

## Fecal microbiota transplantation and prednisone for severe eosinophilic gastroenteritis

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### Abstract

Eosinophilic gastroenteritis is a rare disease of unknown etiology. It is characterized by patchy or diffuse eosinophilic infiltration of the bowel wall to a variable depth and various gastrointestinal manifestations. We describe a case of severe eosinophilic gastroenteritis presenting as frequent bowel obstruction and diarrhea in a 35-year-old man. The patient was misdiagnosed and underwent surgery because of intestinal obstruction when he was first admitted to a local hospital. Then he was misdiagnosed as having Crohn's disease in another university teaching hospital. Finally, the patient asked for further treatment from our hospital because of the on-going clinical trial for treating refractory Crohn's disease by fecal microbiota transplantation. Physical examination revealed a slight distended abdomen with diffuse tenderness. Laboratory investigation showed the total number of normal leukocytes with neutrophilia as 90.5%, as well as eosinopenia, mono-

cytopenia and lymphocytopenia. Barium radiography and sigmoidoscopy confirmed inflammatory stenosis of the sigmoid colon. We diagnosed the patient as having eosinophilic gastroenteritis by multi-examinations. The patient was treated by fecal microbiota transplantation combined with oral prednisone, and was free from gastrointestinal symptoms at the time when we reported his disease. This case highlights the importance of awareness of manifestations of a rare disease like eosinophilic gastroenteritis.

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**Key words:** Eosinophilic gastroenteritis; Bowel obstruction; Diarrhea; Fecal microbiota transplantation; Prednisone

**Core tip:** We report a case of severe eosinophilic gastroenteritis presenting as frequent bowel obstruction and diarrhea in a 35-year-old man. The patient was misdiagnosed and underwent surgery because of intestinal obstruction when he was first admitted to a local hospital. Then he was misdiagnosed as having Crohn's disease in another hospital. Here we present our experience of diagnosis and treatment with fecal microbiota transplantation and oral prednisone for this case. This case is characterized by the unusual features of eosinophilic gastroenteritis and effects of novel therapy.

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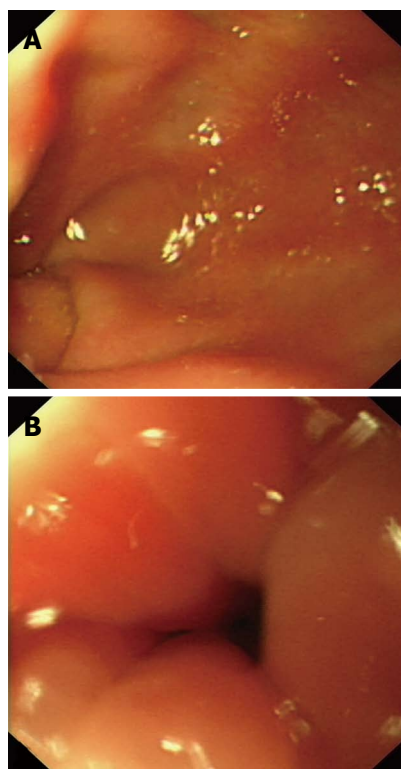
### INTRODUCTION

Eosinophilic gastroenteritis is a rare disease characterized

by patchy or diffuse eosinophilic infiltration of the bowel wall to a variable depth and symptoms associated with the gastrointestinal tract<sup>[1,2]</sup>. The first description of the disease was made by Talley *et al*<sup>[3]</sup>. The pathogenesis and etiology of the disease remain unknown<sup>[4,5]</sup>. Diagnostic criteria include demonstration of eosinophilic infiltration of the bowel wall, lack of evidence of extra-intestinal disease, and exclusion of various disorders that could mimic a similar condition<sup>[1]</sup>. Here we present our experience of diagnosis and novel therapy for a case of severe eosinophilic gastroenteritis presenting as frequent bowel obstruction and diarrhea.

