CASE REPORT

Emergency colectomy for massive rectal bleeding in a patient with well-controlled ulcerative colitis receiving Vedolizumab

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ABSTRACT

Ulcerative colitis (UC) is a chronic inflammatory condition, with a relapsing-remitting course. The case presented poses some valid questions regarding short-term and long-term management of patients with UC, and if the outcome (colectomy) could have been delayed or even prevented. Rectal bleeding is a cardinal symptom in patients with UC and it occurs among all patients during active disease. Massive rectal bleeding is an uncommon, but serious, complication of UC accounting for 0.1-1.4% of admissions. It is, nonetheless, noteworthy that instances of acute significant lower gastrointestinal bleeding accompanied by hemodynamic instability are infrequent. The rate of colectomy appears to be positively impacted by biological treatment. However, a refractory condition is still the primary reason for surgery, indicating a pressing need for new treatment approaches. Here we present the case of a young male patient who developed massive rectal bleeding and underwent emergent colectomy with ileostomy while having clinical and biological remission (normal calprotectin levels) at week 10 of Vedolizumab treatment.

KEYWORDS: ulcerative colitis; massive rectal bleeding; emergency colectomy; calprotectin value

INTRODUCTION

Ulcerative colitis (UC) is a chronically-remitting inflammatory bowel disease (IBD) characterized by continuous colonic inflammation affecting the rectum and to a variable extent the colon [1]. The significance of the anatomical extent of the disease in relation to both the clinical course and the risk for colectomy is widely acknowledged [2]. Patients who fail to have a reasonable quality of life (QoL), experience side effects from the medication prescribed, or are diagnosed with dysplasia or cancer during follow-up colonoscopy are prime candidates [3]. Substantial efforts have been made in discovering noninvasive biomarkers and prediction scores to foresee these life-threatening complications. However, the ideal marker is yet to be discovered.

The traditional biomarkers used in assessing UC activity are serum C- reactive protein (CRP) levels and fecal calprotectin (FC) levels [1-3]. Although imperfect and unspecific for UC, they offer a better understanding and may provide a discriminatory power of the degree of intestinal inflammation.

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When analyzing the frequency of life-threatening complications, severe intestinal bleeding is surprisingly a rare occurrence in IBD with a reported incidence ranging from 0%-6%, but only 0.1% in UC [4]. In patients with extensive UC, bleeding can occur from diffuse areas of active inflammation, where mucosal ulceration or even ulceration of pseudo-polyps are identified [5]. It is often observed that the occurrence of substantial disease activity and symptomatic UC is associated with a greater frequency of lower gastrointestinal (GI) bleeding. However, current evidence indicates that hemorrhagic events can also transpire among individuals who are in a state of clinical remission [1-3].

Here we present the case of a young male patient who developed massive rectal bleeding and underwent emergent colectomy with ileostomy while having clinical and histological remission under VDZ treatment.

CASE PRESENTATION

A 38-year-old male patient with a history of UC was admitted to the Emergency Department of our institution for increased bowel movements (up to 8 stools/day), dizziness, and rectal bleeding. He was diagnosed two years ago with left-sided UC and managed conservatively with corticosteroids

followed by oral mesalamine (5-ASA, 4g/day), for maintenance of remission, with favorable clinical response.

One year after the initial diagnosis, the patient was readmitted for bloody diarrhea (up to 7 stools/day), fever, and abdominal pain without signs of peritonitis. The colonoscopy showed extensive colitis and was classified as a grade 3 Mayo endoscopic score. Laboratory findings showed a hemoglobin (Hb) level of 11.5g/dl, a platelet count of 800.000/MMC, a CRP level of 5mg/dl, and normal ferritin and albumin levels. An extensive work-up was performed to rule out any infections and VDZ 300 mg iv was initiated. Venous thrombosis prophylaxis was also started with low molecular weight heparin (LMWH). By week 10 of treatment, his FC levels were within normal range, with excellent clinical response (2 stools/day without any bloody discharge). After 14 weeks of VDZ treatment, a routine follow-up showed mild thrombocytosis, and normal Hb, ferritin, CRP, FC, and albumin levels. He was in clinical and histological remission. However, by week 26, the patient is readmitted with massive lower GI bleeding. A colonoscopy is performed showing erythema and a large amount of fresh blood in the lumen without identifying the source (Figure 1).

