Case Report

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Synbiotic therapy for diversion colitis after ileostomy with radical resection of rectal cancer: a case report

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Background: As the defunctioned segment of the colon after ileostomy (diverted colon) sometimes exhibits severe mucosal damage, there is concern about the occurrence of bacterial translocation after stoma closure. Therefore, a definitive treatment for diverted colon mucosal disorders prior to stoma closure is needed.
Case presentation: A 48-year-old male rectal cancer patient underwent ileostomy with double orifices. He subsequently underwent preoperative chemoradiotherapy prior to undergoing a laparoscopic low anterior resection, right seminal vesicle complication resection, and bilateral lymph node dissection. Six months after the radical resection, recurrence free, he was referred to our hospital for stoma closure. Colonoscopy performed before the closure revealed that the mucosa of the diverted colon bled easily, with severe mucosal atrophy and colitis. Therefore, GFO (glutamine, fiber, oligosaccharides; Otsuka, Tokushima) and MIYA-BM (Clostridium butyricum MIYARI; Miyarisan Pharmaceutical, Tokyo) were administered via the stoma as synbiotic therapy twice a week for 4 weeks. Posttreatment colonoscopy showed a marked improvement in the mucosa of the diverted colon, so stoma closure was performed.
Conclusion: Synbiotic therapy performed via the stoma as treatment for atrophic mucosa of diverted colon prior to stoma closure proved to be an easy and effective method.

Key words: rectal cancer, stoma closure, synbiotic therapy

Background

During rectal cancer surgery, a temporary stoma may be constructed for the purpose of prevention or treatment of anastomotic leakage. Neoadjuvant chemoradiation therapy (NCRT), which is the standard treatment for rectal cancer in Europe and the United States, helps to avoid the use of a permanent stoma during rectal cancer surgery.[1] The number of facilities utilizing NCRT in Japan is increasing, and there have also been an increasing number of rectal cancer cases. As a result, it is expected that in future procedures there will be a larger number of temporary stomas created after radical resections.

During the stoma-constructed state, the mucosa of the defunctioned segment of the colon after ileostomy (diverted colon) sometimes atrophies. This deterioration of the large intestine mucosa may be conspicuous, especially in cases in which NCRT has been given or in cases where the period until stoma closure is especially long. Due to stoma closure, the subsequent influx of stool into an environment with impaired intestinal function can lead to melena and bacterial translocation.

We herein report a case of severe atrophy of the diverted colon mucosa during stoma formation, which was improved by synbiotic therapy prior to the stoma closure.

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Case presentation

A 48-year-old man visited a nearby hospital with a complaint of stool abnormality. After being diagnosed with rectal cancer with severe stenosis, he underwent ileostomy with double orifices. After the postoperative course became stable, he underwent NCRT. The treatment regimen consisted of tegafur, gimeracil, and oteracil potassium (80 mg/m^2/day, days 1－5) and irinotecan (80 mg/m^2, day 1). A 1-week regimen was considered as 1 course, and a total of 4 courses were given.

Radiotherapy was performed at a margin of 1 cm around the tumor, with a daily dose of 1.8 Gy for 25 days. Four months after NCRT, he underwent a laparoscopic low anterior resection, right seminal vesicle complication resection, and bilateral lymph node dissection. The pathological diagnoses were ypT4b, ypN0, ypM0, and ypStage IIc.[2] Six months after radical resection (1 year after ileostomy), no recurrence was observed, and the patient was referred to our hospital for stoma closure.

During the preoperative examinations, Gastrografin enema examination and colonoscopy were performed. Gastrografin enema examination revealed no evidence of anastomotic leakage. Although colonoscopy showed there was no evidence of stenosis at the anastomotic site, the large intestine was prone to bleeding, with highly atrophic inflammation observed throughout the area (Figure 1).

Although there were no findings of anastomotic leakage, there was severe mucosal damage of the diverted colon. Therefore, we decided to use synbiotic therapy for the purpose of improving the mucositis prior to the stoma closure.

