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Letter to the Editor

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Is it reasonable to perform Fecal Microbiota Transplantation for recurrent *Clostridium difficile* Infection in patients with liver cirrhosis?

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Sir,

Fecal Microbiota Transplantation (FMT) is a successful procedure that in recent years has been accelerated and oversimplified, to the point that in the near future it will be probably used in more patients and much earlier in the natural history of CDI [1, 2].

Advanced liver cirrhosis (LC) is a well-known cause of bacterial translocation and bacteremia [3-5] and also in LC patients CDI is frequent, severe and recurrent [6]. Even when LC is not a formal contraindication of FMT, the number of patients with LC who underwent a FMT that have been reported in the medical literature are very scarce and the few episodes reported appear only listed and not described in detail [7].

We report four cases of LC patients with multiple recurrent CDI who received FMT and their clinical outcome (table 1).

Case 1

A 72-year-old woman with LC and hepatocellular carcinoma due to Hepatitis C virus (HCV) had a MELD score of 13 and was classified as Child Pugh C. She had suffered hepatic encephalopathy several times as a result to different infections and received several courses of antimicrobial agents over the course of three months. Other comorbid conditions included multifactorial pancytopenia, esophageal variceal bleeding and severe malnutrition.

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In January 2015, she had a first episode of CDI caused by a strain of ribotype 027 which was treated with full dose oral vancomycin, followed by vancomycin tapering. She had four more recurrences and the patient received vancomycin tapering in the first, third and fourth recurrences and fidaxomicin in the second one. Finally, the patient ended up with continuous low doses of vancomycin to control the diarrhea, to enable her to perform her basic activities of daily life. She received a FMT by colonoscopy from which she recovered uneventfully, without any further episodes of CDI during the five months of follow up, with a clear-cut increase in her quality of life.

Case 2

A 60-year-old woman had cirrhosis and hepatocellular carcinoma due to HCV. She had a MELD score of 9 and was classified as Child Pugh C. She also suffered hepatic encephalopathy. Her first episode of 027 CDI was treated with vancomycin tapering. She had a first recurrence that was treated with fidaxomicin and the second one was treated with vancomycin, followed by a FMT via colonoscopy. Three days after the FMT, she developed a single episode of fever with *Escherichia coli* bacteremia without a clear focus of origin other than bacterial translocation. She received ceftriaxone for 10 days with a favorable outcome and no further recurrences of CDI were detected after eleven months follow-up. It should be noted that the patient never had episodes of bacteremia or spontaneous bacterial peritonitis previously.

Case 3

A 57-year-old man had alcoholic cirrhosis with a MELD score of 9 and was classified as Child Pugh B. He had suffered gastrointestinal bleeding due to esophageal varices. In April 2017, he had a Fournier´s gangrene requiring surgery and received long-term antibiotics. He had his first episode of CDI treated with metronidazole; subsequently, he had four recurrences which were treated with metronidazole, vancomy-

Table 1 **Clinical cases**

Case	Age (years)	Sex	Causes	Comorbidities	Child-Pugh score	MELD score	Ribotype	Number of recurrences	Treatment received	Route of administration	Complications	Follow up (months)
1	72	F	Hepatitis C virus	Hepatocellular carcinoma, Pancytopenia, Esophageal variceal bleeding, Encephalopathy, Malnutrition	C	13	27	4	Vancomycin tapering, Fidaxomicin	Colonoscopy	No	5
2	60	F	Hepatitis C virus	Encephalopathy episodes, Hepatocellular carcinoma	C	19	27	2	Vancomycin tapering, Fidaxomicin	Colonoscopy	*Escherichia coli* bacteremia	11
3	57	M	Alcohol	Esophageal varices	B	9	no 027	4	Metronidazole, Vancomicycin tapering, Fidaxomicin	Colonoscopy	No	4
4	84	F	Hepatitis C virus	Hepatocellular carcinoma , Hepatopulmonar syndrome, Cholangitis	C	11	no 027	5	Metronidazole, Vancomycin tapering, Fidaxomicin	Nasogastric tube	Death due to collangitis	N.A.

cin, fidaxomicin and vancomycin tapering respectively. In the last recurrence, he received a FMT via colonoscopy. No complications have been seen during the recent four months of follow-up.

Case 4

An 84 year-old woman with LC and hepatocellular carcinoma had a MELD score of 11 and was classified as Child Pugh C. She also suffered from hepatopulmonar syndrome and choledocolitiasis with several cholangitis episodes.

In June 2013, she had a first episode of CDI that was treated with metronidazole. She had six recurrences; three were treated with vancomycin standard dose, the fourth with fidaxomicin, the fifth with vancomycin tapering and in the last one treated with vancomycin followed by FMT by nasogastric tube. Seven days later, the patient died due to a new episode of cholangitis but blood cultures had not been obtained.

Advanced liver cirrhosis (LC) was present as an underlying condition in approximately 25% of our patients who received a FMT.

Out of our four cases with advanced LC that were treated with FMT, in our report, two patients had severe complications post procedure and one of them died.

There is no question that the severity of the previous underlying conditions of our four candidates can explain episodes of superinfection at any time which may endanger their lives.

Bacterial translocation and bacteremia is relatively common in advanced LC without the contribution of FMT but the coincidence of FMT in our second patient is a cause of concern. We were surprised by the very low number of LC patients that appear in large series of patients with FMT. We speculate that the risk aversion towards some complications seen in some of our patients may have accounted for a reluctance of some physicians to perform the FMT.

Our literature research highlights one clinical trial that used FMT in LC patients to treat hepatic encephalopathy. However, it is not applicable to our possible future patients, as the methodology was not designed to treat CDI, used a small quantity of stool and an antibiotic prophylaxis prior to FMT [8].

Bacteremia, as a complication of FMT has been reported only anecdotally [3].

Cholangitis after FMT in the fourth patient, it is quite possible that it was a mere coincidence. However, focusing in the second case, a proven episode of superinfection out of our four cases appears to be striking.

As a contrast to our concerns, the three cases who survived the FMT, were free of recurrent CDI episodes in the ongoing follow up periods of eleven, five and one months.

Despite the fact that the advanced LC is not a formal contraindication of FMT, this report is advisory in its intent and

recommends the need for a careful follow up with a systematic review of complications of FMT in cirrhotic patients.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest

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