ACG CASE REPORTS JOURNAL

CASE REPORT | COLON

# Avoiding Premature Antibiotic Use in Recurrent *Clostridioides difficile* Infection After Fecal Microbiota Transplant

Rahim A. Burdette, BS[1], Caroline C. Whitt, MD[2], Brian W. Behm, MD[3], and Cirle A. Warren, MD[4]

[1]*School of Medicine, University of Virginia, Charlottesville, VA*
[2]*Department of Physical Medicine and Rehabilitation, University of Virginia, Charlottesville, VA*
[3]*Division of Gastroenterology, University of Virginia, Charlottesville, VA*
[4]*Division of Infectious Diseases and International Health, University of Virginia, Charlottesville, VA*

## ABSTRACT

Recurrent *Clostridioides difficile* infection (rCDI) remains a major clinical challenge, often requiring fecal microbiota transplantation (FMT) after conventional treatment fails. An 86-year-old woman with rCDI underwent FMT after failing multiple antibiotic therapies. Shortly after FMT, she experienced diarrhea and abdominal pain, alongside positive *C. difficile* stool tests. Antibiotics were withheld because of clinical improvement, and she achieved complete resolution of symptoms without further treatment. This case demonstrates the potential benefit of withholding antibiotics in rCDI patients soon after FMT to allow sufficient time for donor microbiota engraftment and underscores the need for further research to optimize post-FMT management.

**KEYWORDS:** *Clostridioides difficile*; fecal microbiota transplant; recurrent *C. difficile* infection; antibiotics; case report

## INTRODUCTION

*Clostridioides difficile* infection (CDI) is a significant public health concern, causing approximately 223,900 hospitalizations in the United States annually and more than 12,800 deaths.[1] Recurrent *C. difficile* infections (rCDI) occur in up to 35% of patients after initial treatment and 60% of those with previous recurrence.[2] Fidaxomicin or vancomycin is recommended for initial or recurrent CDI treatment. Fecal microbiota transplant (FMT) is reserved for patients with multiple recurrences.[3] For FMT to be successful, donor bacteria must be engrafted and incorporated into the recipient's microbiome.[4] Variables that lead to improved engraftment and treatment efficacy are not fully understood but include FMT delivery through lower gastrointestinal endoscopy, whereas significant predictors of failure include advanced age, severe CDI, inflammatory bowel disease, peri-FMT use of non-CDI antibiotics, previous CDI-related hospitalizations, inpatient status, and poor quality of bowel preparation.[5–9] We present this case to highlight the need for further research to understand microbiota engraftment and its implications for FMT efficacy.

## CASE REPORT

**Patient demographics and comorbidities:** An 86-year-old woman with a history of congestive heart failure, atrial fibrillation, chronic obstructive pulmonary disease, hyperlipidemia, and hypertension was referred to the complicated *C. difficile* clinic (CCDC) for management of rCDI.

**CDI history:** The patient had 4 distinct episodes of CDI (Figure 1) where for each episode she presented with diarrhea and abdominal pain with either nausea, vomiting, or weakness. For each of the first 3 episodes, 2-step testing for *C. difficile* was positive, and computed tomography imaging of the abdomen revealed colitis. She received anti-CDI antibiotics, which were typically followed by improvement in symptoms. The fourth episode of diarrhea was treated empirically as rCDI, and her symptoms resolved.

*ACG Case Rep J* 2025;12:e01660. doi:10.14309/crj.0000000000001660. Published online: April 3, 2025