The state of the patient progressively worsens and he becomes hemodynamically unstable. He is transferred into de ICU unit for monitoring, and a CT scan is performed showing active diffuse arterial bleeding from multiple sites at the descendent and the sigmoid colon (Figure 2).

Urgent subtotal colectomy and splenectomy with preservation of the rectum and terminal ileostomy are performed. A total of 120 cm of the colon were surgically removed (Figure 3).

The histopathology report of the resected colon did not identify malignancy or dysplasia, but it showed severe and continuous active disease with diffuse erosions, fissuring ulcers, and focal transmural inflammation in the proximity of deeply ulcerated areas. The postoperative treatment consisted of topic 5-ASA and LMWH (significant post-splenectomy thrombocytosis), but shortly after switched to infliximab biosimilar (IFX-B) 5mg/kg of weight. Seven days of IFX- B, the patient had minor rectal bleeding, but without any hemodynamic repercussions. The clinical outcome was favorable, and the patient was discharged and continued IFX-B therapy with the maintenance of remission. Three months into IFX-B treatment, the patient developed a septic complication, an abdominal abscess. The patient underwent a CT scan and was taken to surgery for drainage of an underlying abscess, with a good surgical outcome. The endoscopy report showed Mayo 2 lesions, confirming active

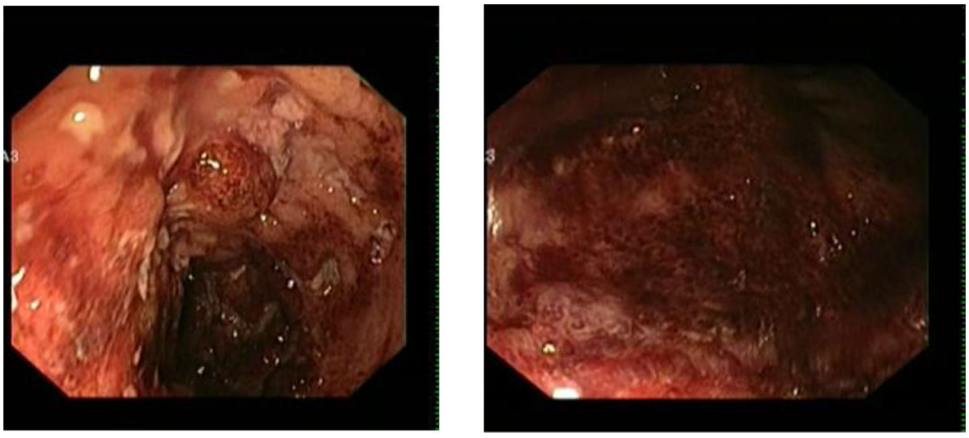

Fig. 1. Endoscopic aspect of active disease.

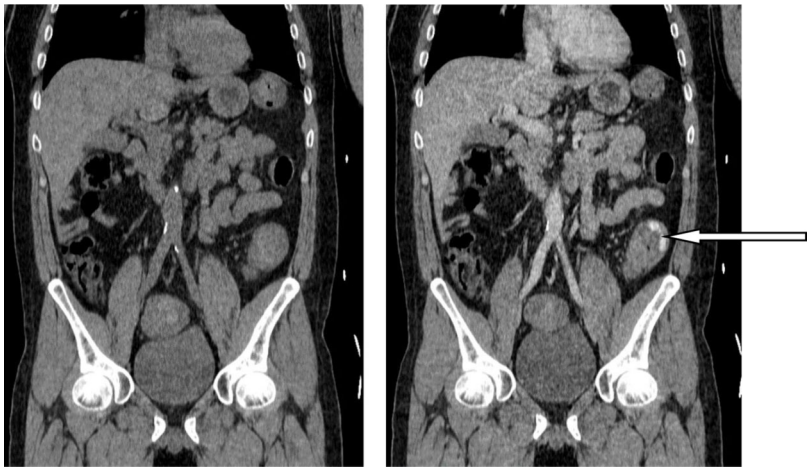

Fig. 2. Active bleeding from diffuse areas from the sigmoid and descending colon.

