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Single Case

Colonic Dilatation Complicating Acute Severe Ulcerative Colitis Managed Successfully with Accelerated Infliximab Dosing

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Keywords
Acute severe ulcerative colitis · Colonic dilatation · Accelerated infliximab regimen · Anti-interleukin-17 agents

Abstract
Lately, emerging data suggest an association between the development of inflammatory bowel disease and anti-interleukin-17 therapy. Megacolon is a life-threatening complication of acute severe ulcerative colitis (ASUC), but its treatment has not yet been established in current practice guidelines. We report a rare case of known psoriasis treated by secukinumab in a patient who presented with ASUC and colonic dilatation. Neither steroids nor standard infliximab regimen was effective. Finally, rescue therapy with accelerated infliximab strategy resulted in excellent recovery. In certain cases of steroid-refractory ASUC complicated by megacolon, accelerated infliximab regimen can be an alternative to surgery.

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Introduction

Recently, a few reports have stated that the incidence rate of developing inflammatory bowel disease (IBD) after treatment with anti-interleukin-17 (anti-IL-17) agents is low, which ranges from 0.4 to 0.7% [1–3]. In real-world evidence, there are eight cases of secukinumab-related ulcerative colitis that have been described from 2018 to 2021 [4–10]. In terms of acute severe ulcerative colitis (ASUC) complications, megacolon without toxicity has not been well characterized with only 3 case reports [11, 12]. These cases, however, had colonic dilatation of less than 10 cm. We herein present a unique case of ASUC with transverse colon dilatation of 11 cm after exposure to secukinumab which was successfully managed by accelerated infliximab regimen.

Case Report

A 22-year-old man with a past medical history of plaque psoriasis who was being treated with secukinumab was admitted to our hospital due to bloody diarrhea. He was diagnosed with severe plaque psoriasis 4 years ago. At first, he did not respond to steroids, so he was started on secukinumab, which induced remission and was maintained at 150 mg monthly. Four months prior to this admission, he developed lower left quadrant abdominal pain accompanied by hematochezia, 2–3 bowel movements per day. At a local hospital, colonoscopy was performed, which revealed marked erythema and friability in the rectal and sigmoid colon. Pathology from the sigmoid colon showed chronic, undetermined colitis. Low-dose mesalamine was commenced for colitis in parallel with secukinumab. Two months later, his symptoms worsened, so the dose of mesalamine was increased to 3 g per day, but no improvement was observed. One week before admission, he described his stools as more frequent, with 30–40 per day, small volume, bloody and tenesmus, while his colonoscopy displayed lesions extending to the transverse colon (shown in Fig. 1). His condition deteriorated rapidly, so he was admitted to our hospital.

His abdomen was moderately distended with lower left quadrant tenderness on palpation. The remainder of the physical examination was normal. Computed tomography of the abdomen with intravenous contrast material revealed air-filled small bowel and colon with 8 cm diameter (shown in Fig. 2a). Laboratory test results were significant for a white blood cell count of 24.92 G/L with 88.7% polymorphonuclear leukocytes, high C-reactive protein (CRP) (152.8 mg/L), hypoproteinemia (52 g/L), and hypoalbuminemia (22.8 g/L). Fecal calprotectin was moderately elevated at 214 μg/g. Enteric pathogens, including *Clostridium difficile*, were all negative based on stool studies. Cytomegalovirus inclusions were undetectable on colonic biopsy specimens 1 week prior to this admission (shown in Fig. 3a–d). After excluding some common colonic distention triggers such as electrolyte disturbances, adverse effects of antidiarrhea or opiates, the diagnosis of colonic dilatation complicating ASUC was established and methylprednisolone 60 mg per day was initiated. Three days later, although CRP slightly decreased (98.4 mg/L), his abdomen and bowel movement did not improve. A plain film radiograph of the abdomen showed severe transverse colon dilatation of 11 cm (shown in Fig. 2b). It was now steroid-refractory ASUC with megacolon, so steroid was stopped, infliximab (5 mg/kg) was utilized, and surgeons were consulted. Six days after infliximab initiation, the hematochezia nearly disappeared, but his abdominal distension was intact (shown in Fig. 2c). Colorectal surgical review was made again, but his family members firmly refused to accept it, so the accelerated infliximab regimen, the second dose of which started less than 1 week after the first one, was initiated. One week following the second infliximab dose, both of his symptoms, inflammatory

