

CASE REPORT

Diversion colitis: a trigger for ulcerative colitis in the in-stream colon?

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Abstract

The aetiology of ulcerative colitis is unknown. Two patients without pre-existing inflammatory bowel disease in whom end colostomy for faecal incontinence was complicated by diversion colitis in the defunctioned rectosigmoid colon, are described. In both instances, colitis with the clinical, colonoscopic, and microscopic features of ulcerative colitis developed about a year later in the previously normal in-stream colon proximal to the colostomy. These cases suggest that diversion colitis may be a risk factor for ulcerative colitis in predisposed individuals and that ulcerative colitis can be triggered by anatomically discontinuous inflammation elsewhere in the large intestine.

(*Gut* 1999;44:279–282)

Keywords: ulcerative colitis, diversion colitis

The aetiology of non-specific ulcerative colitis is obscure. Recently, reports of the frequent occurrence of discontinuous appendiceal inflammation,^{1,2} and the low prevalence of appendectomy in patients with ulcerative colitis,³ have raised the possibility that inflammation in one site of the large intestine may trigger ulcerative colitis at a different site in predisposed individuals.

Inflammation in the defunctioned colon, diversion colitis, develops in a substantial proportion of patients following surgical bypass of the colorectum: the incidence of diversion colitis varies in different reports, and according to whether the inflammation is defined by symptoms, sigmoidoscopic appearances, or microscopic mucosal abnormalities. While most patients are asymptomatic, a minority have troublesome passage of blood and/or mucus per rectum, often with tenesmus.^{4,5} The macroscopic and microscopic appearances of diversion colitis overlap with idiopathic and infectious colitides.⁶ Favoured hypotheses for its pathogenesis include changes in bacterial flora, and deprivation of luminal nutrients for colonocytes, in particular short chain fatty acids.⁷ Diversion colitis is usually reversed by surgical reanastomosis.⁸ Successful treatment with topical short chain fatty acids,⁹ aminosallylate enemas,¹⁰ and corticosteroid enemas¹

has also been reported but the efficacy of these treatments has not been universal.⁸

We describe here two patients in whom symptomatic diversion colitis in the defunctioned rectosigmoid colon developed after colostomy for faecal incontinence. In both cases, symptomatic, colonoscopic, and microscopic ulcerative colitis developed in previously normal in-stream colon proximal to the colostomy, a sequence of events with implications for the aetiopathogenesis of ulcerative colitis.

Patient 1

A 60 year old Caucasian non-smoking woman presented in 1993 with a five year history of urge faecal incontinence. She had a past history of insulin dependent diabetes mellitus complicated by peripheral and autonomic neuropathy, retinopathy, nephropathy, and has well compensated cirrhosis due to hepatitis C. There was no family history of inflammatory bowel disease. Both barium enema and colonoscopy including multiple biopsies were normal. Anorectal physiology studies revealed severe pudendal neuropathy and dysfunction of the external anal sphincter, abnormalities thought to account for her faecal incontinence. A postanal repair was performed but she continued to suffer from faecal incontinence, which led to a sigmoid end colostomy in May 1996.

She presented in September 1996 with blood and mucus per rectum. Rigid sigmoidoscopy revealed an oedematous mucosa with bloodstained mucopurulent exudate. Rectal biopsy in January 1997 showed an active chronic colitis with focal cryptitis and crypt abscesses. The haemoglobin concentration was 11 g/dl, the serum albumin was 35 g/dl, and other blood tests were normal. A diagnosis of diversion colitis was made. However, treatment with corticosteroid and mesalazine enemas was ineffective.

In May 1997, a flexible sigmoidoscopy showed granular, congested, and erythematous mucosa with mucopurulent exudate in the entire diverted segment of colon. The in-stream colon examined through the colostomy was endoscopically normal. On histology,

Abbreviations used in this paper: ANA, antinuclear antibody; pANCA, perinuclear antineutrophilic cytoplasmic antibody.