**Correspondence:** Rahim A. Burdette, BS (aax6rw@uvahealth.org).

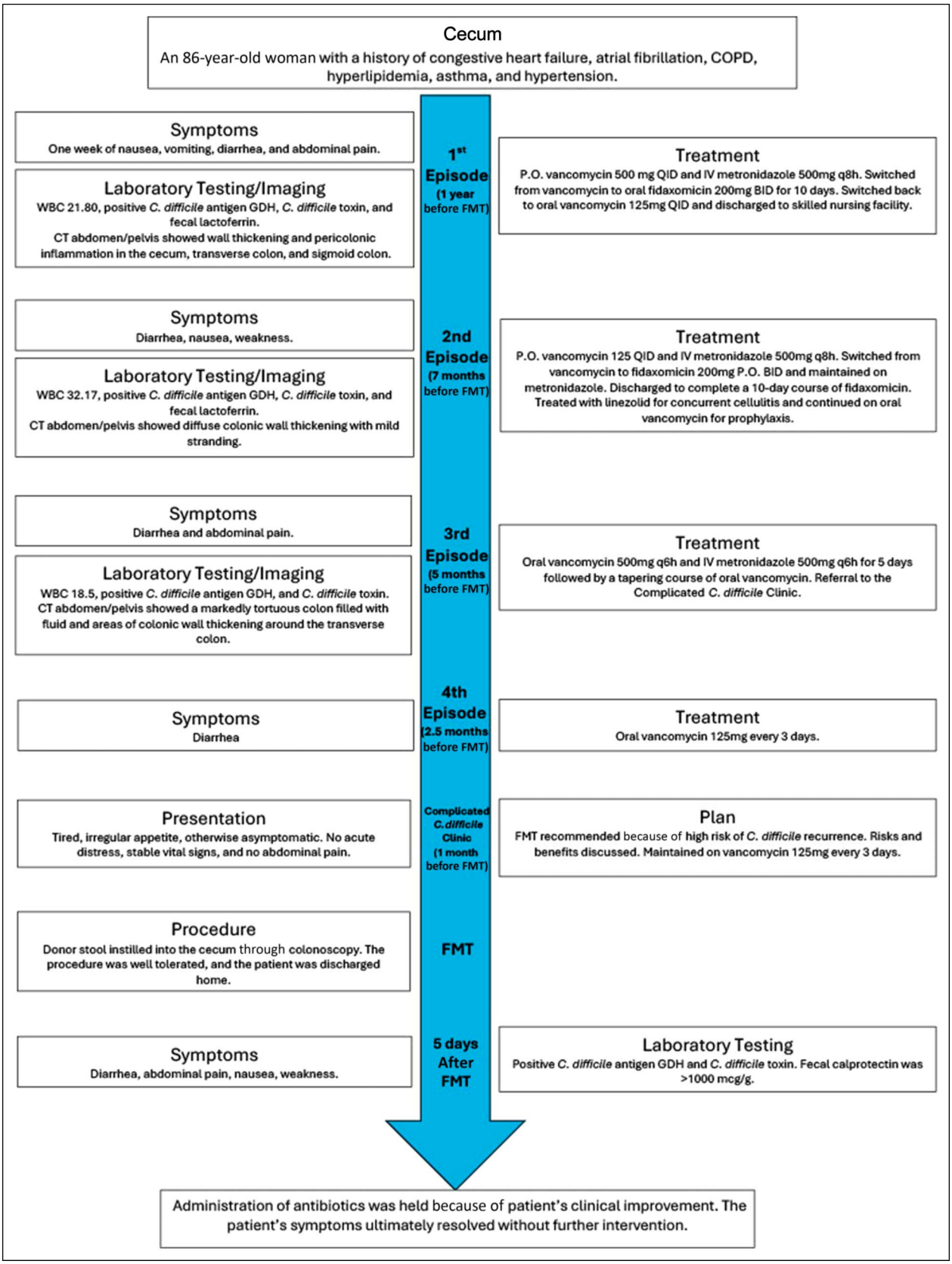


**Figure 1.** Chronological timeline of care that the patient received from the first episode of CDI until the eventual FMT and resolution of symptoms/recurrences. CDI, *Clostridioides difficile* infection; COPD, chronic obstructive pulmonary disease; CT, computed tomography; FMT, fecal microbiota transplantation; GDH, glutamate dehydrogenase; WBC, white blood cell.

