One Year of Infliximab Therapy Successfully Improved a Case of Refractory Pouchitis without the Use of Antibiotics

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Abstract

A 29-year-old woman with ulcerative colitis underwent total colectomy with ileal-pouch-anal canal anastomosis in 1999. After the surgery, she developed refractory pouchitis. We administered metronidazole, mesalamine and ciprofloxacin; however, her clinical symptoms improved only very slightly. We initiated treatment with infliximab in June 2011 and discontinued the antibiotics. Thereafter, the patient’s abdominal symptoms quickly improved. We discontinued the infliximab therapy in June 2012, after which time, the patient’s abdominal symptoms remained in remission for 40 weeks, without the use of antibiotics. This report suggests that infliximab is useful not only for improving the clinical symptoms of refractory pouchitis, but also for discontinuing antibiotic therapy in such patients.

Key words: ulcerative colitis, pouchitis, infliximab, antibiotic therapy

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Introduction

Pouchitis is the most common complication in patients with ulcerative colitis (UC) who have undergone proctocolectomy and ileal pouch-anal canal anastomosis (IPAA) (1). Anti-tumor necrosis factor α (TNF-α) monoclonal antibody whose use is recommended in cases of severe, treatment-refractory pouchitis, although clinical evidence demonstrating the efficacy of this drug and/or anti-TNF-α antibodies in treating refractory pouchitis is limited (1, 3-9). It is also unclear whether infliximab therapy improves refractory pouchitis without the use of antibiotics and how long such treatment should be continued in cases of refractory pouchitis. We herein present the case of a UC patient with refractory pouchitis that significantly responded to infliximab therapy without the use of antibiotics. In addition, it is noteworthy that our patient remained in remission without the use of antibiotics after discontinuing infliximab therapy. We further show that infliximab treatment completely improved the patient’s ocular symptoms caused by uveitis.

Case Report

A 29-year-old woman with UC underwent total colectomy with ileal-pouch-anal canal anastomosis in 1999 for severe colonic inflammation. After the surgery, she developed pouchitis with perianal fistulas. The pouchitis was diagnosed based on clinical, endoscopic and histological criteria according to the pouchitis disease activity index (PDAI) (10). The patient subsequently developed uveitis in 2004. Although metronidazole was episodically administered, abdominal pain, diarrhea with urgency, perianal fistula formation and ocular symptoms were continuously observed. An endoscopic examination performed in September 2009 revealed severe inflammation with large deep ulcers in the ileal pouch (Fig. 1A). At that time, the patient’s PDAI score was 12. Prepouch ileitis was not detected on the endoscopic examination. A histological examination demonstrated acute moderate to severe inflammation in the ileal mucosa, al-

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though no granulomas were noted. We thus administered metronidazole (250-500 mg/d) and mesalamine (1,500 mg/d), with ciprofloxacin (400 mg/d) given occasionally. The patient’s clinical symptoms slightly improved with this therapy, although the large ulcer in the ileal pouch remained. She subsequently underwent magnetic resonance imaging (MRI), which showed a fistula near the site of anastomosis, without obvious intrapelvic infection. We initiated treatment with infliximab (5 mg/kg) in June 2011. Infliximab was administered at zero, two and six weeks, and then every eight weeks thereafter. We discontinued the administration of antibiotics after the initiation of infliximab therapy. The patient’s abdominal symptoms and perianal fistulas quickly improved, and her ocular symptoms completely disappeared. An endoscopic examination performed in June 2012 revealed a significant improvement in the large ulcers and inflammation in the ileal pouch (Fig. 1B), and the patient’s PDAI score improved to 5. Since she wished to stop the infliximab therapy as a result of the significant improvement in her clinical symptoms, we discontinued the dose of infliximab in June 2012. Since that time, her ocular symptoms and abdominal symptoms resulting from the pouchitis have remained in remission for 40 weeks without the use of antibiotics. The clinical course of the patient is shown in Fig. 2.

Although the abdominal and clinical symptoms caused by pouchitis remained in remission (her clinical PDAI score at the time was 0; namely, usual postoperative stool frequency, no fecal urgency, no abdominal cramps, no rectal bleeding and the absence of fever), infliximab therapy was re-started in March 2013, as she wished to resume this treatment due to recurrence of the perianal fistulas and ocular symptoms.
Discussion

In this report, we showed that scheduled infliximab maintenance therapy significantly ameliorated both the clinical symptoms and endoscopic features of UC in a patient with refractory pouchitis who was treated without the use of antibiotics. In addition, it is of note that the pouchitis remained in remission for 40 weeks without the administration of antibiotics after discontinuing infliximab therapy, which had been administered for one year. In this context, Viazis et al. (6) demonstrated that after one year of infliximab treatment, 5/7 (71.4%) of their patients achieved a complete clinical response. With regard to the mid-term efficacy of infliximab, Barreiro-de Acosta et al. (5) showed that 27% of their chronic refractory pouchitis patients achieved a complete response at weeks 52. Barreiro-de Acosta et al. (7) also analyzed the efficacy of adalimumab, a fully human monoclonal antibody to TNF-α, in patients with chronic refractory pouchitis previously treated with infliximab and showed that 50% of the patients avoided permanent ileostomy, although only 25 achieved remission at week 52. In addition, it is notable that Viazis et al. (6) reported that, three years after the completion of infliximab therapy, all patients with a complete clinical response at one year remained in remission and no patients required any additional treatment for pouchitis; these results are almost similar to those of our case and support the possibility that treatment with one year of infliximab therapy may improve refractory pouchitis without the use of antibiotics, even after the completion of infliximab therapy. It is controversial how long infliximab therapy should be continued in UC cases associated with intractable pouchitis. Although we have presented only one case in this report, our case together with those of Viazis et al. may shed light on this difficult question.

Recent studies suggest that the long-term use of antibiotics increases the patient’s risk of breast cancer (11). A casecontrol study of 2,266 women showed that an increased number of cumulative days of antibiotic therapy, including that involving macrolides, tetracyclines, penicillins, cephalosporins, sulfonamides, nitrofurantoin, metronidazole and quinolones, is associated with an increased risk of incident breast cancer, adjusted for age and length of enrollment (11). In addition, a basic study that analyzed the effect of prolonged antibiotic treatments on tumor development in proto-neu transgenic mice showed that the hazard ratio for breast cancer occurrence in the metronidazole/ciprofloxacin-treated mice was more than triple that observed in the controls (12). In this context, we recommend the use of infliximab, especially in patients with refractory pouchitis.

Uveitis is an extraintestinal complication of inflammatory bowel disease (IBD), and ophthalmologic disorders develop in 2-6% of IBD patients (13). Recent studies have shown that biologic therapy suppresses the development of uveitis associated with various autoimmune disorders, including IBD (13). The present report also demonstrated that infliximab dramatically improved the uveitis associated with UC, supporting the efficacy of infliximab in cases of ophthalmologic complications of IBD.

In conclusion, this case report suggests that infliximab therapy is useful not only for improving the clinical symptoms of refractory pouchitis, but also discontinuing antibiotic therapy in patients with refractory pouchitis that persists even after infliximab therapy. Further clinical trials are needed to validate our results.

The authors state that they have no Conflict of Interest (COI).

References