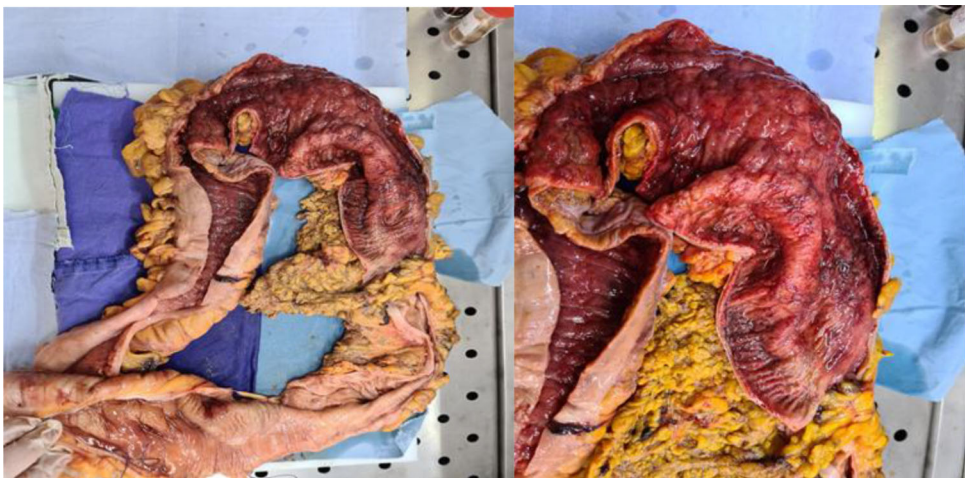

Fig. 3. Postoperative sample of the resected colon.

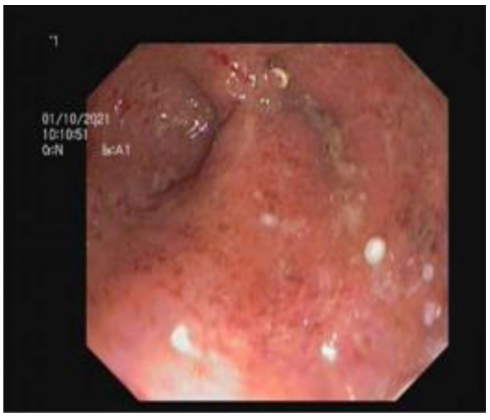

Fig. 4. Endoscopic aspect showing Mayo 2 lesions.

disease with cryptitis and crypt abscesses (Figure 4). The medical team decided to shorten the dosing interval for IFX-B to 4 weeks and add azathioprine (AZA) 2.5mg/kg for a positive and desirable outcome of endoscopic remission. 24 weeks into combo treatment (INF-B + AZA), endoscopic remission was achieved allowing the surgical team to perform a restorative procedure and anastomosis.

DISCUSSION

UC is a chronic inflammatory condition, with a relapsing-remitting course [1]. The case presented poses some valid questions regarding short-term and long-term management of patients with UC, and if the outcome could have been delayed or even prevented. The rate of colectomy appears to be positively impacted by biological treatment. However, a refractory condition is still the primary reason for surgery, indicating a pressing need for new approaches to treatment [1-3]. The severity of UC is frequently associated with the extent of bleeding, which typically manifests as an early consequence throughout the progression of the disease [6,7]. Numerous publications have tried to identify predictive factors for colectomy. The paper by Rodriguez et al. focused on the Navarra cohort, which included 174 patients and a follow-up period of 15.7 years, 8 patients required colectomy, 7 of which were on an emergency basis (megacolon, severe flare, treatment failure) [8]. The IBSEN cohort, which included patients from 4 regions in Norway, reported a 9.8% colectomy rate at 10 years among patients with extensive disease, need for corticosteroids, and significant inflammation (CRP >30mg/dl levels) at diagnosis [9]. Sahami et al. reported an 18.8% colectomy rate during the 10-year follow-up period for UC. Interestingly, proximal disease extension was not a risk factor for colectomy [10]. If we take into consideration the complexity and heterogeneity of UC, it is obvious that no one feature or risk factor can accurately predict the outcome of the illness in every single patient.

