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Case Report

Internal Medicine Section

Acute Severe Ulcerative Colitis: A Case Report of Successful Management with Infliximab

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ABSTRACT

Acute Severe Ulcerative Colitis (ASUC) is a critical, life-threatening condition characterised by more than six bloody stools per day, along with systemic signs of inflammation, such as fever, tachycardia and anaemia. Despite advances in treatment, ASUC remains a significant cause of morbidity. Management typically involves corticosteroids as the first line of treatment; however, a substantial proportion of patients are steroid-refractory, necessitating escalation to rescue therapies like Infliximab (IFX) or Cyclosporine (CyA). The present case report presents the successful management of ASUC using IFX in a steroid-refractory patient. Hereby, the authors present a case report of a 23-year-old male patient presented with a 15-day history of increased stool frequency (10-15 times per day) associated with blood, mucus, abdominal pain and fever. Initial investigations, including Computed Tomography (CT) scans, colonoscopy and histopathology, confirmed a diagnosis of ASUC. Laboratory findings were consistent with severe inflammation. The patient was initially treated with intravenous hydrocortisone (100 mg every 6 hours) but showed no clinical improvement. Following this, IFX (5 mg/kg) was administered on day 6, leading to a significant reduction in stool frequency and a decrease in blood and mucus in the stools. The patient exhibited symptomatic improvement and was discharged with a plan for continued IFX therapy. A repeat episode occurred a few weeks later, but further IFX therapy again resulted in improvement. The present case highlights the importance of timely rescue therapy in steroid-refractory ASUC. IFX demonstrated rapid and sustained clinical improvement in a patient with severe disease, underscoring its efficacy as a vital therapeutic option. Close monitoring and early intervention with biologic therapy can significantly reduce the need for colectomy and improve patient outcomes in ASUC.

Keywords: Acute disease, Life-threatening condition, Rescue therapy, Steroid-refractory

CASE REPORT

A 23-year-old male patient was admitted to the hospital with complaints of loose stools for the past 15 days. He experienced an increased frequency of stools (10-15 times per day), which were mucoid and of small volume, associated with blood, abdominal pain and fever with chills.

Computed Tomography (CT) reports revealed diffuse wall thickening of the entire large bowel, with colonic submucosal oedema and mucosal and serosal hyperemia, along with surrounding stranding and vessel enlargement in the ascending colon, transverse colon, descending colon, sigmoid colon and rectum. Loss of normal haustrations was observed in the descending colon. Calprotectin levels were >1800 mg/kg, indicative of active inflammation. High-resolution Computed Tomography (HRCT) of the thorax revealed no obvious pleuroparenchymal abnormalities. The interventricular septum appeared slightly hyperdense compared to the ventricular lumen, likely indicative of anaemia.

The CT scan was repeated after seven days, which revealed mild surrounding mesenteric fat stranding and vessel enlargement in the ascending colon, transverse colon, descending colon, sigmoid colon and rectum, predominantly around the rectum, sigmoid colon and cecum. Loss of normal haustrations was again noted in the descending colon, while haustrations were well visualised in the ascending and transverse colon. Multiple enlarged lymph nodes were noted along the mesocolon and mesorectum throughout the abdomen, with the largest measuring 15×11 mm in the hypogastric region, likely reactive. Additionally, multiple enlarged lymph nodes were identified in the retroperitoneum, specifically in the pre-aortic, para-aortic, aortocaval, precaval and retrocausal regions, with the largest measuring 12×11 mm in the para-aortic area and 10×8 mm in the precaval region, both likely reactive.

The differential diagnosis considered were inflammatory colitis, with Ulcerative Colitis (UC) being more likely and infective colitis.

Laboratory investigations revealed the presence of Red Blood Cells (RBCs) and pus cells in the stools. No organisms were detected in the stool biofilm. The colonoscopy report indicated superficial ulcers and friable mucosa with loss of vascularity from the rectum to the transverse colon. Biopsy results showed focal crypt shortening and mild crypt distortion, with the lamina propria displaying a mild to moderate increase in inflammatory cells. Aggregate neutrophils were present in the lamina propria. Viral inclusions, granulomas, or parasites were not observed. Colonic tissues tested for cytomegalovirus, herpes simplex virus and a cartridge-based nucleic acid amplification test for Mycobacterium tuberculosis were non reactive. The colonic biopsy revealed severe diffuse active colitis with no significant crypt abnormalities.