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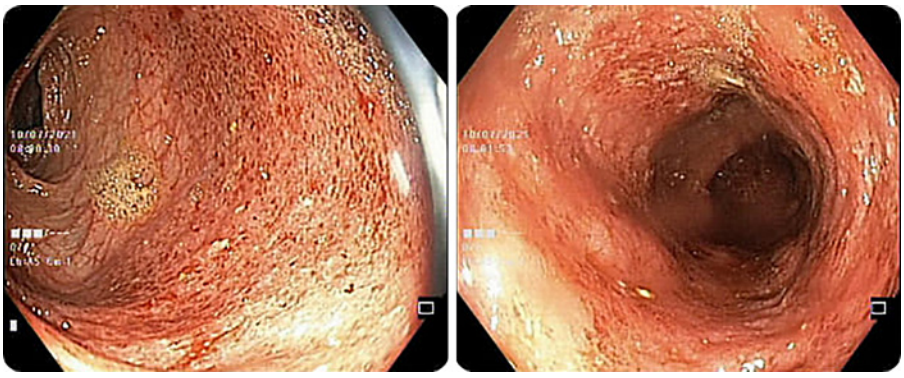

Fig. 1. Colonoscopy revealed marked erythema, absent vascular pattern lesions extending from the rectum to the transverse colon which was compatible with Mayo 2.

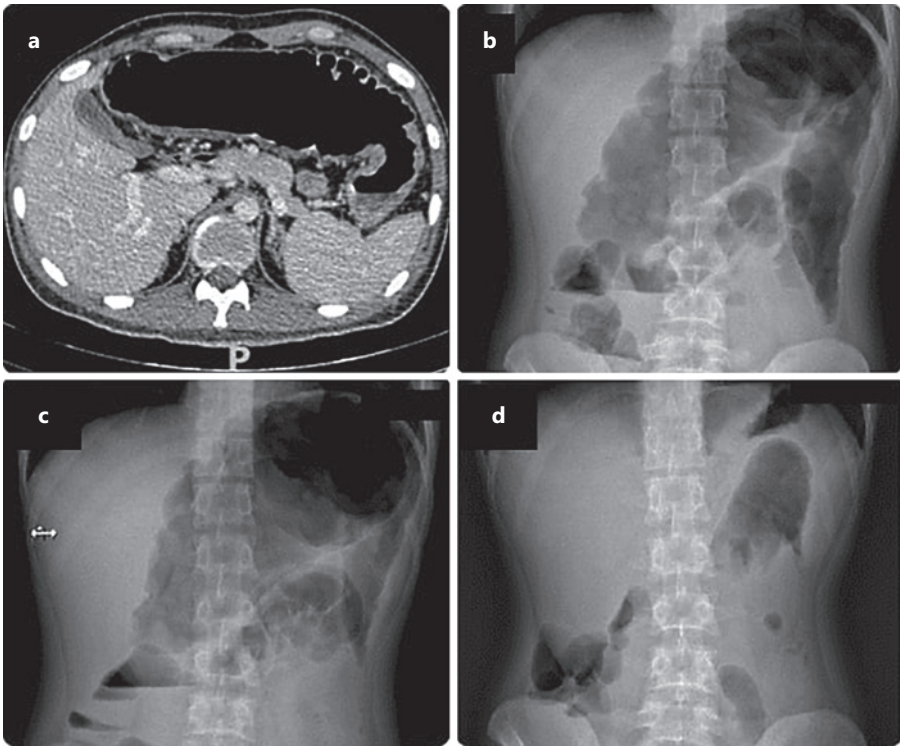

Fig. 2. a Computed tomography scan on admission day showed diffuse, mild thickening of descending colon with endorsement of mesenteric veins. The small bowel and colon were full of air and fluids, with a maximum diameter of 8 cm. However, there are no signs of bowel obstruction. **b** Plain abdominal X-ray on day 3, before starting infliximab. **c** Plain abdominal X-ray on day 9, 6 day after the first dose of infliximab. **d** Plain abdominal X-ray after two accelerated infliximab doses.

markers (CRP of 27 mg/L, white blood cell count of 7.41 G/L), and the dilatation of the transverse colon, significantly improved (shown in Fig. 2d). After 4 doses of induction (weeks 0–2, 4), maintenance of 5 mg/kg infliximab every 8 weeks was used for the treatment of ulcerative colitis and plague psoriasis. One year later, his symptoms had been fully controlled and his colonoscopy revealed mucosa with Mayo 0, many pseudopolyps (shown in Fig. 4).

