gastrointestinal disorders

MDPI

Case Report

Infliximab and Plant-Based Diet as First-Line Therapy Followed by Corticosteroid Therapy for Severe Ulcerative Colitis: A Case Report

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Abstract: We developed infliximab and a plant-based diet as first-line (IPF) therapies for severe ulcerative colitis (UC). It increased the remission rate and decreased the colectomy rate compared to those of current standards. We encountered a case with severe UC in which the consecutive use of IPF therapy and corticosteroid therapy was required to induce remission. A 21-year-old male worker developed diarrhea, abdominal pain, marked weight loss from 70 to 55 kg, and anorexia. He was diagnosed with severe ulcerative colitis. IPF therapy was initiated. Improvement in symptoms and biomarkers was seen soon after the first infusion of infliximab (300 mg). Further improvement in symptoms was observed after both the second and third infliximab infusions. Loose stool and abdominal pain on defecation were still present, however, and biomarkers were above the reference range. Therefore, oral prednisolone (40 mg/day) was consecutively initiated. This resulted in clinical and endoscopic remission. In conclusion, we present a severe UC case in which the response to IPF therapy was insufficient. Consecutive oral prednisolone successfully induced remission. This new stepwise modality will make IPF therapy the first-choice therapy for severe UC.

Keywords: infliximab; plant-based diet; ulcerative colitis; severe; case report; therapy; diet; anti-proteinase 3 antineutrophil cytoplasmic antibodies

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1. Introduction

Together, ulcerative colitis (UC) and Crohn's disease (CD) form inflammatory bowel disease (IBD). IBD was once recognized as a disease of the US and western Europe. The incidence of IBD, however, has been rising since the end of the 20th century in areas where it was previously rare, and thereby IBD has become a global disease. It affects all ages, but the peak incidence is between 15 and 25 years old. The clinical course is characterized by periods of remission and relapse. UC affects mainly the large bowel, whereas CD affects the whole digestive tract. In UC, chronic bloody stool or bloody diarrhea is the main symptom. UC is classified into three types by the extent of inflammation (E1 proctitis, E2 left-sided colitis, and E3 pancolitis) and into four types by severity (S0 clinical remission, S1 mild, S2 moderate, and S3 severe) [1]. Treatments for UC include 5-aminosalicylic acid drugs, glucocorticoids, immunosuppressants, and biologics. The treatment strategy is based on the severity and extent of the disease [2,3].

We assert that the ubiquitous environmental factor in IBD is a westernized diet [4]. Consequently, we developed and began to provide a plant-based diet (PBD) to replace an omnivorous (westernized) diet for IBD patients in 2003 [5]. We published far better outcomes in terms of both induction and relapse rate in both UC and CD as compared with the current standard [5–9]. Consequently, we recommended PBD for IBD [10]. In CD and severe UC, infliximab and PBD are administered as first-line (IPF) therapy [6,8,9].

Severe UC develops in 10–25% of UC patients [2,11,12]. It is a potentially life-threatening disease, with a 1% mortality rate [12–14]. The first choice of treatment for severe UC in the current guidelines is intravenous corticosteroids [3,15]. Second-line rescue therapy in cases unresponsive to corticosteroids is either infliximab or cyclosporine [2,3,12,16]. There are drawbacks to corticosteroid use: between 16 and 34% of the patients are non-responders [13,17–19], long-term use of the drug for a few months, well-known adverse effects of the drug [20], and corticosteroid dependence or surgical intervention in nearly 50% of the patients at 1 year, even though corticosteroids are effective in the induction phase [18]. Therefore, we switched to infliximab and a plant-based diet as first-line (IPF) therapy for severe UC. We experienced a higher remission rate [76% (13/17)] and lower colectomy rate [6% (1/17)] with IPF therapy [8] compared to 40–58% and 18–34%, respectively, achieved with the current intravenous corticosteroid treatment [13,17,19]. There were no cases of corticosteroid dependence or additional colectomy at 1-year follow-up [8]. We subsequently encountered a case with severe UC in which the consecutive use of IPF therapy and corticosteroid therapy was required to induce remission.

