Long-Term Follow-Up of Fecal Microbiota Transplantation for Treatment of Recurrent *Clostridium difficile* Infection in a Dual Solid Organ Transplant Recipient

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Key Words

Long-term follow-up · Fecal microbiota transplantation · Recurrent *Clostridium difficile* infection · Dual solid organ transplant recipient

Abstract

Clostridium difficile infection is one of the most frequent causes of healthcare-associated infections, and its rates are also increasing in the community. Mounting evidence suggests that fecal microbiota transplantation (FMT) may be effective; however, as there is paucity of data regarding the use of FMT in patients with solid organ transplants, we present a case of successful FMT in a patient with dual solid organ transplant.

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Introduction

Clostridium difficile infection (CDI) is one of the most frequent causes of healthcare-associated infections, and its rates are also increasing in the community. The management of CDI has become a major challenge, given growing rates of recurrences and failures with standard antibiotic therapy. A recent systematic review reported that the mean CDI costs for hospitalized patients range from USD 8,911 to USD 30,049 [1]. Mounting evidence suggests that fecal microbiota transplantation (FMT) may be effective; however, as there is paucity of

data regarding the use of FMT in patients with solid organ transplants, we present a case of successful FMT in a patient with dual solid organ transplant.

Case Report

A 62-year-old male with a past history of recurrent CDI, liver and kidney transplant presented to the hospital with shortness of breath. The liver transplantation has been done 10 years before due to cirrhosis caused by hepatitis C infection. The patient had also undergone cadaveric kidney transplantation 3 years after developing renal failure secondary to calcineurin inhibitor-related kidney damage and hepatitis C-induced membranoproliferative glomerulonephritis. The patient was on chronic tacrolimus therapy. He was found to have pneumonia and was started on intravenous vancomycin and cefepime. He developed diarrhea after receiving antibiotics for 2 days, having 8–9 bowel movements per day. Due to the patient's previous episodes of CDI, he was empirically started on oral vancomycin. A stool sample was positive for *C. difficile* toxin. The patient's respiratory symptoms improved and intravenous antibiotics were discontinued.

The patient had four episodes of CDI in the past 10 months prior to this hospitalization. The first episode of CDI was treated by with a course of intravenous metronidazole (500 mg t.i.d. for 14 days) plus oral vancomycin (125 mg q.i.d. for 14 days). The patient's symptoms resolved, but he had a second recurrence of CDI after 1 month. The second episode was treated with an oral vancomycin taper (125 mg q.i.d. for 3 weeks, then 7 days each of 125 mg t.i.d., 125 mg b.i.d., 125 mg daily and finally 125 mg every other day with resolution of diarrhea). The subsequent two recurrences were treated by courses of oral Difcid therapy (200 mg b.i.d. for 10 days). All prior episodes led to symptom resolution after antibiotic therapy for at least 1 month. This was the fifth episode of CDI in the patient. Due to recurrent CDI, evaluation of FMT was done. The patient's spouse was chosen as the donor. The donor's blood was checked for HIV-1, HIV-2, HAV IgM antibody, HBsAg, HBV core antibody, HCV antibody and RPR and was found to be negative. Stool culture and studies for *C. difficile*, Cyclospora, Isospora, Cryptosporidium, ova and parasites were also negative. The donor had no history of inflammatory bowel disease, gastrointestinal malignancy, antibiotic use within the last 6 months or recent hospitalization.

Donor stool was collected. The patient underwent a colonoscopy and 60 ml of donor stool suspension was injected into the terminal ileum, 60 ml was injected into the cecum and finally 60 ml was injected into the ascending colon. Oral vancomycin therapy was discontinued after FMT had been performed. The patient's diarrhea resolved 2 days after the FMT.

The patient was followed up 6 months post FMT. Unfortunately, he passed away after suffering from cardiac arrest 6 months post FMT. During the 6 months, the patient did not have any further recurrence of CDI. The patient's diarrhea completely resolved and he was averaging one bowel movement a day.

Discussion

CDI is one of the most common healthcare-acquired infections. It is currently estimated that three million cases of CDI occur per year in US hospitals [2]. There is increasing evidence that CDI has a substantial impact on the morbidity and mortality in patients receiving immunosuppressive medication for organ transplants [3, 4].

The current treatment regimen for CDI is based on the severity of CDI. Metronidazole therapy is recommended for patients with mild to moderate CDI (diarrhea plus any additional signs or symptoms not meeting severe or complicated criteria). For severe CDI (serum albumin <3.0 g/dl plus either white blood cell count >15,000 cells/mm³ or abdominal tenderness), the treatment of choice is oral vancomycin. Vancomycin 500 mg orally four times a day plus intravenous metronidazole 500 mg three times a day is reserved for patients with severe and complicated disease (admission to the intensive care unit for CDI, hypotension with or without required use of vasopressors, fever >38.5°C, ileus or significant abdominal distention, mental status changes, white blood cell count >35,000/mm³ or <2,000/mm³, serum lactate >2.2 mmol/l and end-stage organ failure) [5]. Recurrence of CDI is treated with a repeat metronidazole course or oral vancomycin pulse regimen. The American College of Gastroenterology recommends that the third recurrence of CDI warrants consideration of FMT [5].

Some studies have reported that hospitalized transplant recipients who have CDI have a mortality rate of 5.5%. The same study in liver transplant recipients reported an increase in length of stay in patients who had CDI to 17.8 days as compared to 7.7 days in liver transplant patients who did not have CDI [6]. The use of FMT has been limited in patients with organ transplants due to concerns of adverse reactions and theoretical risk of infections. At this time, the American College of Gastroenterology does not recommend either for or against FMT for recurrent CDI in patients receiving immunosuppressive therapy for organ transplantation.

There have been reported cases of successful FMT for immunocompromised patients [7–10]. Our case is unique as our patient has two organ transplants, continued to be on immunosuppressive therapy with tacrolimus and did not have any recurrence of symptoms 6 months post FMT.

In conclusion, this case shows that FMT can be a safe treatment modality for recurrent CDI in transplant patients and can help reduce length of stay, cost of hospitalization and mortality in this patient population. However, a prospective cohort study is warranted to assess in detail the risks and benefits of FMT in this patient population.

Disclosure Statement

The authors have no conflicts of interest.

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