**CCDC evaluation:** The patient presented to the CCDC 6 weeks after her last episode of CDI. She was taking vancomycin 125 mg every 3 days on presentation. She reported fatigue and poor appetite, but otherwise felt normal, with 1 bowel movement daily and no abdominal pain. Physical examination findings were unremarkable. FMT was recommended because of her high risk of recurrence. FMT was discussed, including its investigational nature, modes of administration, success rates, adverse events, and unknown long-term sequelae. She was maintained on vancomycin 125 mg once every 3 days until 3 days before FMT, which was scheduled 3 weeks later.

**Fecal microbiota transplant:** After routine bowel preparation, FMT was performed through colonoscopy. During the procedure, moderate hemorrhoids were found on the perianal examination with few diverticula in the sigmoid and ascending colon. No intestinal pseudomembrane was observed. The frozen donor stool was supplied by OpenBiome, thawed per protocol, and instilled (approximately 250 mL) into the cecum. The colonoscopy images are shown in Figure 2. Colon biopsy taken during colonoscopy showed no pathological abnormality. The procedure was tolerated well, and the patient was discharged home, discontinuing vancomycin completely.

**Post-FMT event:** Five days after the procedure, the patient's daughter called for concerns of fatigue and loose stools. Notably, the patient was eating only fruits, vegetables, and plain yogurt after FMT. The next day, the patient reported having multiple episodes of diarrhea, abdominal pain, nausea, and weakness. She was recommended to proceed to the emergency department, but the daughter requested CDI testing instead. The daughter was instructed to ensure adequate hydration and nutrition, and that if the patient's symptoms worsened, she go to the emergency department. Her fecal specimen returned positive for *C. difficile* glutamate dehydrogenase and toxin. Fecal calprotectin was >1,000 mcg/g. The next day, the patient reported improved symptoms. Fidaxomicin was prescribed after positive CDI testing, but administration was held because of the patient's continued clinical improvement to allow time for engraftment. The patient was monitored closely by her caregiver, who updated the provider of the patient's condition. She ultimately experienced symptom resolution without

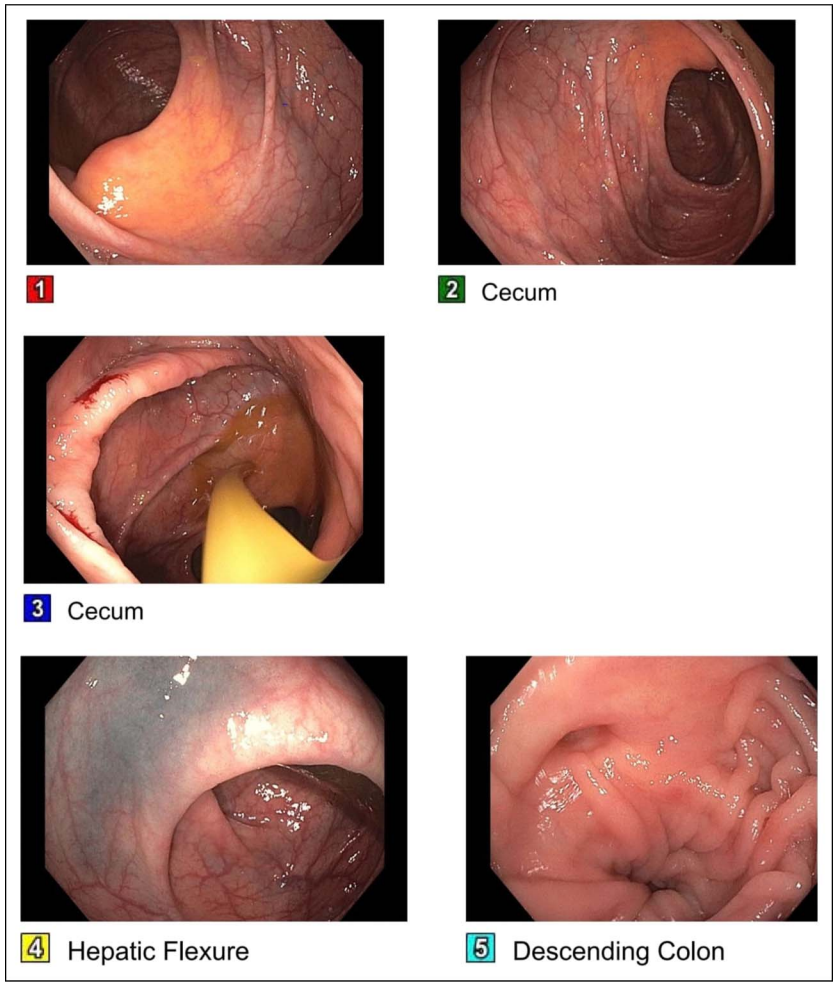


**Figure 2.** Images taken during colonoscopy at the cecum, hepatic flexure, and descending colon.

further intervention and with no CDI recurrences for at least 3 years since the FMT.