The patient was started on intravenous hydrocortisone (100 mg every 6 hours), but he did not respond to this treatment. Subsequently, the patient was administered an injection of IFX at a dose of 5 mg/kg, which reduced the frequency of stools from 15 per day to 5-6 times per day, with minimal blood and mucus. The patient was discharged after six weeks, with repeat endoscopy showing a reduction in friability and nodularity, as well as a decreased stool frequency of 3 per day and overall improvement.

Two weeks after the initial treatment, the patient returned to the hospital, having attempted symptomatic treatment with a local practitioner. When his symptoms did not improve and his condition worsened, he presented to the Outpatient Department (OPD) with complaints of Per Rectal (PR) bleeding persisting for the last 15 days, experiencing 8-10 episodes per day. Fresh blood mixed with stools was present. The patient also reported a low-grade fever with chills over the past 15 days and experienced diffusing abdominal pain that was non radiating.

Upon admission, serum procalcitonin levels were measured at 41.6 ng/mL. The patient was treated with antibiotics, intravenous fluids and blood transfusions. Although the procalcitonin level decreased from 41 to 26 ng/mL, there was no clinical improvement. The patient was started on intravenous steroids but showed no significant improvement.

A sigmoidoscopy performed on admission revealed normal anal sphincteric tone, with patchy loss of vascular pattern, erosions and scarring. A repeat sigmoidoscopy and Histopathologic Examination (HPE) two weeks later suggested the acute phase of Inflammatory Bowel Disease (IBD), likely UC.

The patient was given intravenous IFX at 5 mg/kg (300 mg) over two hours at weeks 0, 2 and 6, followed by doses eight weeks apart. Post-IFX, the patient showed significant improvement, with a stool frequency of three per day and no blood present in the stools. He was discharged afterward and scheduled for follow-up. The patient was discharged after six weeks and was followed up every six weeks for IFX 500 mg doses until remission, which occurred after six months.

DISCUSSION

Ulcerative Colitis (UC) is a common condition in which the colon's mucous membrane becomes inflamed, leading to erosions and ulcers [1]. Experiencing ASUC is considered a critical situation when a patient has more than six bloody stools per day, along with specific medical indicators such as an increased heart rate, high fever, low haemoglobin levels and elevated Erythrocyte Sedimentation Rate (ESR), according to Truelove and Witts criteria [2]. Other severity indices to consider include the modified Mayo classification [3], which takes into account clinical and endoscopic findings and the Montreal classification [4], which is primarily based on Truelove and Witt's criteria. Truelove and Witt's criteria are the primary disease severity index utilised in clinical practice [5-7]. Approximately 20% to 25% of patients with UC experience severe exacerbations that necessitate hospitalisation for urgent therapeutic intervention, with colectomy being considered if medical management fails [8]. Numerous studies have demonstrated that individuals with ASUC carry a significant morbidity burden, with a 30% to 40% likelihood of requiring colectomy following one or more severe exacerbations. Furthermore, 10% to 20% of these patients undergo colectomy during hospitalisation [8-11].

The therapeutic approach to ASUC has evolved considerably over the past decade, incorporating additional treatment modalities such as CyA and IFX alongside conventional intravenous corticosteroids or colectomy. However, ASUC remains a medical emergency requiring prompt hospitalisation and coordinated management by a multidisciplinary team, typically involving a gastroenterologist and a colorectal surgeon. The management of ASUC demands a comprehensive, carefully coordinated approach under the supervision of experienced specialists [8]. First-line therapy typically involves the administration of high-dose intravenous corticosteroids, which are considered the gold standard for initial treatment [12]. However, a substantial proportion of patients exhibit steroid-refractory disease and fail to respond adequately, necessitating escalation to rescue therapies such as IFX or CyA [8,12].

In a report by Halpin SJ et al., IFX has shown significant efficacy in avoiding colectomy in patients with ASUC who are refractory to corticosteroids. A single-centre experience reported that IFX achieved short-term remission in a substantial number of patients, thereby reducing the need for colectomy during the index admission [13]. Another study by Järnerot G et al., which was a randomised placebo-controlled trial, demonstrated that IFX effectively induced clinical remission in ASUC patients, supporting its role as a rescue therapy [14].

The standard dosing regimen (5 mg/kg at weeks 0, 2 and 6) may not be adequate for all patients. Evidence suggests that a higher induction dose or an intensified regimen may improve outcomes in corticosteroid-refractory ASUC [15]. Therapeutic Drug Monitoring (TDM) of IFX is crucial to ensure optimal drug levels, as underdosing has been associated with poorer outcomes, while adequate trough levels correlate with clinical remission and mucosal healing [16]. Monterubbianesi R et al., reported that the three-dose induction regimen in corticosteroid-refractory patients demonstrated both early and late benefits. An early response to IFX was a strong predictor of long-term colectomy-free survival [17].