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Accepted for publication
2 September 1998

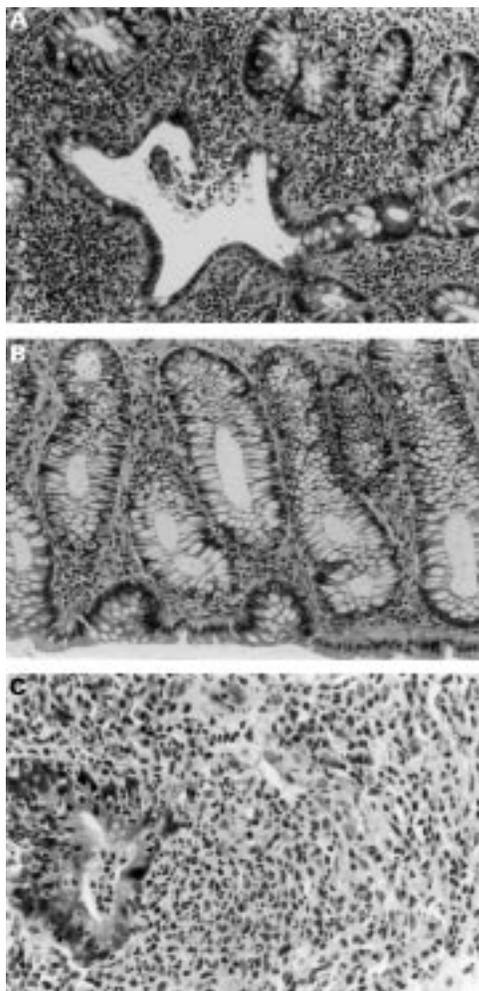


Figure 1 Patient 1: (A) biopsy specimen from rectal stump showing active chronic inflammation with crypt abscesses and distortion of crypt architecture; (B) biopsy specimen of in-stream colon showing no abnormality; (C) biopsy specimen from in-stream colon five months later showing active chronic inflammation.

biopsy specimens of the rectum showed active chronic inflammation with a diffuse lamina propria lymphoplasmacytic inflammatory infiltrate, cryptitis, crypt abscesses, and mild crypt architectural distortion (fig 1A), but biopsy specimens of the in-stream colon were normal (fig 1B). Further investigations including stool culture and *Clostridium difficile* toxin, antiendomysial antibody, and barium follow through were all normal or negative. She also complained of back pain and right sacroiliac joint inflammation was identified on plain x ray. Treatment with ispaghula husk enemas, one sachet at night, as a precursor of short chain fatty acids, had no benefit.

In October 1997, she complained for the first time of bleeding into the colostomy bag. Colonoscopy of the in-stream colon, through the colostomy, revealed a diffusely granular, congested, and erythematous mucosa. Histology showed a diffuse increase in chronic inflammatory cells within the lamina propria with patchy cryptitis, occasional crypt abscesses and moderate gland distortion (fig 1C). Haemoglobin concentration was 6.3 g/dl with a normochromic normocytic picture and the

plasma albumin concentration was 31 g/l. Her serum was pANCA (perinuclear antineutrophilic cytoplasmic antibody) and ANA (antinuclear antibody) (1/80) positive.

A diagnosis of ulcerative colitis involving the in-stream colon was made. She was started on oral prednisolone 30 mg once daily, mesalazine 800 mg three times daily, and mesalazine foam enema 1 g once daily to which she responded well clinically. Further endoscopic assessment showed improvement in both the diverted and in-stream colon. Prednisolone was tapered off over four months and she remained well.

Patient 2

This Caucasian man was born with an imperforate anus. He had been treated as a neonate with a colostomy and subsequently, in infancy, the colostomy was closed and a coloperineal pull through performed. He was a non-smoker. There was no family history of inflammatory bowel disease. In 1991, when he was 16 years old, a series of operations was performed to create a neoanal sphincter. These involved a defunctioning loop ileostomy, transposition of the left gracilis muscle to the neoanal canal, and implantation of an electrical stimulator.

In March 1992, six months after the creation of the ileostomy, he presented with rectal bleeding and passage of mucus. This was attributed to diversion colitis. However, restoration of faecal stream by closure of the loop ileostomy in July 1992 did not improve his symptoms. A flexible sigmoidoscopy to 60 cm showed a granular, erythematous mucosa with contact bleeding. The inflammation was more severe distally. Biopsy specimens showed active inflammation with polymorphs infiltrating crypts and a diffuse increase in lymphocytes and plasma cells in the lamina propria. Stool cultures and *C difficile* toxin were negative. He was started on oral prednisolone 20 mg daily, oral olsalazine 500 mg twice daily, and oral metronidazole 400 mg three times daily. Unfortunately, diarrhoea, faecal incontinence, and perineal excoriation worsened despite the addition of loperamide and readjustment of the electrical stimulator.