However, non-invasive objective biomarkers such as FC and CRP levels are widely available to monitor UC activity at outpatient clinic visits [11]. FC is considered a reliable biomarker for detecting active intestinal inflammation, used for both diagnosing and monitoring UC [12]. False negative results may appear in certain scenarios. Normal FC values are determined by variation in inflammation or the lack of mixing of the calprotectin with stool [11,12]. Furthermore, it should be noted that degrees of variation might exhibit fluctuations on a daily basis, as well as during different time periods throughout the day. Interestingly, these variations can even occur within a single instance of a bowel movement [11]. The passage of feces from the intestinal lumen into the collection container can result in a rapid temperature shift, which has the potential to alter the affinity of FC and subsequently influence molecular alterations [13]. Interestingly, a recent paper by Vicente-Steijn et al. reported that the detection of blood in the feces, including occult bleeding, may have an impact on the quantification of calprotectin levels, leading to a reduction in FC values. The authors noted that the measurement of FC is feces-dependent rather than blood-dependent, indicating that other factors, such as nutrition, may be to blame for the variation [14]. In order to reduce the risk of false results of single markers, strategies using a combination of serum index and fecal biomarkers could be envisioned [15]. The use of fecal immunochemical test (FIT) could be used in combination with FC may enhance the sensitivity of detecting endoscopically active UC. Previous reports stated that in particular, for patients with UC, the combined use of elevated FIT value and high

platelet count is 100% sensitive and 90.9% specific for endoscopically active disease [16]. In the reported case, the negative results of FC was considered as a false determination, as evidenced by the disease outcome and the histology report indicating the presence of active disease. Determination of FIT in conjunction with FC and serological markers would have increased the likelihood of detecting active disease among patients in clinical remission.

CRP is an acute non-specific phase-reactant used in clinical practice to detect inflammatory changes in IBD. CRP can increase in several illnesses unrelated to UC, including one-fifth of the healthy population. Interestingly, normal CRP levels reduce the probability to less than 1% of having UC [16]. However, increased stool frequency and a CRP $\geqslant$45mg/l predict the occurrence of colectomy in more than 85% of cases [17,18]. CRP use in clinical practice has some limitations as it correlates poorly with milder forms of UC [19].

Before the introduction of rescue therapy, patients who fail to respond to iv corticosteroids were candidates for colectomy [20]. Refinement in laparoscopic techniques has progressed towards 'incision-less' totally laparoscopic procedures. However, morbidity and mortality associated with urgent colectomy and ileostomy, regardless of the chosen route, are not neglectable, and patients may develop infections, wound dehiscence, bowel obstruction, and further bleeding shortly after the procedure in about 40% of cases as mentioned by Teeuwen et al. [21]. Unfortunately, our center's surgical department has limited experience regarding the laparoscopic approach in UC patients requiring urgent colectomy which is why the classic abdominal approach was performed. At this point, we are unable to assert if abscess formation was related to the surgical technique, the biological therapy, or as a complication of asplenia leading to an increased risk of infections. In our center, the implementation of endoscopic or radiological intervention, while recognized as viable approaches for addressing active bleeding was not feasible.

In regards to medical therapy, VDZ has proven to be a safe and effective drug having gut-specific mechanisms that make it suitable for use in patients unresponsive to conventional therapy. There are sufficient publications, including the GEMINI trials which offered a clear image of the potential for VDZ in managing patients with moderately to severe UC [22]. Hanzel et al. assessed the relationship between VDZ trough levels and remission in IBD patients. The authors found that a modest 4% of patients who had VDZ trough levels $< 17.0\,\mu g/mL$ at week 6 were able to achieve combination remission by week 54. The combined remission was predicted by a threshold of $22\,\mu g/mL$ at week 6 and $8\,\mu g/mL$ at week 22. The implementation of early therapeutic drug monitoring may facilitate the identification of individuals who are susceptible to unfavorable outcomes, therefore offering an early chance for therapeutic intervention, such as the adjustment of dose intervals [23].

CONCLUSION

The presented case is a real-life illustration of an otherwise straightforward case of UC complicated with massive rectal bleeding and emergent colectomy. It also entails a dangerous reliance on non-invasiveness in surveillance. A good clinical response and normal FC levels assured us that the patient responded favorably to the induction treatment with VDZ. In retrospect, the cause of the massive bleeding was his active disease, with persistence and probably worsening colonic inflammation. Surveillance intervals should be individualized for early detection of lack or loss of response, and rapid implementation of a therapeutic intervention like dosing-interval shortening or switching to alternative agents should be carried out to reduce the risk of life-threatening complications and adverse events. Treatment options should be discussed in a multidisciplinary team involving a surgeon, radiologist, and gastroenterologist in complete agreement with the patient's needs and realistic expectations.

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