Clinical Case Report

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Successful closure of ileostomy in a patient with intestinal Behçet's disease after therapy with adalimumab

A case report

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Abstract

Rationale: Behçet's disease (BD) is a chronic immune-mediated inflammatory disorder involving multiple organ systems. In BD, intestinal ulcers can present as a refractory lesion capable of perforation, which makes the choice of treatment difficult.

Patient Concerns: A 34-year-old male who was diagnosed with intestinal BD and suffered with an ileocecal perforation. He underwent surgery for an ileostomy and was given corticosteroids as treatment. However, the ulcerative lesion remained resistant to the therapy that was provided which delayed the closure operation.

Diagnosis: Intestinal BD with severe post-operative complication.

Interventions: A course of adalimumab (ADa) therapy was started. Subsequently surgery was performed. And ADa and thalidomide were used as a maintenance therapy.

Outcomes: In this case, a course of ADa therapy was given which healed the intestinal ulcers and allowed us to successfully perform the closure operation.

Lessons: This case indicates that ADa may be an effective treatment option in future cases, minimizing complications and allowing the closure operation to be performed successfully.

Abbreviations: Ada = adalimumab, BD = Behçet's disease, PSL = prednisolone, TNF = tumor necrosis factor.

Keywords: adalimumab, closure operation, ileostomal ulcer, intestinal behçet's disease, TNF-α monoclonal antibodies

1. Introduction

Behçet's disease (BD) is a chronic systemic immune-mediated inflammatory disorder characterized by recurrent oral and genital ulcers, uveitis, and cutaneous lesions. In addition, vascular and neurological system, as well as the intestinal track can also be involved in BD.[1,2] Although BD is not a life-threatening disease, vascular, neurological, and intestinal manifestations can cause significant impairment to the patients' health.[3] According to previous data, intestinal BD tends to have a higher prevalence in East Asia compared to Western or Mediterranean regions.[4] To date, BD treatment is mainly dependent on the use of corticosteroids, colchicine, and different disease-modifying antirheumatic drugs (DMARDs), alternative therapies are eventually needed.

In several studies, anti-tumor necrosis factor (TNF)-α monoclonal antibodies, such as adalimumab (ADa) and infliximab have been shown to be effective for intestinal BD. ADa was approved in Japan for intestinal BD in May 2013,[5] but is still not widely used in China. On the whole, these data have allowed an increasing off-label use of these agents in refractory BD manifestations. This report is about a case of BD with intestinal fistulization and refractory intestinal ulcers that were successfully treated with ADa on a Chinese male patient.

2. Case report

The 34-year-old male had a history of recurrent oral aphthous ulcers, uveitis and erythema nodosum since 2012, and was diagnosed with BD in 2013. He was prescribed with oral corticosteroids which relieved his symptoms. However, on June 2016, the patient suffered from severe abdominal pain and was taken to the emergency department of another local hospital. After examination, the patient was diagnosed with diffuse peritonitis because of a small bowel perforation and subsequently underwent partial small bowel resection and ileostomy (Fig. 1A). The

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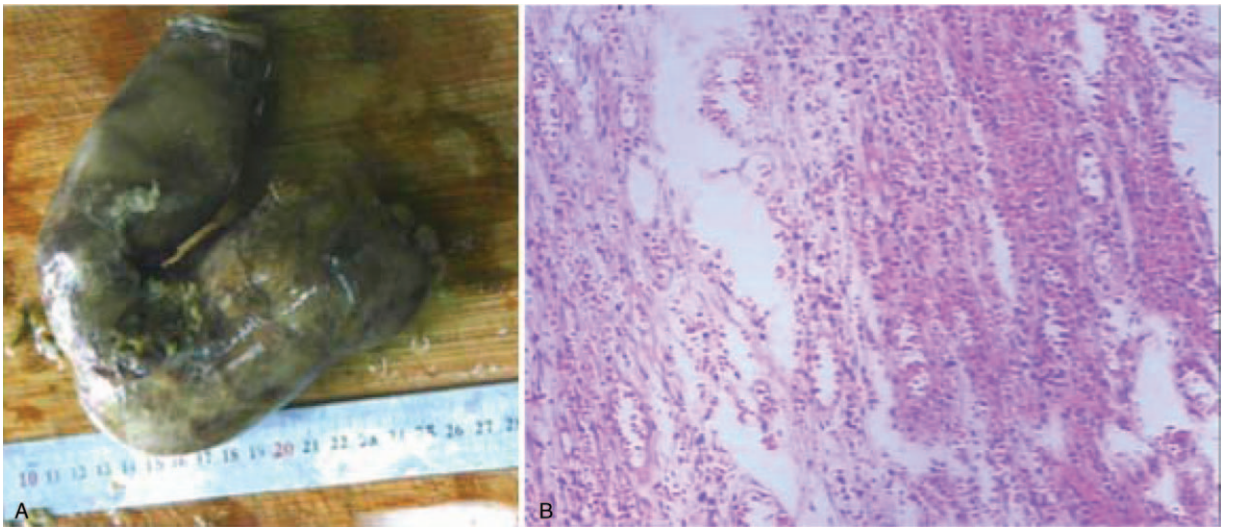