Combination strategies, including early use of immunomodulators and close monitoring of inflammatory markers, may further improve outcomes in patients with ASUC receiving IFX. Early clinical response to IFX, high serum albumin levels and lower C-reactive protein (CRP) levels have been associated with better outcomes. Conversely, a delayed response or persistent endoscopic inflammation predicts eventual colectomy [17]. The need for treatment escalation, including dose intensification or switching to other biologics, should be considered for non responders within the first few weeks [16]. For patients who remain unresponsive to rescue therapy, timely consideration of emergency colectomy is critical. Delaying surgical intervention in this context can lead to increased postoperative morbidity and mortality. Therefore, prompt surgical referral is essential to optimise outcomes and mitigate the risk of severe complications associated with prolonged disease activity and medical failure.

Before the advent of corticosteroid therapy, mortality rates for ASUC were alarmingly high, ranging from 22% to 75% within the first year of diagnosis [12]. The first clinical trial evaluating the use of steroids in severe ulcerative colitis, conducted in the 1950s, reported a marked reduction in mortality rates: 7% in patients treated with steroids compared to 24% in the placebo group [18]. With the advent of specialised medical care, mortality rates for severe ulcerative colitis have dramatically decreased, now falling below 1%. In a retrospective study by Minami N et al., conducted in Japan, the short- and long-term efficacy of Tacrolimus (TAC) and IFX in severe ulcerative colitis was compared [19]. Both therapies demonstrated comparable outcomes in terms of clinical remission at eight weeks and five-year colectomy-free survival, as illustrated by Kaplan-Meier analysis. This data suggests that TAC is a viable therapeutic option for managing ASUC.

Additionally, a network meta-analysis by Komaki Y et al., reviewed eight randomised clinical trials involving steroid-refractory severe ulcerative colitis treated with IFX, cyclosporine (CsA), or TAC [20]. The findings indicated that IFX displayed a slightly superior therapeutic effect in this patient population, while all three agents were effective.

Before the groundbreaking Cyclosporin with IFX in Steroid-Refractory Severe Attacks of Ulcerative Colitis (CYSIF) randomised trial, there was insufficient evidence to determine a significant difference in efficacy between CyA and IFX in the treatment of steroid-refractory severe UC. The CYSIF trial compared two cohorts-43 patients treated with CyA and 49 patients treated with IFX-and demonstrated a lower short-term colectomy rate in the IFX-treated group, providing more clarity on therapeutic decision-making in these cases [21].

In the scenario discussed, the patient did not respond to initial corticosteroid therapy but achieved a favourable outcome with IFX, underscoring its efficacy as a rescue therapy in steroid-refractory ASUC. In the CYSIF trial [22], 111 patients with severe UC who were naïve to thiopurine therapy were randomised to receive either CyA or IFX following five days of intravenous corticosteroids. Those who demonstrated clinical improvement by day 7 were transitioned to oral azathioprine, with a gradual tapering of steroid doses beginning on day 8. By day 7, approximately 85% of patients in both treatment groups had responded favourably. The colectomy rates at day 98 were comparable between the two groups, with 18% in the CyA group and 21% in the IFX group (p=0.66). Similarly, the overall treatment failure rate by day 98 was not significantly

different, with 60% of patients in the CyA group and 54% in the IFX group experiencing treatment failure. The study concluded that neither CyA nor IFX demonstrated clear superiority over the other in managing steroid-refractory severe UC.

CONCLUSION(S)

Treating ASUC is complex and requires high collaboration among doctors, surgeons and patients. Patients who are unresponsive to steroids need immediate evaluation for rescue treatment and careful monitoring to assess their response. Evidence is emerging to support the use of increased IFX dosing in certain patients. Timely recognition and intervention in ASUC are crucial, especially in steroid-refractory cases. The present case highlights the efficacy of IFX as a rescue therapy, demonstrating rapid symptom control, a reduced need for colectomy and improved long-term outcomes with close follow-up and continued therapy.