2. Case Presentation

The present case was a 21-year-old male with chronic diarrhea, anorexia, weight loss, and abdominal pain. He left his hometown after graduating from high school at 18 years old. He has worked for his present employer for almost one year. He had three bowel movements a day and his body weight was around 70 kg. He likes to play basketball. At the beginning of November 2021, he practiced basketball harder than before, preparing for a game after work. He gradually could not do his own cooking and bought ready-made foods. Soon he noticed diarrhea, with the frequency of diarrhea increasing to more than 10 times a day at the end of November (Figure 1). Anorexia then appeared in the middle of December. His body weight decreased to 55 kg. He visited a practitioner in vain and returned to his hometown at the end of December. At the beginning of January 2022, a gastroenterologist in his hometown found diffuse inflammation in the rectosigmoid (Figure 2a) and tentatively diagnosed UC (Figure 1). He was then referred to and admitted to our hospital.

The physical examination was non-contributory. Anal fistula and anal skin tags were absent. He was tentatively diagnosed with severe UC due to his history, mild anemia (hemoglobin 12.1 g/dL), hypoalbuminemia (3.5 g/dL), increased C-reactive protein (CRP) (5.13 mg/dL) (reference range $\leq$ 0.14) and elevated erythrocyte sedimentation rate (ESR) (47 mm/h) (reference range $\leq$ 10). The fecal immunochemical test was more than 1000 ng/mL (reference range $\leq$ 100). IPF therapy with 300 mg of infliximab and 800 kcal of PBD was initiated on the 3rd hospital day (Figure 1). Our PBD was a lacto-ovo-vegetarian diet. Fish was served once a week and meat once every two weeks, both at about half the average amount. The mean $\pm$ SD% of protein, fat, and carbohydrates of the diet was 16.1 $\pm$ 0.5, 18.6 $\pm$ 1.4, and 66.1 $\pm$ 1.6, respectively. In the case of a 2000-kcal diet, it contained 32.4 $\pm$ 2.1 g of dietary fiber, 19.3 $\pm$ 1.3 mg of iron, 10.9 $\pm$ 0.8 g of salt, and 285.9 $\pm$ 72.1 mg of cholesterol [5]. His abdominal pain improved, and the frequency of diarrhea decreased to less than 10 times a day. He became able to eat meals. On the 7th hospital day, CRP decreased to 1.06 mg/dL (Figure 1). The diagnosis of UC was confirmed soon after the IPF therapy. The pathological findings were consistent with UC, i.e., crypt abscesses, goblet cell depletion, and infiltration of polymorphs, lymphocytes, and plasma cells (Figure 3). Negative findings were found for pathogen stool culture, CD Chek (Techlab C Diff Quik Chek Complete; Techlab Inc., Blacksburg, VA, USA), COVID-19 antigen test (HISCL; Sysmex, Kobe, Japan), cytomegalovirus antigenemia, tuberculosis, and hepatitis B infection. On the other hand, he had a low-grade fever in the evenings. The following tests for the fever were normal: T3, T4, thyroid stimulating hormone, immunoglobulin (Ig) G, IgA, IgM, IgG 4, C3, C4, CH_{50}, and KL 6. Monoclonal proteins were absent. Antinuclear antibodies were 80$\times$ (reference $\leq$ 40$\times$), but double-strand DNA antibodies were negative. Anti-proteinase 3 antineutrophil cytoplasmic antibodies (anti-PR3 ANCA) were 124 U/mL

(reference range < 3.5), but anti-myeloperoxidase antineutrophil cytoplasmic antibodies were negative. It seemed to be a favorable course. CRP and ESR, however, did not improve week by week (Figure 4). After a 2nd infusion of infliximab (16th hospital day), further improvement of appetite resulted in an increase in PBD from 1100 kcal/d to 1400 kcal/d. Diarrhea changed to loose stool 4–5 times a day. On the 23rd hospital day, a barium enema study revealed pancolitis (Figure 5). After the 3rd infusion of infliximab (42nd hospital day), the low-grade fever disappeared. At this point, loose stool and abdominal pain on defecation were still present, and CRP and ESR were above the reference range (Figures 1 and 4). Therefore, oral prednisolone (40 mg/d) was initiated on the 48th hospital day. Improvement in symptoms and the above inflammatory markers was seen. The dose of prednisolone (10 mg) was decreased weekly. Sulfasalazine (2 g/d) was initiated to be administered on the 55th hospital day. Normal stool appeared once a day and abdominal pain disappeared by the 63rd hospital day (Figure 1). Azathioprine was initiated to prevent corticosteroid dependence and future relapse. Endoscopic remission was observed on the 73rd hospital day (Figure 2b), and he was discharged (Figure 1). He was advised to continue with the PBD after discharge. Prednisolone was withdrawn 3 days after discharge. He rested at home for one and a half months and then returned to the previous city to restart his work. He was on sulfasalazine and azathioprine and was referred to a doctor in the city.