We inserted a Nelaton catheter (TERUMO, Tokyo) into the anal side intestine using the patient's stoma, and then, via the catheter, administered 1 pack of GFO (glutamine, fiber, oligosaccharides; Otsuka, Tokushima) and 2 g of Miya-BM (Clostridium butyricum MIYARI; Miyarisan Pharmaceutical, Tokyo) dissolved in 100 ml of lukewarm water for 1 hour. We administered this dose twice during the first week, and confirmed that the patient had neither diarrhea nor abdominal pain. Starting on the second week, we administered 2 packs of GFO (Otsuka) and 2 g of Miya-BM (Miyarisan Pharmaceutical) in 200 ml of lukewarm water to the patient twice a week for a total of 4 weeks.

After the synbiotic therapy, colonoscopy showed there was a marked improvement in the mucositis findings (Figure 1). As a result, the patient then underwent stoma closure and was discharged 10 days after the operation without any complications.

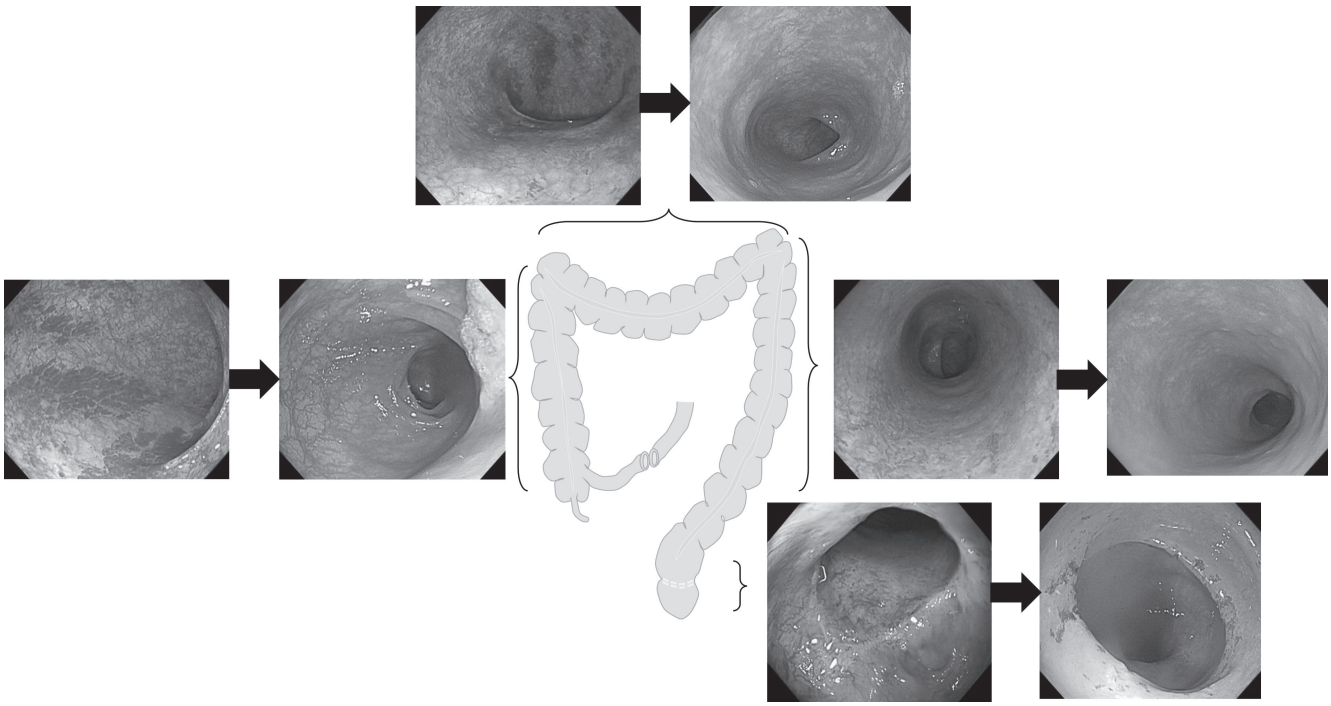

Figure 1. Colonoscopic findings for a diverted colon. Colitis with mucosal atrophy was observed in all areas of the large intestine. After synbiotic therapy, there was significant improvement of the diversion colitis. The photos on the left are from before the treatment, while the ones on the right are from after the treatment.