Figure 1. A. Resected small bowel with perforation. B. Pathological examination of the resected small bowel showed marked infiltration of lymphocytes and neutrophils along the full-thickness of the intestines.

pathology of the resected small bowel showed a marked infiltration of lymphocytes and neutrophils that extended through the whole thickness of the intestinal wall (Fig. 1B). Post-surgery, the patient had persistent refractory bowel and intestinal ulceration associated with intestinal BD. Considering the situation, the return operation was not deemed feasible at that time. Consequently, after the initial surgery, the patient could only survive by fistulization which hindered his daily work and life. So in August 2017, he came to our hospital for further treatment. According to the treatment criterion for intestinal BD proposed by Lee et al,[6] an anti-TNF α agent was considered for this patient, and ADa combined with prednisolone (PSL) and thalidomide was then selected.

Since there is no protocol for the use of anti-TNF-α agents in BD, we followed Japanese guidelines. The dose of ADa for BD therapy was 160 mg at week 0, 80 mg at week 2, and then followed by 40 mg every other week.[5] Before using ADa, ulcers were observed at the opening of the fistula both visually (Fig. 2A) and by endoscopy (Fig. 3A). In response to ADa treatment, the bowel ulcers improved markedly at week 6 after 3 injections (Fig. 2B) and had almost completed remission at week 10 (Fig. 2C) after 5 injections assessed with endoscopy (Fig. 3B). We administered a gradually decreasing amount of PSL during the period of ADa treatment and stopped using PSL for preoperative preparation at week 10 (Fig. 4). A selective closure operation was scheduled for the patient after the endoscopic examination at week 14 (Fig. 3C). Follow-up 6 months post-operation showed that the patient had a full recovery (Fig. 5) without new-onset gastrointestinal manifestations under treatment with ADa 40 mg every other week and 100 mg per day of thalidomide as a maintenance therapy (Fig. 4).