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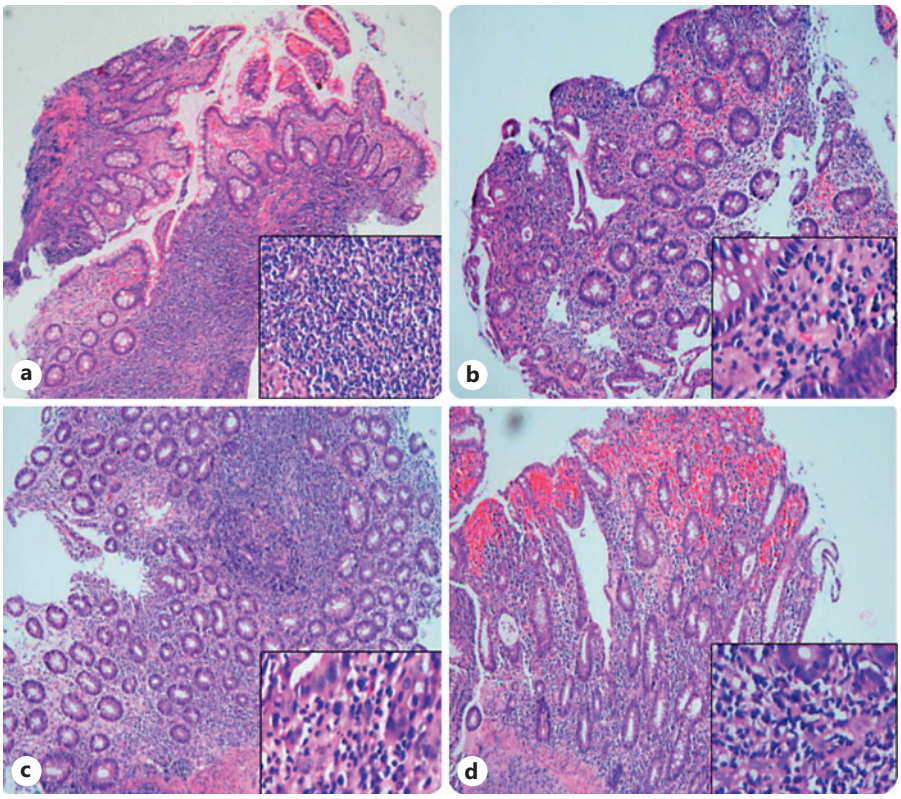

Fig. 3. Specimen biopsies demonstrated cryptitis, some crypt abscesses, and erosive epithelium (**a**), transverse colon (**b**), descending colon (**c**), sigmoid colon (**d**) revealed edema mucosa with severe lymphoid aggregates intermingling with neutrophils in the lamina propria (HE. ×100). The intact figures (HE. ×200) demonstrated dense basally between the lamina muscularis mucosa and crypt bases (basal plasmacytosis). A portion of submucosal specimens revealed less inflammation than those of mucosa. Either normal crypt or dysplasia was not represented in the biopsies of the left colon.

Discussion

The pathogenesis of secukinumab-induced IBD has not been clearly understood. In terms of molecular mechanism, IL-17 overproduction has a negative impact on the skeletal system, while it plays a key role in protecting the gastrointestinal tract from bacterial and fungal infections [13]. Therefore, the inhibition of IL-17 may promote the development of IBD.

We summarized information from eight case reports of ulcerative colitis associated with secukinumab in real-world setting (shown in Table 1). The median time from the onset of secukinumab to the diagnosis of ulcerative colitis was 5 (range: 3–12) months, while it was 24 months in our case. Most cases, including our case, were male and presented with ASUC. Intravenous steroid was the first line of treatment for ASUC, according to current guidelines, but it failed in all of these cases. Infliximab seemed to be effective as rescue therapy because it prevented emergency colectomy in 4 cases. Only one patient underwent surgery due to toxic megacolon associated with *Clostridium difficile*.

Toxic megacolon is a rare but fatal complication of severe colonic inflammation caused by ASUC or some infectious etiologies such as *Clostridium difficile* and *Cytomegalovirus*. According to Jalan et al. [14], the diagnostic criteria of toxic megacolon include radiographic evidence of the dilatation of the colon greater than 6 cm and symptoms of systematic toxicity.

