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**Fecal microbiota transplantation cured epilepsy in a case with Crohn's disease: The first case report**

He Z *et al*. FMT for Crohn's disease comorbid epilepsy

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**Abstract**

Fecal microbiota transplantation (FMT) is a promising strategy that involves reconstruction of gut microbiota. Recently, it has been considered as a treatment of Crohn’s disease (CD) and certain neurological diseases such as intestinal inflammation and neurological diseases. In this study, to the best of our knowledge, we report the first case that used FMT to achieve remission in intestinal and neurological symptoms in a girl with CD and 17 years history of epilepsy. During 20 mo of treatment, FMT has proved its efficiency in preventing the relapse of seizures after withdrawing the antiepileptic drugs. Furthermore, this case highlights the role of microbiota-gut-brain axis and inspires a novel treatment for epilepsy through remodeling gut microbiota.

**Key words: Fecal microbiota transplantation; Epilepsy; Crohn’s disease; Gut microbiota; Brain-gut axis**

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**Core tip:** We report a case of 17 years history of epilepsy fortunately showed improvement as a result of fecal microbiota transplantation (FMT) treatment for Crohn’s disease. This is the first time that FMT has been used in epilepsy treatment. This case might open a new window into disease mechanism focusing on microbiota-gut-brain axis and inspire a novel treatment for epilepsy through remodeling gut microbiota.

He Z, Cui BT, Zhang T, Li P, Long CY, Ji GZ, Zhang FM. Fecal microbiota transplantation cured epilepsy in a case with Crohn's disease: The first case report. *World J Gastroenterol* 2017; In press

**INTRODUCTION**

Considerable evidences showed the effects of microbiota on the neuropsychiatric disorders[1]. However, a very few studies reported the clinical use of microbiota in brain diseases. Fecal microbiota transplantation (FMT), the most effective strategy for reconstruction the gut microbiota, has been considered as a treatment of *Clostridium difficile* infection[2], inflammatory bowel disease[3-5], constipation and other diseases[6]. In this study, we report the first study case that used FMT as a treatment of tong-term epilepsy in a patient with Crohn’s disease (CD). FMT provided seizure freedom without using anti-epileptic drugs.

**CASE REPORT**

A 22-year-old girl, with 17 years history of epilepsy, was referred to the Second Affiliated Hospital of Nanjing Medical University in May 2015 because of the unsuccessful CD treatment. The initial presentation was at the age of six with generalized seizures of loss of consciousness and unexplained chronic diarrhea. She had more than 120 seizures every year between the ages of six to thirteen. After that she was diagnosed as epilepsy by typical electroencephalogram (EEG) and started to take sodium valproate. That treatment achieved extended stabilization in the seizures, but still had 2-3 generalized seizures every year if she forgot to take the anti- epileptic drug. The diagnosis of CD was at the age of 17, at that time she started treatment of the chronic diarrhea and had symptom improvement after oral mesalamine. She had growth retardation, mild malnutrition and started the first menarche at age 17 followed by menstrual cycle disorder.

After administration, abdominal/pelvic magnetic resonance imaging (MRI) showed severe strictures in sigmoid colon and anus with perianal fistula, whereas brain MRI was normal. Crohn's disease activity index (CDAI) was 361 points. The patient underwent Endoscopic balloon dilation for the intestinal strictures, then she got the first FMT through mid-gut by gastroscope (trial: NCT01790061) under anesthesia[7]. The stool for FMT was obtained from a primary school girl and scanned after signing an informed consent from her parents. The laboratory protocol and clinical work flow were noted in our recent reports[8]. The 200 mL fresh fecal microbiota suspension was prepared under an automatic purification system (GenFMTer, FMT medical, Nanjing, China) in our fecal microbiota bank system. After the FMT, she was given professional food instruction related to CD. After FMT, she was given oral Mesalamine 3.0 g per day during the follow–up. She underwent the second endoscopic balloon dilation for colonic stricture before her third FMT. Based on our initial expectation on the role of FMT in epilepsy, we decided to stop sodium valproate after the first FMT and getting her informed consent. Since then, she never had recurrence of epilepsy during twenty months of follow-up and still in a seizure free status without anti-epileptic drugs until this submission. Therefore, there was no need for EEG during the follow-up. The clinical response of CD to the FMT was assessed by decreasing of CDAI to 104 points after twelve months, and this remission maintained after the third FMT until the end of twenty months follow-up. In addition, the patient showed sustained improvement of quality of life and started to work. More interestingly, her menstrual cycle after FMT tended to shorten and became regular every 6 wk with normal menstruation quantity during each cycle. The key clinical parameters before and after the FMT were shown in Table 1.