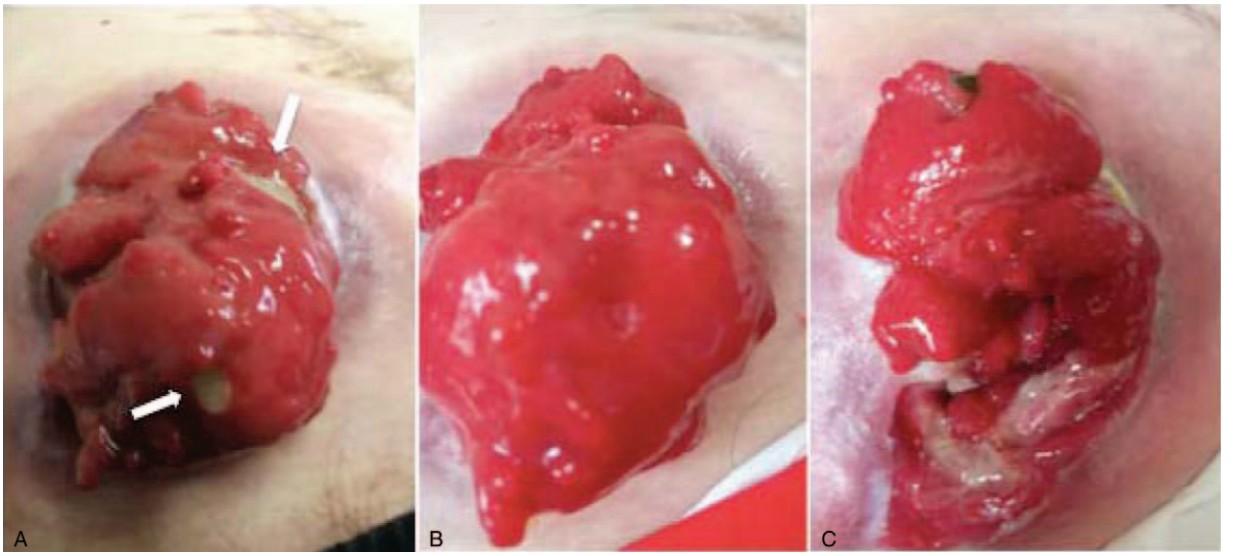

Figure 2. A. Week 0: 2 ulcers in bowel (write arrow) can be observed before treatment with adalimumab; B. Week 6: After therapy with adalimumab for 6 weeks; C. Week 10: After therapy with adalimumab for 10 weeks.

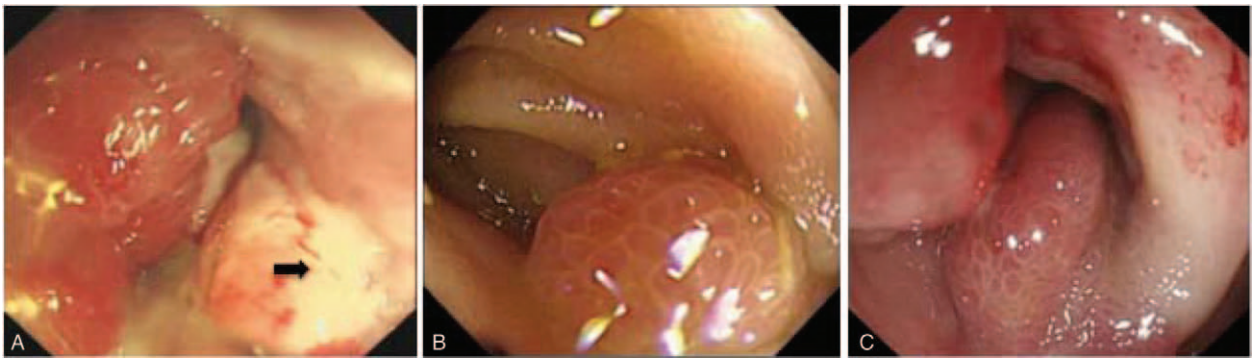

Figure 3. A. Before using Adalimumab, an ulcer of 1.2 cm diameter was observed in the opening of the fistula by endoscopy (black arrow). B. After 10 weeks therapy with Adalimumab, ulcer has been healed. C. After 14 weeks therapy with Adalimumab, ulcer has been completely healed.