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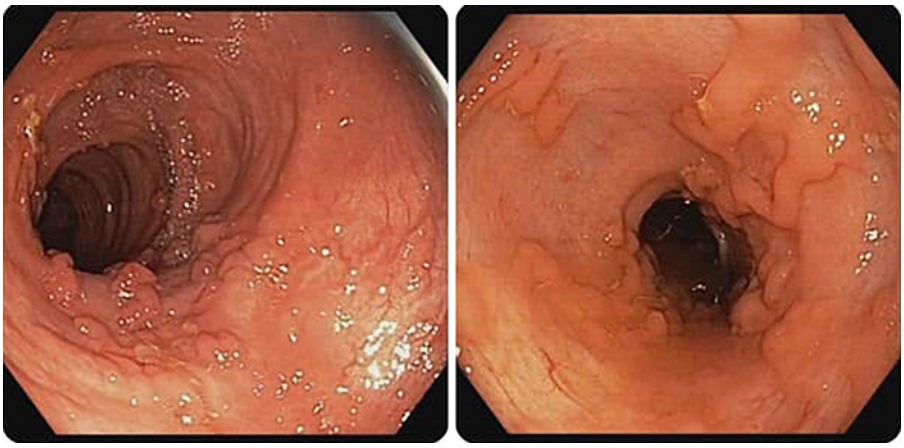

Fig. 4. Colonoscopy showed healed mucosa with multiple pseudopolyps 1 year later.

Table 1. Clinical presentation and treatment of case reports describing patients who developed ulcerative colitis after being treated with secukinumab

Clinical characteristics	
Age, years	40 (22–60)
Psoriasis	4/8
IBD personal history	1/8
Time from secukinumab treatment to onset IBD, months	5 (3–12)
ASUC	5/6 (2 cases did not mention)
First-line treatment	
Mesalamine	1/8
Steroids	6/8
Adalimumab	1/8
First-line treatment failure	8/8
Rescue therapy	
Infliximab	4/8
Adalimumab	1/8
Ustekinumab	2/8
Surgery	1/8

Although there are still some controversies with regard to the timing of surgery, the treatment protocol for toxic megacolon has been well described in the literature. In contrast, colonic dilatation in ASUC scenario, which may be the early stage of toxic megacolon, has limited case reports. Hayashi et al. [11] reported 2 cases of steroid-refractory ASUC with transverse colon dilatation of about 5–5.5 cm. Tacrolimus demonstrated effectiveness in both cases, although ganciclovir was added in one case because of CMV detection. Recently, Garate et al. [12] presented a case of ASUC complicated by *Clostridium difficile*-related megacolon. The dilatation of the transverse colon was rapidly resolved with oral vancomycin and intravenous steroids, but the hematochezia did not improve. Because the diarrhea and rectal bleeding persisted after the first dose of infliximab, the accelerated regimen was initiated with favorable results, which is similar to our case.

For many reasons such as high circulating levels of tumor necrosis factor, fecal loss of infliximab, and rapid drug degradation by the reticuloendothelial system, the standard infliximab regimen may be insufficient in ASUC [15]. In 2015, the retrospective study by Gibson et al. [16] showed that the accelerated regimen reduced the rate of early colectomy more than the standard one. Many later studies, however, did not demonstrate similar results [17, 18]. Disagreement in data could be due to differences in disease severity, dosing, starting time, and attending physician's decision. The British Society of Gastroenterology endorsed the accelerated regimen for patients who are not responding to a 5 mg/kg dose after 3–5 days, while the American Gastroenterological Association and American College of Gastroenterology did not [19–21]. High CRP/albumin ratio, like in our case, is a predictor of high-risk patients who will benefit from the accelerated regimen [22]. In addition, therapeutic drug monitoring may aid in choosing the most suitable candidate for this strategy as reported by Garate et al. [12].

In ASUS, colonic dilatation can be managed with medical treatment but should be closely monitored by a multidisciplinary team. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000529152).

Statement of Ethics

Informed written consent was obtained from the patient for the publication of their information and imaging in this journal. Consent is available to the editor upon request. Ethical approval is not required for this study in accordance with local or national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Nguyen CD, corresponding author, and Dang LM wrote the manuscript and reviewed the literature. Bui HH and Vo DNT edited the manuscript. All authors approved the final version of the manuscript.