**DISCUSSION**

Epilepsy entails a major burden in seizure-related disability, mortality, comorbidities, stigma, and costs[9]. Although the number of available antiepileptic drugs has increased substantially during the past 20 years, about a third of patients remain resistant to medical treatment[10].Despite the development of surgical procedures, epilepsy surgery is still done in a small subset of drug-resistant epilepsy cases. Here, we report a case of 17 years history of epilepsy fortunately showed improvement as a result of FMT treatment for CD. Although she had never got any anti-epileptic drugs after the FMT, she had more than 20 month’s seizure freedom and this status is maintained. Unfortunately, in this case report, there is no confirmed focal pathology, no potential pathogen identification, no microbiome analysis, and no gene mutations detection. There were very few reported cases on epilepsy comorbid Crohn's disease[11,12], which may be the key reason that the mechanism linking intestinal microbiota, intestinal inflammation and epilepsy remains unclear. Crohn's disease with associated nutrient deficiencies could have symptoms like tetany and seizures, which may be related to the deficit of magnesium and/or calcium[12]. However, the present patient in this report was diagnosed as epilepsy at the age of 13 and only had mild malnutrition. Although it has been mentioned that FMT might be helpful for certain neurological diseases[6] and Crohn's disease[7], as far as we know, this article is the first report of successful epilepsy treatment using FMT. It is notable that the level of blood lipid of the patient returned to the almost normal level after FMT. In our previous studies[7, 13], we also found the similar results that the gut microbiota could affect the host lipid metabolism. These evidences suggested that FMT may be one of the therapeutic options for metabolic diseases. Although it has been at least 1700-year old history of using FMT in human diseases[14], as we know, there was no previous report on using FMT in epilepsy. This interesting case might open a new window into disease mechanism focusing on microbiota-gut-brain axis and inspire a novel treatment for epilepsy through remodeling gut microbiota.

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**COMMENTS**

***Case characteristics***

AChinese girl with long term epilepsy was referred to our hospitalbecause of unsuccessful treatment for Crohn’s disease.

***Clinical diagnosis***

Clinical symptoms showed chronic diarrhea, growth retardation, mild malnutrition and menstrual cycle disorder.

***Differential diagnosis***

Her differential diagnosis included intestinal tuberculosis and viral infection.

***Laboratory diagnosis***

Laboratory evaluation revealed low hemoglobin and elevated erythrocyte sedimentation rate.

***Imaging diagnosis***

Magnetic resonance imaging confirmed the severe strictures in sigmoid colon and anus with perianal fistula, and negative finding in brain.

***Pathological diagnosis***

The patient was diagnosed definitely with no pathological examination, although this was important.

***Treatment***

The patient underwent three times offecal microbiota transplantation and twice endoscopic balloon during 12 mo after the first visiting.

***Related reports***

There was no report on fecal microbiota transplantation for epilepsy.

***Term explanation***

Fecal microbiota transplantation involves infusing healthy donor microbiota into the intestines of a patient to restore the intestinal microbiota.

***Experiences and lessons***

This case highlights the disease mechanism focusing on microbiota-gut-brain axis and inspires a novel treatment for epilepsy through remodeling gut microbiota.

***Peer-review***

The paper is well written. The nutrient deficiencies associated with Crohn’s disease is usually subclinical but, occasionally, can cause weight loss, growth retardation, anemia and, even, tetany and seizures.

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Grade D (Fair): 0

Grade E (Poor): 0

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| **Table 1 Clinical parameter changes of the patient during follow-up** |
| **Parameter** **(normal range)**  | **Before the 1st FMT** | **After the 1st FMT** |
| **1 m** | **3 m** | **6 m** | **12 m** | **15 m** | **20 m** |
| CDAI score  | 361 | 174 | 158 | 87 | 104 | 112 | 131 |
| Body weight (kg) | 42 | 42 | 43 | 47 | 49 | 50 | 52 |
| Hemoglobin (110-160, g/L) | 95 | 99 | 120 | 117 | 113 | 103 | 111 |
| CRP (0-10,mg/mL) | 8 | 3 | 7 | 10 | 1 | 3 | 10 |
| ESR (0-20, mm/h) | 59 | 51 | 27 | 30 | 36 | 21 | 61 |
| Album (g/L) | 39.6 | ND | 47.7 | 39.7 | 45.5 | 48.4 | 41.5 |
| Total cholesterol (≤ 5.2 mmol/L) | 4.08 | ND | 4.98 | ND | ND | 5.71 | ND |
| Triglycerides (≤ 2.3 mmol/L) | 1.68 | ND | 1.03 | ND | ND | 0.32 | ND |
| HDL-C (≥ 0.9 mmol/L) | 0.7 | ND | 1.2 | ND | ND | 1.8 | ND |
| IgA (0.70-4.00, g/L) | 5.71 | ND | 5.47 | 4.39 | ND | ND | 5.4 |
| Menstrual cycle length (d) | 60-75 | ND | 45 | 45 | 45 | 45 | 30 |
| CDAI: Crohn’s disease activity index (remission: < 150, moderate: 150-450, severe: > 450); CRP: C reactive protein; ESR: Erythrocyte sedimentation rate; HDL-C: High density lipoprotein-cholesterol; LDL-C: Low density lipoprotein-cholesterol; ND: No detect; FMT: Fecal microbiota transplantation. |