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Fecal microbiota transplantation for severe complicated *C. difficile* colitis in a patient with acquired immunodeficiency syndrome[☆]



Trasplante de microbiota fecal en el tratamiento de colitis grave complicada por *C. difficile* en un paciente con síndrome de inmunodeficiencia adquirida

Clostridium difficile infection (CDI) continues to be the main cause of hospital-acquired diarrhea and one of the main causes of nosocomial infection. For the last two decades, CDI burden has increased in terms of incidence, morbidity, mortality, and costs.¹ The wide spectrum of CDI manifestations ranges from asymptomatic patients to fulminant presentations with toxic megacolon.² Treatment strategies should be based on disease severity, previous history of CDI, and individual patient risk for recurrence.

Vancomycin is the treatment of choice for severe or complicated CDI. Metronidazole is appropriate for mild disease, and fidaxomicin is a therapeutic option for patients with recurrent CDI or with a high risk for recurrence. Fecal microbiota transplantation (FMT) has been associated with recurrent CDI symptom resolution, but its role as primary treatment and in severe CDI has not been established.³ There is a subgroup of CDI patients that develop fulminant presentations that are refractory to conventional treatments.⁴ We present herein the case of a patient with HIV infection and colitis due to *Clostridium difficile* that was successfully treated through fecal microbiota transplantation.

A 28-year-old man was diagnosed with stage C3 human immunodeficiency virus/AIDS (CD4+ T-lymphocyte count of 41 cells/ μ l and viral load of 127,305 copies/ml), treated

for central nervous system toxoplasmosis and hospital-acquired pneumonia with pyrimethamine, clindamycin, and piperacillin-tazobactam. At the tenth day of treatment, the patient developed diarrhea, abdominal distension, and hyperleukocytosis with 61,400 cells/ μ l. PCR for *Clostridium difficile* toxins was positive for the hypervirulent 027/NAP1/BI strain (Cepheid Xpert® *C. difficile* assay, USA). Treatment was begun with 125 mg PO of vancomycin every 6 h and 500 mg IV of metronidazole every 8 h. Due to lack of improvement at 48 h, we increased the dose of vancomycin to 500 mg PO every 6 h. After 12 days of treatment, the patient had clinical deterioration manifested as increased abdominal pain and distension (fig. 1). Therefore, we began the protocol for fecal microbiota transplantation. The donor was the patient's mother, who had no history of chronic disease and whose body mass index was 24. She was screened for hepatitis viruses A, B, and C and for HIV. Stool culture, ova and parasite exam, and *Clostridium difficile* toxin stool test were negative. Fifty grams of stool were collected from the donor and suspended in 100 ml of 0.9% saline solution. The sample was homogenized through a filter until a liquid solution was produced. Two days prior to the procedure all antibiotics were suspended, including the metronidazole and vancomycin. After the patient signed a statement of informed consent, he was infused with 100 ml of the prepared sample through a nasojejunal catheter, given that no urgent colonoscopies were available at that time. Forty-eight hours after the infusion, the patient showed dramatic clinical improvement, with resolution of pain and abdominal distension and a decrease in leukocytes from 62,000 to 12,000 cells/ μ l (fig. 2). The patient was released and has not presented with disease recurrence at the one-year follow-up.

In a systematic review that included a total of 536 patients from 36 clinical trials, FMT efficacy was 87% after the first procedure. Resolution of diarrhea varied according to the infusion site: when the FMT was infused in the stomach, efficacy was 81%; in the duodenum/jejunum it was 86%; in the cecum/ascending colon it was 93%; and in the distal colon it was 84%.⁵ The number of reports that support the use of FMT in the acute phase of severe cases is on the rise.⁶ However, there is concern with respect to the greater potential risk for sepsis and infections following FMT. A recent retrospective multicenter study on 80

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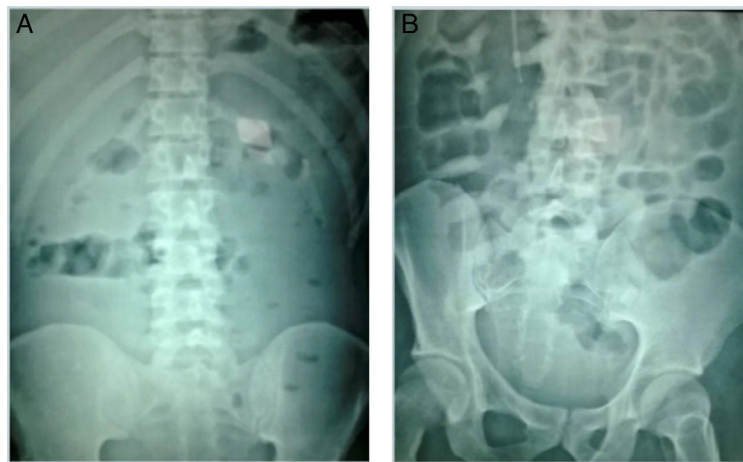


Figure 1 Radiographic progression of the patient, showing a normal radiographic pattern on the 5th day of treatment for *C. difficile* infection (A). However, on the 12th day of antimicrobial treatment, the patient presented with clinical worsening and important bowel segment dilation can be seen (B).