Data Availability Statement

All data that support the findings of this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Orrell KA, Murphrey M, Kelm RC, Lee HH, Pease DR, Laumann AE, et al. Inflammatory bowel disease events after exposure to interleukin 17 inhibitors secukinumab and ixekizumab: postmarketing analysis from the RADAR ("research on adverse drug events and reports") program. J Am Acad Dermatol. 2018 Oct;79(4):777–8.
2 Schreiber S, Colombel JF, Feagan BG, Reich K, Deodhar AA, McInnes IB, et al. Incidence rates of inflammatory bowel disease in patients with psoriasis, psoriatic arthritis and ankylosing spondylitis treated with secukinumab: a retrospective analysis of pooled data from 21 clinical trials. Ann Rheum Dis. 2019 Apr;78(4):473–9.
3 Caron B, Jouzeau JY, Miossec P, Petitpain N, Gillet P, Netter P, et al. Gastroenterological safety of IL-17 inhibitors: a systematic literature review. Expert Opin Drug Saf. 2022 Feb 1;21(2):223–39.
4 Fobelo Lozano MJ, Serrano Giménez R, Castro Fernández M. Emergence of inflammatory bowel disease during treatment with secukinumab. J Crohns Colitis. 2018 May 9;12(9):1131–3.
5 Ehrlich D, Jamaluddin N, Pisegna J, Padua D. A challenging case of severe ulcerative colitis following the initiation of secukinumab for ankylosing spondylitis. Case Rep Gastrointest Med. 2018;2018:9679287.
6 Lee ASW, Levell NJ, Shah SN, Gaffney K, Tremelling MAW. Severe colitis complicating secukinumab (Cosentyx ®) therapy. Clin Exp Dermatol. 2020 Apr;45(3):344–5.
7 Achufusi TG, Harnee PS, Rawlins S. A rare case of new-onset ulcerative colitis following initiation of secukinumab. Case Rep Med. 2019 Jul 31;2019:2975631.
8 Vernero M, Astegiano M, Ribaldone DG. New onset of inflammatory bowel disease in three patients undergoing IL-17a inhibitor secukinumab: a case series. Am J Gastroenterol. 2019 Jan;114(1):179–80.
9 Johnston DN, Veettil R. A case of new onset ulcerative colitis following secukinumab treatment. Br J Hosp Med. 2019 Sep 2;80(9):544–5.
10 Uchida S, Oiso N, Komeda Y, Kudo M, Kawada A. Paradoxical ulcerative colitis during treatment with secukinumab for psoriasis. Eur J Dermatol. 2019 Aug;29(4):444–5.
11 Hayashi R, Ueno Y, Tanaka S, Sagami S, Nagai K, Shigemoto N, et al. Two cases of severe ulcerative colitis with colonic dilatation resolved with tacrolimus therapy. Case Rep Gastroenterol. 2015 Jul 31;9(2):272–7.
12 Garate ALSV, Rocha TB, Almeida LR, Quera R, Barros JR, Baima JP, et al. Treatment of acute severe ulcerative colitis using accelerated infliximab regimen based on infliximab trough level: a case report. World J Clin Cases. 2021 May 6;9(13):3219–26.
13 Fauny M, Moulin D, D'Amico F, Netter P, Petitpain N, Arnone D, et al. Paradoxical gastrointestinal effects of interleukin-17 blockers. Ann Rheum Dis. 2020 Sep;79(9):1132–8.
14 Jalan KN, Sircus W, Card WI, Falconer CW, Bruce J, Crean GP, et al. An experience of ulcerative colitis. I. Toxic dilation in 55 cases. Gastroenterology. 1969 Jul;57(1):68–82.
15 Rosen MJ, Minar P, Vinks AA. Review article: applying pharmacokinetics to optimise dosing of anti-TNF biologics in acute severe ulcerative colitis. Aliment Pharmacol Ther. 2015 Jun;41(11):1094–103.
16 Gibson DJ, Heetun ZS, Redmond CE, Nanda KS, Keegan D, Byrne K, et al. An accelerated infliximab induction regimen reduces the need for early colectomy in patients with acute severe ulcerative colitis. Clin Gastroenterol Hepatol. 2015 Feb;13(2):330–5.e1.
17 Sebastian S, Myers S, Nadir S, Subramanian S. Systematic review: efficacy and safety of accelerated induction regimes in infliximab rescue therapy for hospitalized patients with acute severe colitis. Dig Dis Sci. 2019 May;64(5):1119–28.
18 Nalagatla N, Falloon K, Tran G, Borren NZ, Avalos D, Luther J, et al. Effect of accelerated infliximab induction on short- and long-term outcomes of acute severe ulcerative colitis: a retrospective multicenter study and meta-analysis. Clin Gastroenterol Hepatol. 2019 Feb;17(3):502–9.e1.
19 Lamb CA, Kennedy NA, Raine T, Hendy PA, Smith PJ, Limdi JK, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut. 2019 Dec;68(Suppl 3):s1–106.
20 Feuerstein JD, Isaacs KL, Schneider Y, Siddique SM, Falck-Ytter Y, Singh S, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. Gastroenterology. 2020 Apr;158(5):1450–61.
21 Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG clinical guideline: ulcerative colitis in adults. Am J Gastroenterol. 2019 Mar;114(3):384–413.
22 Gibson DJ, Hartery K, Doherty J, Nolan J, Keegan D, Byrne K, et al. CRP/Albumin ratio: an early predictor of steroid responsiveness in acute severe ulcerative colitis. J Clin Gastroenterol. 2018 Jul;52(6):e48–52.