REFERENCES

[1] Baumgart DC, Sandborn WJ. Inflammatory bowel disease: Clinical aspects and established and evolving therapies. Lancet. 2007;369:1641-57.
[2] Truelove SC, Witts LJ. Cortisone in ulcerative colitis; preliminary report on a therapeutic trial. Br Med J. 1954;2:375-78.
[3] D'Haens G, Sandborn WJ, Feagan BG, Geboes K, Hanauer SB, Irvine EJ, et al. A review of activity indices and efficacy end points for clinical trials of medical therapy in adults with ulcerative colitis. Gastroenterology. 2007;132:763-86.
[4] Silverberg MS, Satsangi J, Ahmad T, Arnott ID, Bernstein CN, Brant SR, et al. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: Report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. Can J Gastroenterol. 2005;19(Suppl A):5A-36A.
[5] Rice-Oxley JM, Truelove SC. Ulcerative colitis course and prognosis. Lancet. 1950;255:663-66.
[6] Edwards FC, Truelove SC. The course and prognosis of ulcerative colitis. Gut. 1963;4:299-315.
[7] Nakase H, Sato N, Mizuno N, Ikawa Y. The influence of cytokines on the complex pathology of ulcerative colitis. Autoimmun Rev. 2022;21:103017.
[8] Dinesen LC, Walsh AJ, Protic MN, Heap G, Cummings F, Warren BF, et al. The pattern and outcome of acute severe colitis. J Crohns Colitis. 2010;4:431-37.
[9] Aratari A, Papi C, Clemente V, Moretti A, Luchetti R, Koch M, et al. Colectomy rate in acute severe ulcerative colitis in the infliximab era. Dig Liver Dis. 2008;40:821-26.
[10] Lynch RW, Lowe D, Protheroe A, Driscoll R, Rhodes JM, Arnott ID. Outcomes of rescue therapy in acute severe ulcerative colitis: Data from the United Kingdom inflammatory bowel disease audit. Aliment Pharmacol Ther. 2013;38:935-45.
[11] Jain S, Kedia S, Sethi T, Bopanna S, Yadav DP, Goyal S, et al. Predictors of long-term outcomes in patients with acute severe colitis: A northern Indian cohort study. J Gastroenterol Hepatol. 2018;33:615-22.
[12] Hardy TL, Bulmer E. Ulcerative colitis: A survey of ninety-five cases. Br Med J. 1933;2:812-15.
[13] Halpin SJ, Hamlin PJ, Greer DP, Warren L, Ford AC. Efficacy of infliximab in acute severe ulcerative colitis: A single-centre experience. World J Gastroenterol. 2013;19(7):1091-97. Doi: 10.3748/wjg.v19.i7.1091.
[14] Järnerot G, Hertervig E, Friis-Liby I, Blomquist L, Karlén P, Grännö C, et al. Infliximab as rescue therapy in severe to moderately severe ulcerative colitis: A randomized, placebo-controlled study. Gastroenterology. 2005;128(7):1805-11. Doi: 10.1053/j.gastro.2005.03.003.
[15] Fiske J, Conley T, Sebastian S, Subramanian S. Infliximab in acute severe colitis: Getting the right dose. Frontline Gastroenterol. 2020;11(6):427-29. Doi: 10.1136/flgastro-2020-101407.
[16] Gordon BL, Battat R. Therapeutic drug monitoring of infliximab in acute severe ulcerative colitis. J Clin Med. 2023;12(10):3378. Doi: 10.3390/jcm12103378.
[17] Monterubbianesi R, Aratari A, Armuzzi A, Daperno M, Biancone L, Cappello M, et al. Infliximab three-dose induction regimen in severe corticosteroid-refractory ulcerative colitis: Early and late outcome and predictors of colectomy. J Crohns Colitis. 2014;8(8):852-58. Doi: 10.1016/j.crohns.2014.01.006.
[18] Jakobovits SL, Travis SP. Management of acute severe colitis. Br Med Bull. 2005;75-76:131-44.
[19] Minami N, Yoshino T, Matsuura M, Koshikawa Y, Yamada S, Toyonaga T, et al. Tacrolimus or infliximab for severe ulcerative colitis: Short-term and longterm data from a retrospective observational study. BMJ Open Gastroenterol. 2015;2:e000021.
[20] Komaki Y, Komaki F, Micic D, Yamada A, Suzuki Y, Sakuraba A. Pharmacologic therapies for severe steroid refractory hospitalised ulcerative colitis: A network meta-analysis. J Gastroenterol Hepatol. 2017;32:1143-51.
[21] Sjöberg M, Walch A, Meshkat M, Gustavsson A, Järnerot G, Vogelsang H, et al. Infliximab or cyclosporine as rescue therapy in hospitalised patients with steroid-refractory ulcerative colitis: A retrospective observational study. Inflamm Bowel Dis. 2012;18:212-18.
[22] Laharie D, Bourreille A, Branche J, Allez M, Bouhnik Y, Filippi J, et al. Ciclosporin versus infliximab in patients with severe ulcerative colitis refractory to intravenous steroids: A parallel, open-label randomised controlled trial. Lancet. 2012;380:1909-15.

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