Ulcerative Proctitis in a Patient With a History of Fecal Microbiota Transplant for *Clostridioides difficile* Infection

Michael Massaro, MD\(^1\), Jhanvi Vansia, BS\(^2\), and Sarah McGill, MD, MS\(^2\)

\(^1\)Division of Gastroenterology and Hepatology, University of Alabama at Birmingham, Birmingham, AL
\(^2\)Division of Gastroenterology and Hepatology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC

**ABSTRACT**

Fecal microbiota transplantation (FMT) effectively treats *Clostridioides difficile* infection and alters the gut microbiota in the long term, but potential adverse effects are poorly understood. We report a man with a family history of ulcerative colitis who developed ulcerative proctitis within a year of FMT.

**INTRODUCTION**

*Clostridium difficile* is a toxin-forming and spore-forming bacillus that was once believed to be commensal but has become an important pathogen causing major morbidity and mortality\(^1\). Recurrence of *C. difficile* after specific therapy for the organism is common, and over 20% of patients recur shortly after the initial infection\(^2\). Fecal microbiota transplantation (FMT) has been successful in the treatment of recurrent *C. difficile* in 85%–95% of cases and is now strongly recommended for patients with multiple recurrences who have failed antibiotic therapy\(^3\). After FMT, the microbiota of the colon increase in diversity, and donor microbiota persist in recipients up to 2 years after FMT\(^4\). The effects of these changes related to long-term health are poorly understood.

**CASE REPORT**

A 63-year-old man with a medical history of recurrent pituitary adenoma who underwent transphenoidal resection presented after 2 months of new-onset abdominal pain and diarrhea. He tested positive for *C. difficile* polymerase chain reaction (PCR) toxin and was treated with 2 weeks of metronidazole. He had received perioperative antibiotics 2 months previously at the time of his surgery. His diarrhea resolved, but at 3 months from surgery, his diarrhea resumed and was *C. difficile* PCR-toxin-positive. He was treated with 2 weeks of vancomycin with the resolution of symptoms. Four months after surgery, diarrhea returned and treated empirically with vancomycin, this time with a long pulse and then taper. The patient had resolution of symptoms, but after the taper, diarrhea returned after previous resolution and was *C. difficile* PCR-toxin-positive as well as glutamate dehydrogenase enzyme-linked immunosorbent assay positive, and the decision was made to perform FMT. FMT was performed via colonoscopy with stool from a commercially available stool bank from healthy donors without relevant medical history. During the colonoscopy, there was no evidence of ulcerative colitis (UC), though random biopsies of the normal-appearing mucosa were not performed. FMT was considered successful because he remained symptom-free without antibiotics 2 months after the treatment.

Ten months after FMT, the patient developed persistent abdominal pain and diarrhea. Infectious stool studies, including *C. difficile* were negative. Repeat colonoscopy showed findings consistent with ulcerative proctitis, with moderately erythematous, eroded, friable, and ulcerated mucosa from the anal verge to the proximal rectum (Figure 1). Pathology from rectal biopsies was read as severe chronic active proctitis without evidence of *C. difficile*. He was started on hydrocortisone enemas and balsalazide for ulcerative proctitis and had a quick resolution of abdominal pain, cramps, and diarrhea. Of particular interest, the patient’s sister had...
undergone total colectomy for UC refractory to medical management in her 20s, decades ago. Otherwise, there was no family or personal history of inflammatory bowel disease (IBD).

DISCUSSION
We describe a patient with a family history of UC who developed ulcerative proctitis 10 months after FMT. FMT has emerged as a standard treatment for patients with recurrent C. difficile, with reported cure rates greater than 90% in many studies.5–7 C. difficile frequently presents after disruption of the native gut flora by antibiotics. One study found that a single dose of clindamycin was enough to cause the loss of up to 90% of the taxa of gut microbiota.8 Gut microbiota can take up to 2 weeks or longer to return to preantibiotic diversity after an antibiotic course. Although the key to FMT’s efficacy in recurrent C. difficile is still unknown, FMT does restore the diversity of the gut microbiota, and in many patients, engraftment of donor flora persists long term.9 Reported adverse effects of FMT have included mild diarrhea, abdominal cramps, and low-grade fever in 5%–10% of patients.10

The development of IBD is believed to be multifactorial, and both improvements in and flares of disease after FMT have been reported. A systematic review and first meta-analysis of FMT in patients with IBD revealed that 45% showed clinical remission, although the results were significantly heterogeneous because of the low numbers.11 Genetic susceptibility and dysregulation of the immune system that leads it to respond inappropriately to intestinal microbiota are believed to play important roles in the pathogenesis of IBD.12 In experiments, mouse models that lack parts of adaptive and innate immunity predisposing them to colitis appear to require interaction with gut microbiota, as evidenced by mice kept in germ-free environments not developing colitis.13 Among 4 published randomized, controlled clinical trials that used FMT to treat UC, patients had higher rates of clinical remission compared with the control arm in the studies.14–17

