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Successful treatment of chronic Pouchitis utilizing fecal microbiota transplantation (FMT): a case report

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Dear Editor

Ulcerative colitis (UC) is a chronic debilitating inflammatory condition medically treated with corticosteroids, aminosalicylates, immunomodulators, and biologics. Almost one third of UC patients ultimately require surgical interventions because of fulminant colitis, dysplasia, cancer, or medical refractory diseases. Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) is the current standard surgical intervention for severe chronic ulcerative colitis with failed medical treatment. Anastomotic leak, pouch failure, pelvic sepsis, and pouch ischemia can occur after the procedure. The most common long-term complication is pouchitis, an idiopathic inflammatory condition involving the ileal reservoir. Common presentations of pouchitis include increased stool frequency, urgency, incontinence, bloody stools, abdominal or pelvic discomfort, fatigue, malaise, and fever. The prevalence of pouchitis ranges from 23 to 46 %, with an annual incidence up to 40 %. Though the majority of initial cases of pouchitis can be easily managed with a short course of antibiotics, in about 5 % of patients, inflammation of the pouch becomes chronic and a challenging problem to manage.

Fecal microbiota transplantation (FMT) is a novel therapy to transfer normal intestinal flora from a healthy donor to a patient with a medical condition potentially caused by disrupted homeostasis of intestinal microbiota or dysbiosis. FMT has been widely used in refractory *Clostridium difficile* infection (CDI) and recently it has gained popularity for treatment of inflammatory bowel disease (IBD). Previous studies suggested that manipulating the composition of intestinal flora through antibiotics, probiotics, and prebiotic achieved significant results for treating acute episodes of UC-associated pouchitis. However, currently there is no established effective treatment for chronic antibiotic-dependent or refractory pouchitis. In this report, we described a case of chronic antibiotic refractory pouchitis successfully treated with FMT through pouchoscopy. The effect has been sustainable at 6 months post-FMT.

Case report

The patient is a 39-year-old Caucasian male with a history of chronic pan-colonic UC and extraintestinal manifestations of bilateral arthritis of the knees and fingers diagnosed 20 years ago. It was poorly controlled with medical treatment. The patient also had a history of allergy to infliximab. Bilateral knee arthritis was controlled with certolizumab; however, recurrent rectal bleeding, anemia, diarrhea, significant weight loss, and compressive lumbar fractures due to chronic corticosteroid use led to frequent hospitalizations for intravenous steroids, blood transfusions and the ultimate recommendation for total colectomy. He underwent total colectomy in August 2011, IPAA in November 2011, and diverting ileostomy closure in March 2012. At 2 months after ileostomy closure and restoration of his digestive continuity, the patient was doing well with fecal continence and having approximately five to six bowel movements per day. However, in May 2012, he developed intermittent fever, rectal bleeding, abdominal pain, high frequency of watery diarrhea up to 20 times per day. Pouchoscopy revealed patent ileo-anal anastomosis with mucosal erythema at, above, and below the staple line. *Clostridium difficile* PCR and biopsies for cytomegalovirus were negative. A diagnosis of pouchitis was made, and a course of ciprofloxacin was started. Initially the symptoms of pouchitis improved; however, the patient later developed chronic antibiotics refractory pouchitis (CARP) with relapsing and remitting pattern. He was constantly rotating on courses of antibiotics.

A series of pouchoscopies revealed loss of vascular pattern, granularity and erythema of pouch mucosa consistent with chronic pouchitis. Histology demonstrated lamina propria infiltration of lymphocytes and monocytes and focus of crypt abscess suggesting chronic inflammation. There was no evidence of non-caseating granulomas or cytomegalovirus. The patient had a total modified Pouchitis disease activity index (mPDAI) score of 10 with the clinical portion score of 6. We evaluated patient's quality of life through short inflammatory bowel disease questionnaires (SIBDQ) and Cleveland global quality of life (CGQL), which resulted in a score of 30 and 0.47, respectively. The decision was then made to proceed with FMT for chronic antibiotic refractory pouchitis, after informed consent was obtained from the patient and the patient was screened negative for CDI, common enteric pathogens, and antibiotics were stopped for 48 h prior to FMT. An IND was obtained from the FDA #15893.

The donor was screened negative for hepatitis A, B, and C, HIV, and the donor stool was also negative for *C. difficile* and other enteric pathogens. The stool sample was then mixed with sterile saline and diluted to 250 ml. FMT was performed through flexible sigmoidoscopy, and the fecal fluid was instilled 40 cm into the afferent limb and pouch body via a spray catheter. During 1-month follow-up, the patient still experienced usual symptoms of pouchitis with a clinical mPDAI score of 5 both at 2-week and 4-week follow up, compared to clinical mPDAI score of 6 at baseline. However, the patient was off his usual antibiotics for pouchitis during the entire follow-up, and the watery diarrhea was moderately controlled with antidiarrheal medication. After 2 months of FMT, the patient's stool frequency decreased from 20 to 5 times per day without urgency or rectal bleeding. At 3-month follow-up, clinical PDAI score decreased to 0, SIBDQ and CGQL score increased to

52 from 30 and 0.75 from 0.47, respectively Both pouchitis symptoms and patient's quality of life improved on validated scales.

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