Discussion

The number of cases of rectal cancer in Japan is steadily increasing, with the number of cases in 2018 exceeding 50,000.[3] With the development of automatic anastomotic devices, anus-conserving surgery has become widespread in rectal cancer surgery.[4] In recent years, NCRT has increased the possibility of anal preservation.1 In contrast, anastomotic leakage after low anterior resection for rectal cancer is one of the most troublesome complications, with a reported frequency of approximately 10% to 15% according to the National Clinical Database in Japan and a similar database in the United States.[5,6] It has also been reported that use of a diverting stoma is recommended for anastomoses that are within 5 cm of the anal verge when a low anterior resection is performed.[7] This temporary stoma is positioned and used as a way of preventing aggravation of anastomotic leakage when it occurs.[8]

Under conditions where the gastrointestinal tract is not used, such as during fasting, the intestinal mucosa atrophies, which in turn leads to deterioration of mechanical and immunological barrier functions.[9,10] This can be a factor in bacterial translocation.[11] The diverted colon has been shown to have a similar environment.[12] Furthermore, if chemotherapy is administered before or after surgery, this area will be further exposed to an environment that causes drug-induced mucosal damage.[13] Therefore, prior to the stoma closure, mucosal evaluation of the diverted colon is considered essential, and when colitis is observed, treatment is required.

The main energy substrate of the small intestine mucosal cells is glutamine, with most of the involved pathways directly incorporated into cells through the brush border membrane.[14] Furthermore, the colonic epithelium derives much of its energy supply from fatty acids that are present in the colonic lumen, especially butyric acid, which is the result of bacterial fermentation of carbohydrates.[15] Therefore, in order to improve the mucosal function of the diverted colon, it is necessary to administer treatments with an understanding of these background factors. As a result, we have adopted the use of synbiotic therapy. We used Miya-BM (Miyarisan Pharmaceutical) as the probiotic and GFO (Otsuka) as the prebiotic. GFO (Otsuka) is a food that contains glutamine, dietary fiber and oligosaccharides. Water-soluble fibers and oligosaccharides are metabolized by intestinal bacteria to produce short-chain fatty acids (SCFAs). SCFAs are used as the main energy source for the colonic mucosal cells. For these reasons, we used GFO (Otsuka). Miya-BM (Miyarisan Pharmaceutical) is a probiotic that uses Clostridium butyricum MIYARI and produces SCFAs. Among the SCFAs, butyric acid has been reported to be not only the main energy source of intestinal epithelial cells, but also has been shown to play a role in growth promoting, anti-inflammatory and anti-ulcer effects on intestinal epithelial cells in rats.[16,17]

At our hospital , we not only evaluate the anastomotic site but also the diverted colon mucosa by colonoscopy prior to the stoma closure. We use the Mayo score,[18] as it allows for ease of evaluation of endoscopic findings, with synbiotic therapy prior to stoma closure considered to be indicated if a score of 2 (moderate) or higher is observed. We have performed synbiotic therapy in 2 cases, including this present case, prior to stoma closure. In both cases, the results have shown there was remarkable improvement of the severe mucosal damage of the diverted colon. Although there have also been other reported treatments, such as 5-aminosalicylic acid (5-ASA) enema and steroid enema,[19] potential side effects need to be carefully evaluated in all patients. When inflammation is localized to the anal side in ulcerative colitis and Crohn's disease, topical treatments such as 5-ASA enema and steroid enema are used. The side effects of 5-ASA are wide-ranging and can include allergic reactions and chemical toxicity. Symptoms observed during usage include fever, diarrhea, abdominal pain, bloody stools, liver dysfunction and rash, among others.[20] Although steroid enema can reduce the amount absorbed into the whole body, observed side effects can include moon face, diabetes, acne vulgaris, infectious diseases, gastrointestinal symptoms such as stomach pain and bloating, among others. In contrast, there are no peculiar side effects that have been reported for Miya-BM (Miyarisan Pharmaceutical). Thus, the results found for the present treatment method can be considered to be indicative of a therapeutic approach that demonstrates superior facility, safety, and efficacy.

Because NCRT utilization is expected to increase in the near future, it is likewise expected that temporary stoma construction will increase in conjunction with radical resection procedures for rectal cancer. Therefore, reducing the complications of stoma closure will be an important challenge to tackle. Examination of the indications for preoperative synbiotic therapy and the effect of synbiotic therapy on reducing postoperative complications after stoma closure are issues that will need to be further examined by evaluation of more cases. However, if diversion colitis is observed, the method described herein can be easily performed and may be exceedingly useful to improve atrophy.

Conflicts of Interest: None

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