):2450-69.
- Tarasiuk-Rusek A, Shah KJ. *Clostridium difficile* ileitis in a patient, after total colectomy. *BMJ Case Rep*. 2016 Feb 22;2016:bcr2015214319.
- Vesoulis Z, Williams G, Matthews B. Pseudomembranous enteritis after proctocolectomy: report of a case. *Dis Colon Rectum*. 2000;43(4):551-4.
- Wee B, Poels JA, McCafferty IJ, et al. A description of CT features of *Clostridium difficile* infection of the small bowel in four patients and a review of literature. *Br J Radiol*. 2009;82(983):890-5.
- Williams RN, Hemingway D, Miller AS. Enteral *Clostridium difficile*, an emerging cause for high-output ileostomy. *J Clin Pathol*. 2009;62(10):951-3.
- Yafi FA, Selvasekar CR, Cima RR. *Clostridium difficile* enteritis following total colectomy. *Tech Coloproctol*. 2008;12(1):73-4.
- El Muhtaseb MS, Apollos JK, Dreyer JS. *Clostridium difficile* enteritis: a cause for high ileostomy output. *ANZ J Surg*. 2008 May;78(5):416.
- Kayal M, Tixier E, Plietz M, et al. *Clostridioides Difficile* Infection Is a Rare Cause of Infectious Pouchitis. *Inflamm Intest Dis*. 2020;5(2):59-64.
- Seril DN, Shen B. *Clostridium difficile* infection in patients with ileal pouches. *Am J Gastroenterol*. 2014;109(7):941-7.
- Li Y, Qian J, Queener E, et al. Risk factors and outcome of PCR-detected *Clostridium difficile* infection in ileal pouch patients. *Inflamm Bowel Dis*. 2013;19(2):397-403.
- Shen BO, Jiang ZD, Fazio VW, et al. *Clostridium difficile* infection in patients with ileal pouch-anal anastomosis. *Clin Gastroenterol Hepatol*. 2008;6(7):782-8.
- Shen B, Goldblum JR, Hull TL, et al. *Clostridium difficile*-associated pouchitis. *Dig Dis Sci*. 2006;51(12):2361-4.
- Mann SD, Pitt J, Springall RG, et al. *Clostridium difficile* infection--an unusual cause of refractory pouchitis: report of a case. *Dis Colon Rectum*. 2003;46(2):267-70.
- Martinez Ugarte ML, Lightner AL, Colibaseanu D, et al. *Clostridium difficile* infection after restorative proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis. *Colorectal Dis*. 2016;18(5):O154-7.
- Shen B, Remzi FH, Fazio VW. Fulminant *Clostridium difficile*-associated pouchitis with a fatal outcome. *Nat Rev Gastroenterol Hepatol*. 2009;6(8):492-5.