In this patient, the onset of ulcerative proctitis appears to be a new development because there was no endoscopic evidence of UC during the colonoscopy for FMT, although no biopsies were taken at that time. Although there is no direct causal link between the development of UC and the patient’s previous FMT, FMT may have played a role in altering his gut microbiota and immune response. Although the development could be coincidental in a patient who might have developed UC, regardless in light of his family history, this case raises questions and suggests that more research is needed to predict the response to FMT among patients with IBD and those at risk for developing IBD.

DISCLOSURES
Author contributions: M. Massaro wrote the manuscript. J. Vansia edited the manuscript. S. McGill edited and revised the manuscript for intellectual content and is the article guarantor.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received October 21, 2019; Accepted February 11, 2020

REFERENCES
1. Lessa FC, Mu Y, Bamberg WM, et al. Burden of Clostridium difficile infection in the United States. N Engl J Med. 2015;372(9):825–34.
2. Eyre DW, Walker AS, Wyllie D, et al. Predictors of first recurrence of Clostridium difficile infection: Implications for initial management. Clin Infect Dis. 2012;55(Suppl 2):S77–87.
3. Norris AH, Shrestha NK, Allison GM, et al. Infectious Diseases Society of America Clinical Practice Guideline for the management of outpatient parenteral antimicrobial therapy. Clin Infect Dis. 2019;68(1):1–4.
4. Kumar R, Yi N, Zhi D, et al. Identification of donor microbe species that colonize and persist long term in the recipient after fecal transplant for recurrent Clostridium difficile. NPJ Biofilms Microbiomes. 2017;3:12.
5. Kao D, Roach B, Silva M, et al. Effect of oral capsule- vs colonoscopy-delivered fecal microbiota transplantation on recurrent Clostridium difficile infection: A randomized clinical trial. JAMA. 2017;318(20):1985–93.
6. Kelly CR, Khoruts A, Staley C, et al. Effect of fecal microbiota transplantation on recurrence in multiply recurrent Clostridium difficile infection: A randomized trial. Ann Intern Med. 2016;165(9):609–16.
7. van Noord E, Vrieze A, Nieuwdorp M, et al. Duodenal infusion of donor feces for recurrent Clostridium difficile. N Engl J Med. 2013;368(5):407–15.
8. Bufﬁe CC, Jarchum I, Equinda M, et al. Profound alterations of intestinal microbiota following a single dose of clindamycin results in sustained susceptibility to Clostridium difficile-induced colitis. Infect Immun. 2012;80(1):62–73.
9. Staley C, Kaiser T, Vaughn BP, et al. Durable long-term bacterial engrafment following encapsulated fecal microbiota transplantation to treat Clostridium difficile infection. mBio. 2019;10(4).
10. Brandt LJ, Aroniadis OC, Mellow M, et al. Long-term follow-up of colonoscopic fecal microbiota transplant for recurrent Clostridium difficile infection. Am J Gastroenterol. 2012;107(7):1079–87.
11. Anderson JL, Edney RJ, Whelan K. Systematic review: Fecal microbiota transplantation in the management of inflammatory bowel disease. Aliment Pharmacol Ther. 2012;36(8):503–16.
12. Sartor RB, Wu GD. Roles for intestinal bacteria, viruses, and fungi in pathogenesis of inflammatory bowel diseases and therapeutic approaches. Gastroenterology. 2017;152(2):327–39.e4.
13. Ni J, Wu GD, Albenberg L, Tomov VT. Gut microbiota and IBD: Causation or correlation? Nat Rev Gastroenterol Hepatol. 2017;14(10):573–84.
14. Rossen NG, Fuentes S, van der Spek MJ, et al. Findings from a randomized controlled trial of fecal transplantation for patients with ulcerative colitis. Gastroenterology. 2015;149(1):110–8.e4.
15. Moayyedi P, Surette MG, Kim PT, et al. Fecal microbiota transplantation induces remission in patients with active ulcerative colitis in a randomized controlled trial. Gastroenterology. 2015;149(1):102–9.e6.
16. Paramsothy S, Kamm MA, Kaakoush NO, et al. Multidonor intensive faecal microbiota transplantation for active ulcerative colitis: A randomised placebo-controlled trial. Lancet. 2017;389(10075):1218–28.
17. Costello SP, Hughes PA, Waters O, et al. Effect of fecal microbiota transplantation on 8-week remission in patients with ulcerative colitis: A randomized clinical trial. JAMA. 2019;321(2):156–64.