

Ulcerative Colitis After Complicated Diverticulitis

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ABSTRACT

It has been recently shown that inflammatory bowel disease may follow an episode of acute complicated diverticulitis. We report 3 cases of ulcerative colitis after acute complicated diverticulitis that required surgery. All cases occurred in elderly patients with moderate-to-severe disease and 1 individual who also received treatment with biologics. These cases highlight the need for older patients to be strictly monitored after an episode of perforated diverticulitis requiring surgery because of the risk of developing ulcerative colitis.

KEYWORDS: acute complicated diverticulitis; surgery; ulcerative colitis

INTRODUCTION

Although the prevalence of diverticulosis and diverticular disease (DD) is stable in Western countries,¹ complicated diverticulitis (CD) seems to have increased progressively over the past decade.²

It is estimated that cases of inflammatory bowel disease (IBD) are rising worldwide,³ especially in pediatric and older populations.⁴

Rahman et al⁵ report that some patients may develop IBD after an episode of CD. In particular, ulcerative colitis (UC) may develop more often than Crohn's disease and may require treatment with biologics. IBD occurrence after CD is very important from a clinical point of view because similar cases have been observed recently.

CASE REPORTS

Case 1: A 63-year-old woman with myasthenia gravis presented with acute abdominal pain and was admitted to hospital in April 2018. Her concomitant medication included continuous maintenance therapy with 5-mg prednisone daily for her neurological disease. Abdominal computed tomography found diffuse diverticulosis of the left colon, with sigmoid inflammation and perforation. After resection of the sigmoid colon by colostomy (with Hartmann procedure), she was diagnosed with CD associated with perforation. No histological evidence of IBD was found in the resected section (Figure 1). She was a smoker but ceased after her diagnosis. In October 2018, she underwent reanastomosis and was stable for approximately 2 years, at which point she developed diarrhea and urgency, often with blood in the stools. In January 2021, fecal calprotectin (FC) levels were 991 $\mu\text{g/g}$. A colonoscopy revealed hyperemia and erosions affecting the entire colon, including the anastomosis area approximately 15 cm from the anus. Histopathological features confirmed a diagnosis of UC (Figure 1). A course of steroids and mesalazine successfully induced remission until a recurrence at 3 months. In June 2021, azathioprine 2.5 mg/kg daily was started, giving partial benefit. Five months later, an endoscopic review found the persistence of inflammation, and FC levels had increased to 1332 $\mu\text{g/g}$. Azathioprine was stopped, and in January 2022, the patient began treatment with vedolizumab 300 mg at baseline, at 2 and 6 weeks, and then every 8 weeks. Vedolizumab was selected because her neurologist had advised against other biologics. She did not benefit from this treatment (Figure 1) and was switched to ustekinumab in May 2022, to which an immediate response was seen. At her last examination (July 2022), she reported only 3 bowel movements daily with no diarrhea or blood, and her FC had dropped to 229 $\mu\text{g/g}$.

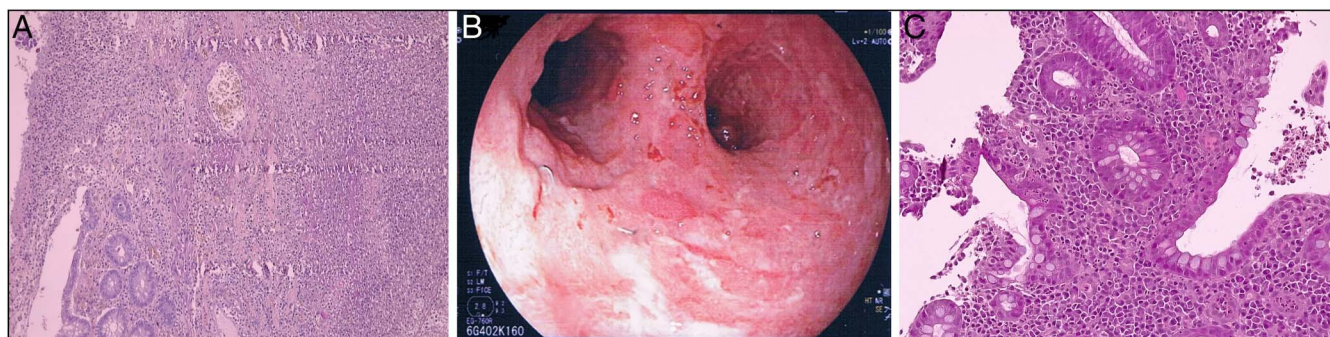


Figure 1. (A) Histopathology of the surgical resected segment (April 2018). It showed acute-chronic inflammatory infiltrate, which extended through, and diverticular abscess (Hematoxylin & Eosin, 10 \times). (B) Colonoscopy under vedolizumab (May 2022). Severe inflammation can be seen. (C) Histopathology of the colocolonic anastomosis. Severe acute-chronic infiltrate, with plasmacytosis, cryptitis, and crypt abscesses can be seen (Hematoxylin & Eosin, 40 \times).