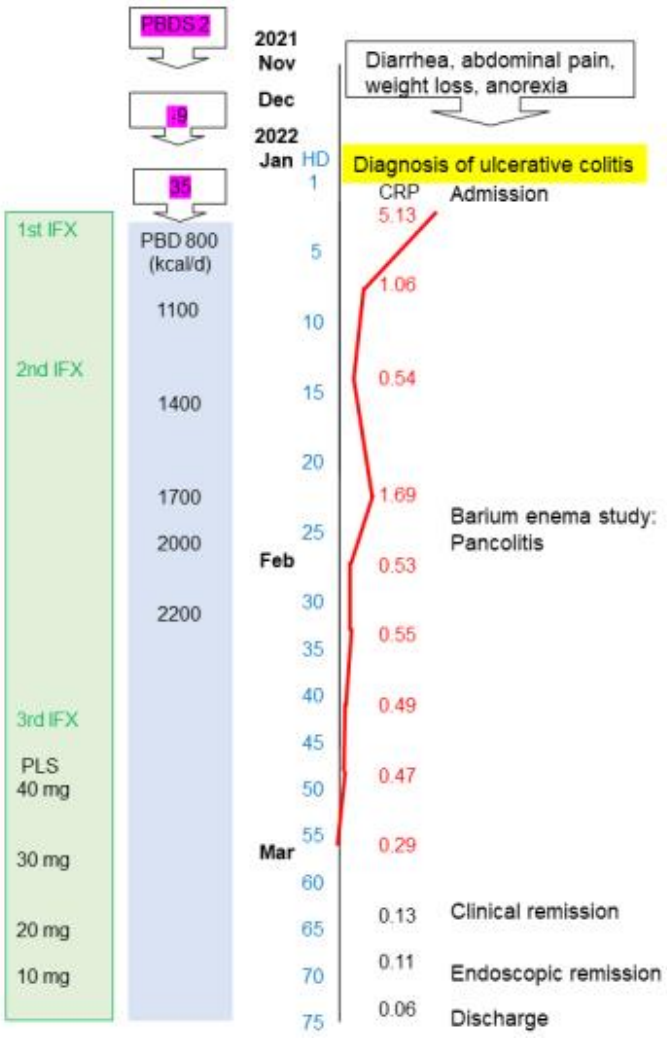

Figure 1. Timeline of the case. IFX, infliximab; PLS, prednisolone; PBD, plant-based diet; PBDS, plant-based diet score; HD, hospital day; CRP, C-reactive protein. Abnormal CRP (normal range $\leq$ 0.14 mg/dL) levels are shown in red.

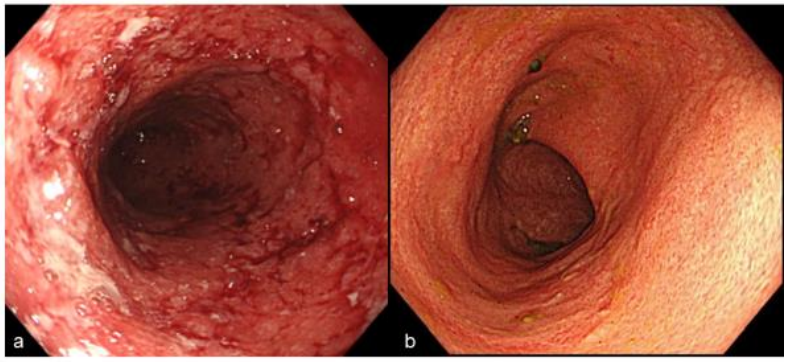

Figure 2. Colonoscopic images before (**a**) and after (**b**) treatment. Diffuse continuous rough-surfaced mucosa was observed in the sigmoid colon. Adherent mucous, redness, and blood clots were seen (**a**). Smooth-surface mucosa was observed in the sigmoid colon. Active findings before treatment were no longer seen (**b**).