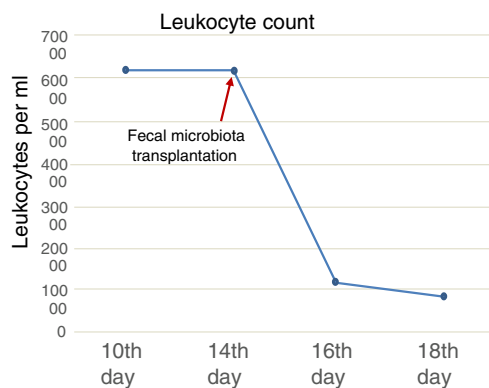


Figure 2 The leukocyte count decreased to 12,000 cells/ml 48 h after fecal microbiota transplantation.

immunosuppressed patients that underwent FMT suggests that it is an effective modality (a 78% cure rate with a single procedure), with few adverse effects and no infectious complications in those high-risk patients.⁷ In addition, there is concern about potential long-term complications secondary to FMT. A higher risk for developing obesity, diabetes, colon cancer, atherosclerosis, irritable bowel syndrome, fatty liver, asthma, and autism has been reported.⁸ It is essential that clinical follow-up of the patients that undergo FMT be carried out over the years to determine the strength of association of the respective reports.

Very few cases have been published on patients with HIV that have received FMT as treatment for CDI, and the majority of those reports are in relation to disease recurrence.^{7,9,10}

FMT is a simple, efficacious, and relatively inexpensive option to be considered in severe cases of CDI, especially those in which broad-spectrum antibiotics cannot be suspended. Clinical trials should be conducted to demonstrate the efficacy of FMT as first-line treatment in immunosuppressed patients with severe disease.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Perforation of Meckel's diverticulum by a foreign body[☆]



Perforación de divertículo de Meckel por cuerpo extraño

Meckel's diverticulum (MD) is a vestigial remnant of the omphalomesenteric duct that consists of a saccular dilation of the small bowel, located at the antimesenteric border, generally at fewer than 60-100 cm from the ileocecal valve. It is the most common malformation of the small bowel and has a prevalence of 2-3%. Symptomatic MD is more frequent in males than in females.¹ It is composed of all the bowel wall layers and therefore is a true diverticulum. Up to 60% of the cases can present with heterotopic tissue of the gastric, pancreatic, colonic, or duodenal mucosa.²

We present herein an unusual case of MD perforated by a foreign body.

A 71-year-old man with a past medical history of COPD and peptic ulcer sought medical attention for abdominal pain in the right iliac fossa of 24-h progression, associated with hyporexia. There was no other accompanying symptomatology. Physical examination revealed pain in the lower hemiabdomen with guarding, as well as the Blumberg's sign and Rovsing's sign. Laboratory results reported leukocytosis (11,280/ μ l) with 63.3% segmented neutrophils and a slightly increased C-reactive protein level (1.2 mg/dl). Clinical diagnosis of acute appendicitis was made, indicating urgent surgery. A cecal appendix with normal characteristics was observed through a pararectal incision, and so the small bowel was explored. An 80-cm MD of the ileocecal valve was identified, with inflammatory signs secondary to perforation by a foreign body, suggestive of a fish bone, with fragments of fibrin in the surrounding area (fig. 1A). Appendectomy was performed along with a Meckel diverticulectomy, sectioning its base with a linear stapler (fig. 1B). The histopathologic study confirmed the normality of the vermiform appendix, as well as the inflammatory changes in the MD. The patient

had favorable postoperative progression and was released on day 6 after the surgery. He was asymptomatic at month 6 of follow-up.

MD is generally asymptomatic and only 4.2-16.9% have clinical manifestations.³ It is usually an incidental finding, identified in imaging studies or interventions performed for a different indication. When symptoms do present, they tend to be similar to those of acute appendicitis or those derived from a complicated MD. Bowel obstruction (35%), gastrointestinal bleeding (32%), diverticulitis (22%), umbilical fistula (10%), or perforation secondary to a foreign body (5%) are among the possible complications.⁴ The differential diagnosis for MD should include acute appendicitis, peptic ulcer, gastroenteritis, biliary colic, and colonic diverticulitis.⁵

Plain abdominal x-ray, ultrasound, and computed tomography are complementary studies, and even though they are not very specific, they can aid in the differential diagnosis of acute abdomen. They are also useful in cases in which the MD presents as an obstruction or perforation.⁵ Tc-99m scintigraphy has high sensitivity and specificity, but the number of false positives and false negatives increases with patient age, most likely due to technical difficulty and the overlap of the gallbladder over the area of the MD.⁵ Thus, it is not a study that is routinely used, but it is considered the technique of choice in cases of lower gastrointestinal bleeding in children suspected of having a MD.

Management of asymptomatic MD is controversial. According to a review from the Mayo Clinic on patients seen within the time frame of 1950 and 2002, prophylactic resection is not recommended, except in cases presenting in males under 50 years of age, with a MD that is longer than 2 cm or has heterotopic tissue.⁶ However, in a study by Cullen et al., they recommend prophylactic resection in all patients under 80 years of age, considering that 6.4% of patients with MD can develop complications.⁷ In contrast, there is agreement that all symptomatic MDs should be surgically treated. The most widely used techniques are diverticulectomy and bowel resection. Diverticulectomy is the method of choice, as long as complete extirpation is certain, or the perforation is far from the base. It can be performed through wedge resection or with linear staplers. Bowel resection is indicated in cases of bleeding, diverticulitis, perforation close to the base, tumor, and in wide-based MDs or those in which wedge resection

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