## CASE REPORT

A 35-year-old man was first admitted to a local hospital in March 2012 for progressing abdominal pain and distension. Computer tomography scan demonstrated marked wall thickening and stenosis of the intestine in the lower right abdomen. An emergency laparotomy was performed for the consideration of acute appendicitis. Exploration revealed focal stricture in the ileocecal junction. Segmental resection of the ileocecum and end to end anastomosis were performed. After the operation, diarrhea and incomplete ileus still occurred frequently, and symptomatic treatment had little effect. Severe intestinal obstruction recurred in September 2012, at which time doctors in another university teaching hospital reviewed previous surgical biopsy and diagnosed the patient as having Crohn's disease. After eliminating infection, two weeks prednisone and two months nasogastric tube feeding of enteral nutrition and azathioprine did not improve the symptoms. He suffered from diarrhea over twenty times a day. Finally, the patient asked for further treatment from our hospital in November 2012 because of the on-going clinical trial (NCT01793831) for treating refractory Crohn's disease by fecal microbiota transplantation (FMT). The patient had no history of drug allergy, asthma, or allergic rhinitis. Physical examination revealed a slight distended abdomen with diffuse tenderness. Laboratory investigation showed the total number of normal leukocytes, with neutrophilia of 90.5%, eosinopenia of 0%, monocytopenia of 2.2%, lymphocytopenia of 7.2%, erythrocyte sedimentation rate 42 mm/h, and C-reactive protein 69 mg/L. Blood and stool bacterial culture were negative. Blood tests for Cytomegalovirus and Epstein-Barr virus were negative. Sigmoidoscopy revealed an obvious stenosis and a smooth, diffusely inflamed sigmoid mucosa from which multiple biopsies were taken (Figure 1). Barium radiography confirmed a stricture of the sigmoid colon (Figure 2). Previous surgical biopsy showed a dense infiltration of eosinophils throughout the entire thickness of the bowel wall (Figure 3). After excluding the possibilities of malignancy by surgical pathology, parasitic disease by stool examination, and autoimmune disease by immunological tests, eosinophilic gastroenteritis was diagnosed. Antibiotics was used, but there was no clinical improvement. The patient strongly

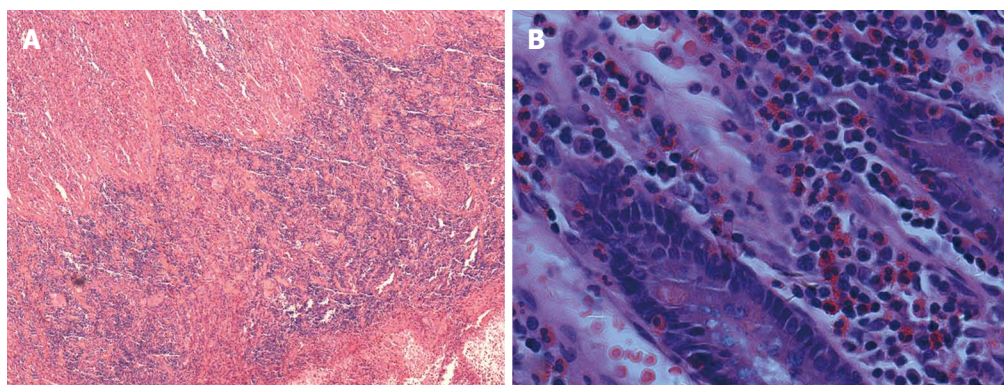


**Figure 1** Endoscopic picture of the sigmoid colon. A: Multiple biopsies were taken from the diffusely inflamed mucosa and revealed eosinophilic infiltration; B: Stricture of the sigmoid colon and smooth mucosa.



**Figure 2** X-ray barium radiography discloses significant stenosis of the sigmoid colon.

demanded FMT treatment for his disease, and the donor of the feces was his 9-year-old healthy daughter. The routine screening for potential pathogens was performed in all donors. After single standardized FMT through the mid-gut by gastroscopically, referring to our previous protocol<sup>[6]</sup>, the frequent diarrhea was dramatically reduced within one week. However, the stenosis still existed. For consideration of combined therapy, prednisone 35 mg/d was used in the first three weeks and gradually reduced until it was terminated within seven weeks. The patient recovered well and was free from gastrointestinal symptoms until six weeks after he stopped steroids. Diarrhea recurred but the stricture of the sigmoid colon disap-



**Figure 3** Microscopy of the resected ileocecal revealing eosinophilic infiltration from the submucosa to the subserosa. A: Boundary of muscular and serosal layer become indistinct (HE  $\times$  40); B: Dense eosinophilic infiltrates in the mucosa (HE,  $\times$  400).

peared during colonoscopy. A steroid was used again for six weeks. The patient was completely free of recurrence during the follow-up 11 mo, at which time he regained 10 kg and had normal working capability.