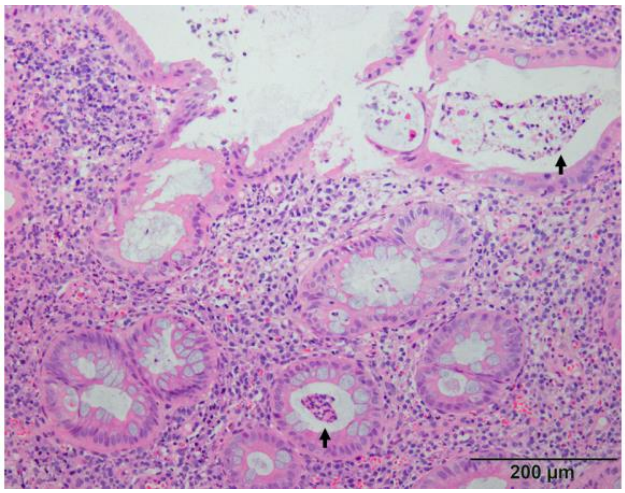

Figure 3. Photomicrograph of the biopsy specimen from the sigmoid colon. Crypt abscess (arrows), goblet cell depletion, and mononuclear cell infiltration were observed.

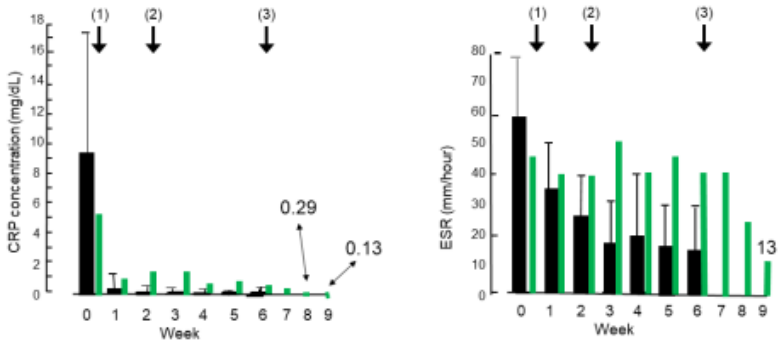

Figure 4. Change in C-reactive protein (CRP) concentration (left panel) and erythrocyte sedimentation rate (ESR) (right panel) before and after infliximab and plant-based diet as first-line (IPF) therapy followed by corticosteroid therapy for severe ulcerative colitis. The solid black bar denotes the mean, and the thin line shows SD in 13 patients with severe ulcerative colitis who achieved clinical remission with infliximab and plant-based diet as first-line (IPF) therapy [8]. The green solid bar denotes the values in the present case. Arrows with a number in brackets indicate three infliximab infusions, at weeks 0, 2, and 6. In a previous study [8], the normal range of CRP concentration was $\leq$0.3 mg/dL, and it was $\leq$0.14 in the present study. The normal range of ESR in males and females is $\leq$10 mm/h and $\leq$15 mm/h, respectively.

