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Case Report
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Ulcerative Proctosigmoiditis Exacerbated by Recurrent *Clostridium colitis*: Case Report

Rafaelle Galiotto Furlan[1], Jonathan Soldera[1,2], Rafael Sartori Balbinot[1], Alana Zulian Terres[1], Silvana Sartori Balbinot[1,2] and Raul Angelo Balbinot[1,2]*

[1]*Gastroenterology and Digestive Endoscopy Service, General Hospital of University of Caxias do Sul, Brazil,*

[2]*Department of Gastroenterology, University of Caxias do Sul, Brazil*

Abstract

Ulcerative proctossigmoiditis is one of the presentations of ulcerative colitis, whose main etiological tripod is the modification of the intestinal bacterial microbiota, genetic predisposition and exposure to environmental antigenic factors. Individuals with inflammatory bowel disease are predisposed to severe and recurrent infections with *Clostridium difficile*, presenting high morbidity and mortality rates if treatment is not instituted early. The use of vancomycin as the first line in the therapeutic arsenal was effective in reducing the recurrence of *C. difficile* infection and complications of ulcerative colitis. In cases of relapse and not responsive to antibiotic therapy, fecal microbiota transplantation is used as a safe and effective therapy to restore the mucosal protection barrier through intestinal dacolonization by healthy bacterial flora. This case report confirms the positive therapeutic response to the use of fecal microbiota transplantation in a patient with ulcerative proctosigmoiditis for treatment of recurrent *Clostridium* infection.

Keywords: Proctosigmoiditis; Exacerbated proctosigmoiditis; *Clostridium difficile; Clostridium* recidivant; Ulcerative colitis; Inflammatory bowel disease; Vancomycin; Fecal microbiota transplantation

Introduction

Inflammatory bowel disease is represented by two major entities: ulcerative colitis and Crohn's disease. Both are due to an exaggerated immune response in the intestinal mucosa against the nonpathogenic local microbiota. In ulcerative colitis, the attempt to control exacerbations and maintain remission is performed using glucocorticoids, aminosalicylates, immunomodulators and antibiotics, in order to cease inflammation and reduce the number of colonizing bacteria in the intestinal tract that are in imbalance. The dysfunction of this protective barrier of the mucosa facilitates the infection of the colon by pathogenic bacteria.

Patients with ulcerative colitis are more susceptible to severe and recurrent *Clostridium difficile* colitis and fecal microbiota transplantation has been shown to be highly safe and effective [1-5], for the control of this condition due to the restoration of flora diversity and bacterial barrier intestinal. We report the case of a patient with ulcerative proctosigmoiditis, one of the presentations of mesalazine-dependent ulcerative colitis, presenting recurrent diarrhea, who developed recurrent *C. difficile* colitis even after reduction of vancomycin therapy and who had remission of symptoms after transplantation of fecal microbiota.

Case Presentation

A 36-year-old male patient sought care in October 2015 for having severe diarrhea for three months, associated with a loss of 11 kg, beginning after appendectomy. He reported using antiparasitic and antimicrobial drugs without improvement. Laboratory tests revealed absence of lactose intolerance, serological tests for celiac disease, faecal parasitological examination, coproculture, fecal leukocyte detection and *Clostridium* toxin A and B, and calprotectin: 51 µg/g.

The patient underwent upper digestive endoscopy, evidencing small hiatal hernia and gastritis with negative *Helicobacter pylori* research; and ultrasonography of the abdomen with presence of gallbladder polyp 6 mm. Due to the persistence of the clinical picture, a colonoscopy with a biopsy was performed, which revealed reigramitis, with severe enanthemous, without ulcers (Figure 1 and 2). There were no risk factors for gonococcal or chlamydial proctitis, moderate to anatomopathological and entero-resonance without changes.

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Correspondence:
Raul Angelo Balbinot, Gastroenterology and Digestive Endoscopy Service, General Hospital of University of Caxias do Sul, Brazil;
E-mail: raulbalbinot77@gmail.com

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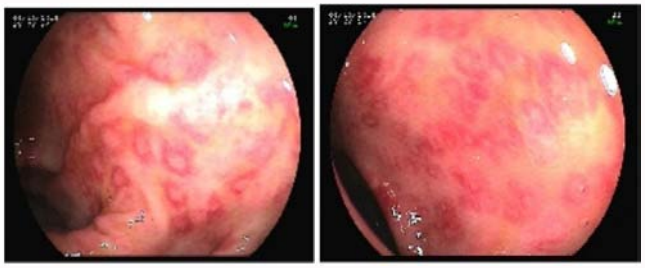

Figure 1: Rectum.

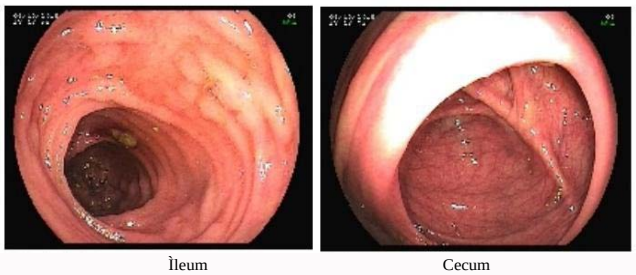

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Figure 2: Sigmoid colon.