## DISCUSSION

FMT is considered a standard, and often superior, alternative to antibiotic treatment when managing rCDI.[3,10,11] Several strategies exist to manage recurrent infection after FMT, including reinstatement of anti-CDI antibiotics followed by a repeat FMT (preferred) or indefinite antibiotic treatment with vancomycin (alternative).[9] Our case demonstrates the potential importance of delaying treatment of rCDI immediately after an FMT to allow adequate time for the donor microbiome to engraft and provide resolution of the condition. This patient ultimately did not require further antibiotic treatment for CDI. Premature administration of antibiotics when her symptoms initially recurred may have prevented engraftment of the freshly administered microbiota and the long-term resolution of rCDI.

After FMT, the recipient's microbiome undergoes significant changes, typically shifting toward a composition more similar to that of the donor microbiome. This includes an increase in microbial diversity and the restoration of beneficial bacterial populations that were depleted because of antibiotics and CDI.[12–14] Donor and recipient strains can coexist for extended periods, with donor strains often achieving successful colonization and contributing to the restoration of a healthy microbiome.[15] This engraftment of donor strains is crucial for the long-term success of FMT. Engraftment of donor microbiota after an FMT for CDI has been shown to occur within as little as 3 days and can be stable for at least 4 months after FMT.[16] Most patients exhibited high levels of donor microbiota engraftment within the first week, which were sustained over the long term.[17] Engraftment timeline is likely not uniform in all patients though because studies have indicated a more gradual engraftment process with some bacteria increasing in abundance rapidly, whereas others do so at a slower pace.[18] In addition, the method of transplant may affect the time required for engraftment to take place.[19]

This case underscores the potential benefit of delaying antibiotic treatment in patients with recurrent CDI shortly after FMT. The patient's spontaneous symptom resolution without further intervention suggests that engraftment of the donor microbiome is sufficient to control rCDI. Further research is needed on how to ensure effective microbiota engraftment to maximize long-term success of FMT.

## DISCLOSURES

Author contributions: AR Burdette: substantial contributions to data curation, visualization, and critical revision of the manuscript for intellectual content. CC Whitt: substantial contributions to data curation, drafting the initial manuscript, and final approval of the version to be published. BW Behm: substantial contributions to investigation, supervision of the work, and critical revision of the manuscript for intellectual content. CA Warren: substantial contributions to conceptualization, supervision, critical revision of the manuscript for intellectual content, and final approval of the version to be published. CA Warren is the guarantor of this manuscript and accepts full responsibility for the integrity of the work and the conduct of the study.

Funding: CA Warren is partially funded by NIH AI145322.

Financial disclosure: CA Warren and BW Behm are UVA site investigators for Rebyota Observational Study Registry (ROAR, Ferring Pharmaceuticals). The rest of the authors have nothing to disclose.

Informed consent was obtained for this case report.