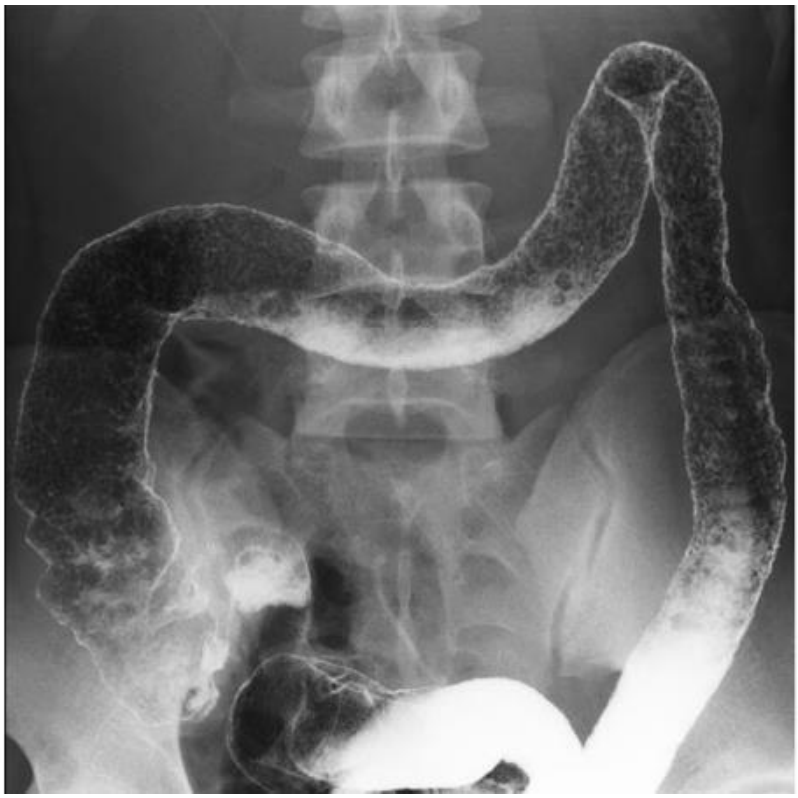

Figure 5. Roentgenogram of a double-contrast barium enema study on the 23rd hospital day. Coarse mucosa, irregular border, shortening of the bowel, and loss of haustration in the right and transverse colon were observed. It indicated active pancolitis.

His plant-based diet score (PBDS) [21], which evaluates adherence to PBD, was 2 when he cooked his own meals and −9 after he stopped cooking his own meals (Figure 1). His PBDS during hospitalization was 35. A higher PBDS indicates greater adherence to PBD.

3. Discussion

There were some characteristic findings in the present case. He did not notice any bloody stool, but stool occult blood was strongly positive (>1000 ng/mL). The absence of bloody stool might have delayed his visit to a practitioner, and it seemed that hemoglobin did not decrease below 10.5 g/dL, one of the criteria for severe UC [1], due to the absence of bloody diarrhea. Although his body temperature was lower than 37.5 °C, another one of the criteria for severe UC [1], a low-grade fever in the evenings became apparent after the 1st infliximab infusion. On the other hand, anorexia and marked weight loss were dominant in the present case. These are not the typical manifestations of UC. His baseline PBDS, i.e., 2 and −9, when he cooked his own meals and after he stopped doing so, respectively, were exceptionally low compared 10.9 ± 9.5 (mean ± SD) of 159 UC patients [21]. This means that his diet was extremely unhealthy as compared to the average UC patient. The Anti-PR3 ANCA was positive in this patient. According to Imakiire et al., PR3 ANCA positive UC was more severe than its negative UC [22]. The PR3 ANCA titer in our patient was 124, which is higher than that in the 45 positive patients in the study by Imakiire et al. [22].

The above factors may have influenced disease severity and the response to IPF therapy. Each of the three infliximab infusions was effective in improving symptoms. Improvement of biomarkers, i.e., CRP and ESR, however, was different from those shown in patients who achieved remission with the same IPF therapy in our previous study (Figure 4). Consequently, prednisolone was consecutively administered. Because his condition was not severe, 40 mg/d instead of 60 mg was orally given. This corticosteroid therapy resulted in successful clinical and endoscopic remission.

In conclusion, we recommend IPF therapy for severe UC. If its efficacy is insufficient, a corticosteroid can be consecutively administered to induce remission, as in the present case.

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Informed Consent Statement: Informed consent was obtained from the patient to publish this paper.

Data Availability Statement: The authors confirm that the data supporting the findings of this study are available within the article.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

Anti-PR3 ANCA	Anti-proteinase 3 antineutrophil cytoplasmic antibody
CD	Crohn's disease
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate
IBD	Inflammatory bowel disease
Ig	Immunoglobulin
IPF	Infliximab and plant-based diet as first-line
PBD	Plant-based diet
PBDS	Plant-based diet score
UC	Ulcerative colitis

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