Initiated prednisone 40 mg/day and mesalazine 4 g/day on suspicion of inflammatory bowel disease. After a gradual reduction of steroid therapy for four months, the patient presented diarrheal disease after maintenance of mesalazine VO, not presenting new findings in his laboratory tests and stool analysis. A mesalazine 1 g suppository was associated with symptom control.

After another four months, the patient returns to diarrhea, associated with mucus and blood, starting after the use of tetracycline for the treatment of acne and ketoprofen for low back pain. Prescribed ciprofloxacin, metronidazole and nitazoxanide. At the end of the antibiotic therapy, the patient seeks care again for recurrence of the condition. New colonoscopy and biopsy were performed, suggesting the presence of an infectious process, confirmed by anatomopathological study. New laboratory: calprotectin: 589 µg/g; *Clostridium* toxin A and B positive. Made new cycle of metronidazole for 14 days, returning symptoms after one week of suspension. Prescribed oral vancomycin, in gradual reduction for two months, as suggested by the guideline of the American Society of Infectious Diseases (IDSA) [6].

Fifteen days after the end, he again presented diarrhea with intense dehydration, with vancomycin restarted and sent to a fecal microbiota transplant. The patient progressed with significant improvement of the condition. In the colonoscopy performed for transplantation, retossigmoiditis was identified. It maintained mesalazine 4 g daily, as an isolated therapy for three months. He again had diarrhea that responded positively to the reintroduction of the suppository.

Discussion

Ulcerative colitis is an idiopathic, multifactorial chronic inflammatory disease that affects the large intestine, with a variable clinical presentation depending on the extent of the disease in the colon and higher incidence in developed countries. It mainly affects individuals in the third and fourth decades of life, with no difference between the sexes. The etiology of ulcerative colitis remains unknown, but it is believed to be multifactorial where the interaction between genetic susceptibility, host immunity and environmental factors alter the regulation of the enteric immune response.

It is currently believed that the pathogenesis of inflammatory bowel disease is a result of the antigenic action of the intestinal bacterial microbiota in genetically susceptible patients, inducing a chronic inflammatory process due to imbalance between protection and damage of intestinal bacteria, dysbiosis and a reduction in flora biodiversity, leading to the growth of pathogenic bacteria that induce the production of pro-inflammatory cytokines, causing an increased T-cell response in the organ wall. Patients with inflammatory bowel disease are considered a risk group, compared to the general population, for *C. difficile* colitis, especially those with ulcerative colitis, use of a proton pump inhibitor, previous use of antibiotics and albumin of less than 3 g/dL [7] and have more unfavorable outcomes. Clinical manifestations of *C. difficile* colitis may be indistinguishable from exacerbation of ulcerative colitis or cytomegalovirus colitis, and screening for *C. difficile* and cytomegalovirus colitis has been recommended in exacerbation episodes [8,9]. Studies report that although *C. difficile* is present in exacerbations of inflammatory bowel disease, it is not considered the triggering factor and is not directly associated with the activity and change of inflammatory bowel disease over time [10,11]. However, *C. difficile* colitis considerably increases the risk of colectomy, postoperative complications, and mortality [12,13].

Currently the recommended treatment for *C. difficile* colitis in patients with ulcerative colitis is the use of demetronidazole in mild cases and vancomycin in severe infections. However, in a study by the American Society of Microbiology, vancomycin therapy had lower rates of recurrence, hospital readmission, and length of stay, regardless of the severity of the infection [2,14].

The repetitive prescription of antimicrobials as an attempt to control exacerbations of the underlying disease, associated with the use of aminosalicylates, corticosteroids and biological therapies, increases the predisposition to recurrent *C. difficile* colitis, which develops with low response to vancomycin use, worsening quality of life and increased morbidity and mortality of the patient [5].

TMF has been described and disseminated for the treatment of recurrent *C. difficile* colitis. It consists of the infusion of fecal suspension obtained by a healthy donor into the gastrointestinal tract of the patient with *C. difficile* colitis, with the objective of restoring the natural intestinal microflora [4,15]. Although most gastroenterologists still have limited experience with fecal microbiota transplantation, widely available, is an effective and safe method and is considered as a treatment alternative for recurrent and vancomycin-refractory *C. difficile* colitis in patients with well-controlled inflammatory bowel disease [16].

The efficacy after single MPT for treatment of recurrent *C. difficile* colitis is proven, with a cure rate of more than 78% in patients with controlled ulcerative colitis. Only 14% of transplant recipients present exacerbation of inflammatory bowel disease shortly after the procedure, requiring pharmacological treatment of colitis [17,18].

From these outcomes, the action of fecal microbiota transplantation on the induction of ulcerative colitis was questioned for restoring the gastrointestinal ecosystem. It was verified that the sustained response is directly related to the donor fecal microbiota profile, inflammatory status and the capacity of restoration, maintenance and diversity of the recipient flora. Although the efficacy

of this management for inflammatory bowel disease has not yet been confirmed, new studies have been developed seeking better results and new treatment fronts [19-23].

Conclusion

Ulcerative proctosigmoiditis is an entity of multifactorial etiology. The recurrent use of antibiotics, glucocorticoids and aminosalicylates to control exacerbations favors the breakdown of the intestinal mucosal barrier and, consequently, the colonization of the gastrointestinal tract by pathogenic bacteria, especially *C. difficile*. In patients who develop relapsed *C. difficile* colitis and are not responsive to antibiotic therapy, fecal microbiota transplantation is widely indicated because it is proven to be effective and safe only with a single procedure.

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