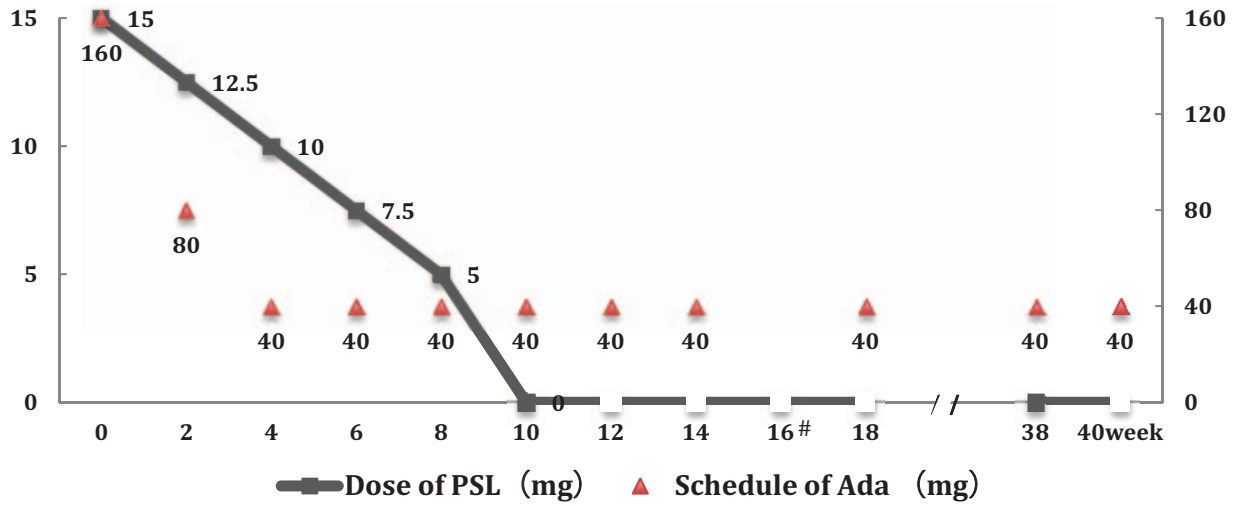

Figure 4. Schedule of therapy for the patient. PSL: prednisolone, Ada: adalimumab. #Closure operation was performed at week 16. To avoid postoperative infection, both Ada and thalidomide were suspended at the week of operation. Ada 40 mg every other week and thalidomide 100 mg/d were used as a maintenance therapy until now (week 40).

3. Discussion

BD is a chronic immune-mediate inflammatory disorder involving multiple organ systems. The main clinical manifestations include oral or genital ulcers, ocular inflammation, and skin lesions. In addition, gastrointestinal and neurological manifestations can also occur.[1] The diagnosis of intestinal BD is usually based on clinical symptoms and typical gut ulcerative lesions.[7] Although the diagnosis of intestinal BD is

Figure 5. A. Whole view of patient's abdomen before surgery. B. Whole view of patient's abdomen after surgery. C. 1 month after closure surgery.

highly definitive, the treatment for gut lesions is still troublesome due to refractory intestinal ulceration and perforation.[8,9] Recurrent gut lesions are also a post-operative complication that requires precise protocols regarding the treatment strategy.

Intestinal BD is associated with abnormal T-cell immune response and T helper type 1 associated cytokines such as TNF-α will play a critical role in disease.[10] Based on this mechanism and clinical data, in 2014, the 2nd edition of consensus states that anti-TNF-α agents should be considered as standard therapy for intestinal BD.[11] To date, several observational studies performed in Japan and Italy indicate a long-term safety and efficacy of ADa in BD patients.[12,13] Infliximab has also been proved effective for recurrent ulcers complicated with BD.[14,15] In 2015, ADa was approved for treatment of intestinal BD in Japan.[5] Therefore, more studies on anti-TNF-α agents for treatment of intestinal BD,[16] particularly information of the therapeutics effects, should be accumulated to expand the new treatment guidelines.

Crohn's disease (CD) is also a chronic inflammatory disorder, which has similar pathogenesis and clinical features to intestinal BD. Fistula, which is a common complication of CD, may also be difficult to manage. Infliximab was first used to treat a patient with Crohn's disease accompanied by duodenopancreatic fistula in 2009 with great success,[17] opening a new vision of CD treatment. In 2016, ADa was first used to successfully treat a patient with Crohn's disease accompanied duodenobiliary fistula. This was also the second attempt to use anti-TNF-α agents to treat CD patients complicated fistula.[18] In this case, the patient was resistant to the systematic administration of corticosteroid and immunosuppressant treatment. In addition, due to active BD, ileostomy closure operation could not be performed. Ishioka M et al improved the para-ileostomal ulcer with infliximab and enabled the surgery for ileostomy closure.[19] To explore more possibilities, we decided to use ADa for intestinal BD treatment in this case. ADa not only markedly improved and caused remission of the bowel ulcers, it also led to reduced intestinal inflammation and remission of gut lesions, allowing the closure operation to be successfully performed.

To our best knowledge, this is the first reported case of intestinal BD complicated with ileostomy which was treated preoperatively with ADa, and then followed by a successful closure operation. This case indicates that ADa may be considered as a treatment option in cases of ileostomy associated with intestinal BD during the perioperative period, as well as a maintenance therapy.

Author contributions

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Project administration: Qi-Bing Xie.
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