Received January 17, 2025; Accepted March 3, 2025

## REFERENCES

1. Centers for Disease Control and Prevention. *Antibiotic Resistance Threats in the United States, 2019*. Atlanta, GA: Centers for Disease Control and Prevention; https://www.cdc.gov/antimicrobial-resistance/media/pdfs/2019-ar-threats-report-508.pdf (2019).
2. Feuerstadt P, Theriault N, Tillotson G. The burden of CDI in the United States: A multifactorial challenge. *BMC Infect Dis.* 2023;23(1):132.
3. Johnson S, Lavergne V, Skinner AM, et al. *C. difficile* 2021 focused update (https://www.idsociety.org/practice-guideline/clostridioides-difficile-2021-focused-update/). Accessed September 8, 2024.
4. Ianiro G, Punčochář M, Karcher N, et al. Variability of strain engraftment and predictability of microbiome composition after fecal microbiota transplantation across different diseases. *Nat Med.* 2022;28(9):1913–23.
5. Baunwall SMD, Lee MM, Eriksen MK, et al. Faecal microbiota transplantation for recurrent *Clostridioides difficile* infection: An updated systematic review and meta-analysis. *eClinicalMedicine.* 2020;29-30:100642.
6. Staley C, Halaweish H, Graiziger C, et al. Lower endoscopic delivery of freeze-dried intestinal microbiota results in more rapid and efficient engraftment than oral administration. *Sci Rep.* 2021;11(1):4519.
7. Beran A, Sharma S, Ghazaleh S, et al. Predictors of fecal microbiota transplant failure in *Clostridioides difficile* infection: An updated meta-analysis. *J Clin Gastroenterol.* 2023;57(4):389–99.
8. Tariq R, Hayat M, Pardi D, Khanna S. Predictors of failure after fecal microbiota transplantation for recurrent *Clostridioides difficile* infection: A systematic review and meta-analysis. *Eur J Clin Microbiol Infect Dis.* 2021;40(7):1383–92.
9. Kelly CR, Fischer M, Allegretti JR, et al. ACG clinical guidelines: Prevention, diagnosis, and treatment of *Clostridioides difficile* infections. *Am J Gastroenterol.* 2021;116(6):1124–47.
10. Poylin V, Hawkins AT, Bhama AR, et al. The American Society of colon and rectal surgeons clinical practice guidelines for the management of *Clostridioides difficile* infection. *Dis Colon Rectum.* 2021;64(6):650–68.
11. Hvas CL, Dahl Jørgensen SM, Jørgensen SP, et al. Fecal microbiota transplantation is superior to fidaxomicin for treatment of recurrent *Clostridium difficile* infection. *Gastroenterology.* 2019;156(5):1324–32.e3.
12. Hourigan SK, Chen LA, Grigoryan Z, et al. Microbiome changes associated with sustained eradication of *Clostridium difficile* after single faecal microbiota transplantation in children with and without inflammatory bowel disease. *Aliment Pharmacol Ther.* 2015;42(6):741–52.
13. Weingarden A, González A, Vázquez-Baeza Y, et al. Dynamic changes in short- and long-term bacterial composition following fecal microbiota transplantation for recurrent *Clostridium difficile* infection. *Microbiome.* 2015;3(1):10.
14. Björkqvist O, Rangel I, Serrander L, et al. *Faecalibacterium prausnitzii* increases following fecal microbiota transplantation in recurrent *Clostridioides difficile* infection. *PLoS One.* 2021;16(4):e0249861.
15. Li SS, Zhu A, Benes V, et al. Durable coexistence of donor and recipient strains after fecal microbiota transplantation. *Science.* 2016;352(6285):586–9.

16. Shankar V, Hamilton MJ, Khoruts A, et al. Species and genus level resolution analysis of gut microbiota in *Clostridium difficile* patients following fecal microbiota transplantation. *Microbiome.* 2014;2:13.
17. Staley C, Kaiser T, Vaughn BP, et al. Durable long-term bacterial engraftment following encapsulated fecal microbiota transplantation to treat *Clostridium difficile* infection. *mBio.* 2019;10(4):e01586-19.
18. Staley C, Vaughn BP, Graiziger CT, et al. Community dynamics drive punctuated engraftment of the fecal microbiome following transplantation using freeze-dried, encapsulated fecal microbiota. *Gut Microbes.* 2017;8(3):276–88.
19. Jiang ZD, Ajami NJ, Petrosino JF, et al. Randomised clinical trial: Faecal microbiota transplantation for recurrent *Clostridum difficile* infection - fresh, or frozen, or lyophilised microbiota from a small pool of healthy donors delivered by colonoscopy. *Aliment Pharmacol Ther.* 2017;45(7):899–908.