Case 2: A 74-year-old woman with seronegative arthritis, and a history of diverticulosis, was admitted to the hospital in August 2021 because of acute abdominal pain. Her concomitant medication included continuous maintenance therapy with 5-mg prednisone daily. Computed tomography found diffuse diverticulosis of the entire colon, with sigmoid inflammation and perforation. Resection of the sigmoid colon through colostomy, according to Hartmann procedure, was conducted. Based on the histopathology of the resected specimen, a diagnosis of CD associated with perforation was made. In December 2021, she underwent reanastomosis and was stable for around 2 months. In February 2022, she developed diarrhea and urgency, often with blood in the stool, with an FC of 390 $\mu\text{g/g}$. Colonoscopy was performed in April 2022, and the colocolonic anastomosis appeared normal (Figure 2), with mild hyperemia of the right colon. The histopathology features included moderate acute-chronic infiltrate with plasmacytosis, cryptitis, and crypt abscesses across the entire colon (Figure 2). A diagnosis of UC was made. An 8-week course of daily budesonide (9 mg) resulted in significant clinical improvement with 1 bowel movement daily without diarrhea or blood. Her FC dropped to 109 $\mu\text{g/g}$.

Case 3: A 73-year-old man with a history of diverticulosis was admitted to the hospital in March 2021 because of acute

abdominal pain. He was an ex-smoker, taking an angiotensin-converting enzyme inhibitor and topical steroids for hypertension and asthma. An abdominal computed tomography found diffuse diverticulosis of the left colon, with sigmoid inflammation and perforation. The patient underwent resection of the sigmoid colon by colostomy using Hartmann procedure. A diagnosis of complicated diverticulitis associated with perforation was made based on the absence of any histological evidence of IBD in the resected specimen. In September 2021, he underwent reanastomosis, but he developed diarrhea and urgency immediately after the surgical procedure (4–5 bowel movements per day), without any blood in the stools. Although no instrumental investigation was performed, his general practitioner prescribed 2.4-g mesalazine daily, with no significant improvement. Loperamide was often needed to control diarrhea. In March 2022, his FC was 234 $\mu\text{g/g}$, but the patient refused the colonoscopy. Mesalazine was increased to 3.6 g daily plus 4 g topically, resulting in mild improvement. In May 2022, his FC had risen to 567 $\mu\text{g/g}$, but the patient again refused a colonoscopy. An intestinal ultrasonography was performed, showing thickening of the mucosa and submucosa (4.9 mm) and increased color Doppler signal, a typical intestinal ultrasonography finding of active UC.⁶ The patient was treated with 9 mg of budesonide daily for 8 weeks. Within 1 month, significant clinical improvement was reported (2 bowel movements/day without diarrhea or blood), and his FC dropped to 191 $\mu\text{g/g}$.

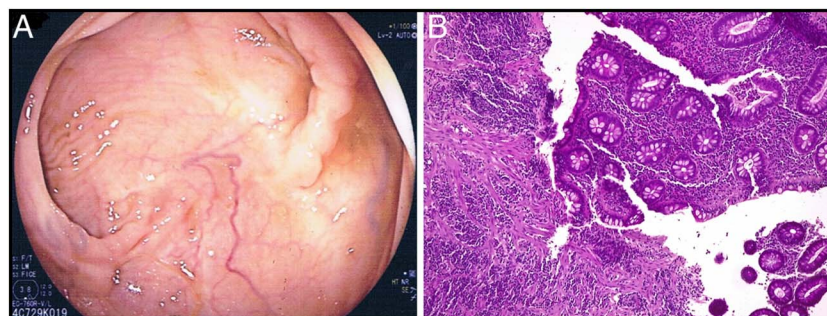


Figure 2. (A) Endoscopic appearance of the colocolonic anastomosis (April 2022): no endoscopic signs of inflammation can be seen. (B) Histopathology of the anastomosis: acute-chronic infiltrate, with plasmacytosis, cryptitis, and crypt abscesses can be seen (Hematoxylin & Eosin, 10 \times).

DISCUSSION

It is unknown why UC occurs after CD. One hypothesis is that smoking cessation, or previous smoking history, could trigger UC.⁷ Lee et al⁸ found that smoking modified the human leukocyte antigen expression; thus, cessation may increase the risk of UC. UC has a higher predominance in females, with a significantly increased risk within 2–5 years of smoking cessation remaining elevated over the following 20 years.⁹

A more intriguing hypothesis that may explain UC occurrence after CD is observed changes in the microbiota of these patients. Some bacterial taxa, including *Escherichia coli*, *Streptococcus* species, *Bacteroides*, and *Clostridium* species, have been isolated from the peritoneal cavity or abscesses in CD cases complicated by perforation.¹⁰ An exaggerated immune response to these luminal antigens could drive UC. A low-fiber diet, often advised after an episode of CD,¹ could also contribute to UC. Although not supported by clear scientific evidence, maintaining a low-fiber diet after an episode of acute diverticulitis may decrease intestinal bacterial diversity, a phenomenon already observed in IBD cases.¹¹ Together with modifications linked to aging, these changes may therefore represent a perfect background for the persistence of an altered immune response. Finally, a significant role may be played by the *Akkermansia muciniphila* species. This is a mucin-degrading and short-chain fatty acid (SCFA)-producing species,¹² which is underexpressed in UC.¹³ However, it is known that *A. muciniphila* is overexpressed in diverticular disease.¹⁴ We can therefore hypothesize that removing the diverticular district may lead to a decrease in *A. muciniphila* abundance, favoring the occurrence of UC.

Whatever the pathophysiological mechanisms may be, these cases show that older patients should be strictly monitored after an episode of perforated diverticulitis requiring surgery because of the risk of developing UC, which sometimes requires biological treatment.

DISCLOSURES

Author contributions: A. Tursi planned and conducted the study and is the article guarantor. A. Tursi, R. Nenna, and V. Papa collected and interpreted data. A. Tursi drafted the manuscript. A. Tursi, R. Nenna, and V. Papa approved the final draft submitted.

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