## DISCUSSION

Eosinophilic gastroenteritis is an uncommon disease and can be seen anywhere in the gastrointestinal tract. In 1970, Klein *et al*<sup>[7]</sup> classified the disease into mucosal, muscular and serosal types based on the depth of involvement. The involvement of different layers usually gives rise to different clinical manifestations. The most common mucosal disease generally presents with diarrhea, bleeding, and protein-losing enteropathy, or malabsorption. Involvement of the muscle layer may cause bowel wall thickening and subsequent intestinal obstruction, which was the manifestation in this patient. The subserosal form usually presents with peritonitis and eosinophilic ascites, with or without any or all of the symptoms associated with mucosal and/or muscle layer disease<sup>[1,8]</sup>.

Because the pathogenesis and etiology of the disease are not clear, there are no standards for the diagnosis of eosinophilic gastroenteritis. Talley *et al*<sup>[3]</sup> have identified three main diagnostic criteria: (1) the presence of gastrointestinal symptoms; (2) biopsies demonstrating eosinophilic infiltration of one or more areas of the gastrointestinal tract, or characteristic radiological findings with peripheral eosinophilia; or (3) no evidence of parasitic or extra-intestinal disease. However, the definitive diagnosis is the histologic demonstration of eosinophilic infiltration of some part of the gastrointestinal tract<sup>[2]</sup>. Rarely, Crohn's disease or ulcerative colitis might be associated with peripheral eosinophilia, but they can usually be excluded by biopsy because of a lack of eosinophilia<sup>[9]</sup>.

There is no consensus about the treatment of eosinophilic gastroenteritis, but long term steroid treatment is the mainstay management so far. It is now well appreciated that intestinal microbiota make up a microbial organ that is integral to overall host physiology, including pivotal roles in metabolism and immune system function<sup>[10]</sup>. The concept of FMT in traditional Chinese medicine has been recorded for at least 1700 years to treat intestinal

diseases<sup>[11]</sup>. Reports of applications outside of *Clostridium difficile* infection are emerging because more patients request treatment and more clinics incorporate FMT into their treatment repertoire, which will pave the way for the use of FMT in several idiopathic conditions<sup>[12]</sup>. After all this comprehensive consideration, we eventually tried the combination treatment of FMT and prednisone, and achieved good clinical effects. We can differentiate between the effects of prednisone and FMT because FMT was used one week before prednisone and dramatically reduced the frequency of diarrhea within several days. This indicated the fast therapeutic role of FMT in eosinophilic gastroenteritis cases presenting as long-term diarrhea. Besides, the patient did not benefit from the two-week treatment with prednisone before he went to our hospital and appeared to respond to our combination treatment judging by the disappearance of the gastrointestinal symptoms. However, it remains unclear whether FMT could cure eosinophilic gastroenteritis or maintain long term clinical remission if prednisone was not given. As far as we know, this is the first report where FMT was used to treat severe eosinophilic gastroenteritis.

## COMMENTS

### Case characteristics

A case of severe eosinophilic gastroenteritis presenting as frequent bowel obstruction and diarrhea.

### Clinical diagnosis

Clinical symptoms and surgical pathology are very important for the diagnosis of eosinophilic gastroenteritis.

### Differential diagnosis

Long term follow-up should be important for confirming or correcting previous diagnosis when it is difficult to make a differential diagnosis between Crohn's disease and severe eosinophilic gastroenteritis.

### Laboratory diagnosis

Peripheral eosinophilia was not observed in this case.

### Imaging diagnosis

X-ray barium radiography discloses typical stenosis of the sigmoid colon.

### Pathological diagnosis

Microscopy of the resected ileocecum, revealing eosinophilic infiltration from the submucosa to the subserosa.

### Treatment

The combination treatment of fecal microbiota transplantation (FMT) and pred-

nisonone achieved good clinical effects after previous failure of treatment with prednisone, azathioprine and enteral nutrition.

### Related reports

Patients with severe intestinal disease might benefit from FMT.

### Term explanation

FMT is a special therapeutic modulation which uses microbiota from stools.

### Experiences and lessons

Manifestations of a rare disease should draw clinical workers great attention.

### Peer review

This is the first report where FMT was used to treat severe eosinophilic gastroenteritis. However, *Helicobacter pylori* (*H. pylori*) was not detected in this case. It is important to evaluate infection by *H. pylori* due to a recent work in which the patient was cured from eosinophilic gastroenteritis just by eradicating the infection.

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