

Utilization of Upper Gastrointestinal Fecal Microbiota Transplant in Fulminant *Clostridioides difficile* Colitis

Techniques to Maximize Success

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Introduction

- Clostridioides difficile (C. diff) colitis is an antibiotic-related infection of the gut that is estimated to cause approximately half a million infections in the United States annually.[1]
- The role of fecal microbiota transplant (FMT) in the treatment of C. diff is unclear.
- However, FMT is currently recommended for patients with severe and fulminant C. diff infections that are unresponsive to antibiotic therapy in patients who are non-surgical candidates.[2]
- FMT is preferably administered rectally as this is associated with higher cure rates than delivery via the upper gastrointestinal tract.[2,3]

Case Description

A 93-year-old female, independent with her activities of daily living at baseline, with a past medical history of stage III chronic kidney disease, hyperlipidemia, and gastroesophageal reflux disease (on chronic proton pump inhibitor (PPI) therapy), who presented to the emergency department for eight-day history of intermittent fevers, 1-2 weeks of loose stools with generalized abdominal pain, nausea and vomiting associated with poor oral intake for 2-3 days prior to presentation. She had no history of recent antibiotic use, although did take omeprazole for reflux. She was vaccinated with the BNT162b2 (Pfizer-BioNTech) Covid vaccine with two doses and a booster prior to presentation.

References

[1] Centers for Disease Control and Prevention. (2021, July 20). What is C. diff? Centers for Disease Control and Prevention. Retrieved April 27, 2022, from https://www.cdc.gov/cdiff/what-is.html

[2] Kelly, Colleen R.; Fischer, Monika; Allegretti, Jessica R.; LaPlante, Kerry; Stewart, David B.; Limketkai, Berkeley N.; Stollman, Neil H. ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of Clostridioides difficile Infections, The American Journal of Gastroenterology: June 2021 - Volume 116 - Issue 6 - p 1124-1147. doi: 10.14309/ajg.00000000001278

[3] Cohen NA, Livovsky DM, Yaakobovitch S, Ben Yehoyada M, Ben Ami R, Adler A, Guzner-Gur H, Goldin E, Santo ME, Halpern Z, Paz K, Maharshak N. A Retrospective Comparison of Fecal Microbial Transplantation Methods for Recurrent Clostridium Difficile Infection. Isr Med Assoc J. 2016 Oct;18(10):594-599.

[4] Gweon, Tae-Geun, et al. "Fecal microbiota transplantation using upper gastrointestinal tract for the treatment of refractory or severe complicated Clostridium difficile infection in elderly patients in poor medical condition: the first study in an Asian country." Gastroenterology research and practice 2016 (2016).

[5] Brandt, Lawrence J MD, MACG1. American Journal of GastroenterologyLecture: Intestinal Microbiota and the Role of Fecal Microbiota Transplant (FMT) in Treatment ofC. difficileInfection. American Journal of Gastroenterology: February 2013 - Volume 108 - Issue 2 - p 177-185. doi: 10.1038/ajg.2012.450

[6] Hong, A. S., Yu, W. Y., Hong, J. M., Cross, C. L., Azab, M., Ohning, G., and Jayaraj, M. (2020) Proton pump inhibitor in upper gastrointestinal fecal microbiota transplant: A systematic review and analysis. Journal of Gastroenterology and Hepatology, 35: 932–940. https://doi.org/10.1111/jih.14958.

[7] Deshpande, A., Pant, C., Pasupuleti, V., Rolston, D. D., Jain, A., Deshpande, N., ... & Hernandez, A. V. (2012). Association between proton pump inhibitor therapy and Clostridium difficile infection in a meta-analysis. Clinical Gastroenterology and Hepatology, 10(3), 225-233.

	Pertinent Initial Labs at Admission	Pertinent Labs upon Discharge	
Lab	Value		Reference Range
WBC	16,800 /uL	6,190 /uL	4,000 to 11,000 /uL
Bands	4.0%	Not noted	<u><</u> 10%
Hgb	10.5 g/dL	8.8 g/dL	12.0 to 16.0 g/dL
Na	130 mmol/L	134 mmol/L	137 to 145 mmol/L
к	5.1 mmol/L	3.8 mmol/L	3.5 to 5.1 mmol/L
Bicarb	19.0 mmol/L	31.0 mmol/L	22.0 to 30.0 mmol/L
BUN	48 mg/dL	34 mg/dL	7 to 17 mg/dL
Cr	2.3 mg/dL	0.8 mg/dL	0.5 to 1.0 mg/dL
Total bilirubin	0.9 mg/dL	0.3 mg/dL	0.2 to 1.3 mg/dL
AST	45 U/L	52 U/L	15 to 46 U/L
ALT	27 U/L	52 U/L	< 35 U/L
Alk phos	74 U/L	86 U/L	38 to 126 U/L
Lactic acid	1.3 mmol/L	Not obtained	0.7 to 2.1 mmol/L
C-reactive protein	326.1 mg/L	11.6 mg/L	< 10.0 mg/L
Sedimentation rate	120 mm/hr	Not obtained	0 to 36 mm/hr
Procalcitonin	22.2 ng/mL	Not obtained	< 0.077 ng/mL



Initial vitals included temperature of 99.7° F, heart rate of 87 bpm, blood pressure of 103/42, and oxygen saturation of 92% on room air.

Initial blood work revealed leukocytosis, elevated creatinine, and elevated inflammatory markers. Initial imaging studies showed evidence of severe diffuse colitis. She was found to be C. diff positive and initially treated with oral vancomycin. Rectal vancomycin and intravenous metronidazole were added in conjunction after she continued to deteriorate clinically. Her hospital course was complicated by poor oral intake, ileus, toxic megacolon, and severe deconditioning.

FMT was considered in this patient, although she was not a candidate for colonoscopic, upper endoscopic, or orally encapsulated delivery due to the high risk of colon perforation and high aspiration risk, respectively. We pursued FMT via nasojejunal tube (NJT). We took measures including ensuring a deep insertion of the NJT [4], with the tip approximately 25-30 cm distal to the ligament of Treitz, stopping all antibiotics for 48 hours before FMT [5], and utilization of a PPI and a pro-kinetic agent at the time of FMT [6], to maximize the chances of a positive outcome.

Since undergoing FMT, the patient, initially critically ill, has had a significant improvement in her symptoms and has returned to her baseline clinical and functional status.

Discussion

- C. diff is one of the most common nosocomial infections among hospitalized patients, although may be community acquired, such as in this case.
- The patient's only risk factor for acquiring C. diff was use of a PPI [7]
- Alternative approaches, such as surgical resection or FMT, may be utilized in cases that are refractory to antibiotic therapies.
- Although evidence supporting FMT is limited, delivery of FMT via the upper gastrointestinal tract is not recommended due to lower efficacy.
- We utilized FMT via NJT in this patient given her high risk for surgery, perforation, and aspiration.
- We took measures to maximize the success of FMT with deep insertion of the NJT, discontinuing antibiotics prior to the procedure, and utilization of a PPI and pro-kinetic agent and believe these steps increased the patient's chances of a positive outcome.

Further studies may further clarify efficacy for FMT via upper gastrointestinal tract utilizing the above-mentioned efforts to attempt to maximize the success rates.

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thickening in the ascending colon and cecum concerning for colitis in axial (A) and coronal (B) planes. (C-E) Repeat non-contrast CT

abdomen/pelvis in axial (C) and sagittal (D, E) planes which showed increase in colonic distention within the transverse colon

measuring up to 7cm (C, E) and increased distention within the cecum and ascending colon (D) concerning for toxic megacolog