The faecal incontinence and perineal excoriation prompted a further colonic diversion by means of a sigmoid loop colostomy in October 1992. The colostomy initially worked well but he continued to pass blood and mucus per rectum. Flexible sigmoidoscopy showed granular, congested, and erythematous mucosa with bleeding in the rectum and sigmoid colon. The endoscope inserted proximally through the colostomy showed normal mucosa macroscopically and on histology. Rectal bleeding and passage of mucus persisted. In January 1993, the defunctioned rectosigmoid was partially removed, leaving the lower rectum and anal canal; the loop colostomy was refashioned into an end colostomy. On histology the excised rectal segment showed areas of chronic mucosal inflammation with ulceration, cryptitis, crypt abscesses, and submucosal fibrosis; the findings were consistent with the diagnosis of diversion colitis.

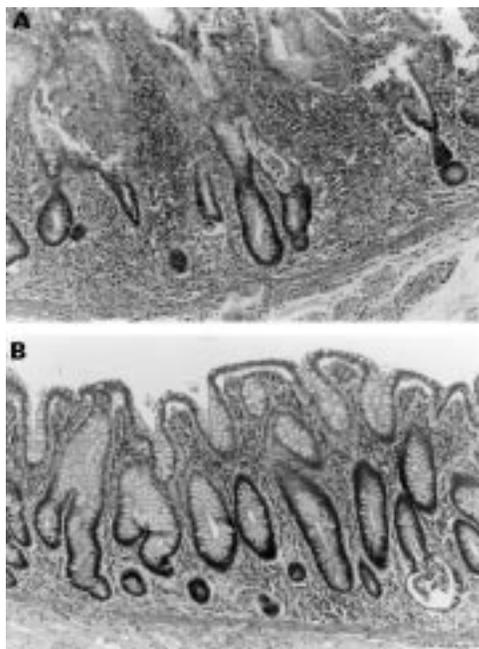


Figure 2 Patient 2: (A) excised rectal stump showing active chronic inflammation with lymphoid follicles, crypt abscesses, and mild crypt architectural distortion; (B) resected in-stream colon showing similar but less severe changes.

In February 1993, he presented for the first time with bleeding and passage of mucus through the colostomy and continued passage of mucus and blood from the residual rectal stump. Treatment with oral corticosteroids was ineffective. A colonoscopy through the colostomy revealed congested and erythematous mucosa up to the splenic flexure with macroscopically normal looking mucosa proximally. Biopsy specimens of the caecum showed active chronic inflammation, which was more severe distal to the splenic flexure.

In March 1994, a colectomy and removal of residual rectal stump and anal canal was performed and an end ileostomy fashioned. Histologically the colectomy specimen showed active chronic inflammation throughout its length with occasional crypt abscesses (fig 2B). The rectal stump showed active chronic inflammation with lymphoid follicles and occasional crypt abscesses (fig 2A). He subsequently made a good recovery and steroid therapy was discontinued.

Discussion

To our knowledge, this is the first description of patients without pre-existing inflammatory bowel disease who having presented originally with diversion colitis, subsequently developed clinical, endoscopic, and histological evidence of ulcerative colitis in the in-stream colon. The possibility that the initial presentation in both patients was merely the onset of ulcerative colitis in the rectosigmoid stump rather than diversion colitis cannot be entirely discounted, but would seem unlikely in view of the temporal relation between colonic diversion and the onset of distal colitic symptoms. Unfortunately histology is neither sufficiently specific nor consistent to be used to explore this possibility

further. Although lymphoid follicles may be unusually prominent in some patients with diversion colitis,⁵⁻⁸ as they were in the rectal stump of patient 2 (fig 2A), the microscopic abnormalities described in diversion colitis may also occur in ulcerative colitis and cannot distinguish between the two diseases in individual patients.

The contention that in each patient diversion colitis and ulcerative colitis developed as two separate and unrelated events is also not compelling. We suggest, on the contrary, that in both patients, diversion colitis in the rectosigmoid stump acted as a trigger for the onset of ulcerative colitis.

Microscopic evidence of mild inflammation affecting the in-stream colon has been described earlier in the majority of 36 patients with diversion colitis in a prospective study.⁵ Although that study showed that inflammation in the diverted bowel can be associated with similar histological changes in anatomically discrete segments of in-stream colon, none of the subjects reported had clinical or colonoscopic signs of colitis, perhaps because they lacked genetic or other predisposing factors for clinically overt ulcerative colitis.

Indirect support for the proposal that inflammation in one site can trigger ulcerative colitis in an anatomically separate part of the colon comes from data reporting the high frequency of discontinuous inflammation in the appendix,^{1,2} and the rarity of appendectomy in patients with ulcerative colitis.³

How might diversion colitis have precipitated the onset of ulcerative colitis in the in-stream colon? Changes in colonic bacterial flora^{11,12} and depletion of luminal short chain fatty acids^{7,9,13} have been proposed as aetiopathogenic factors for both diseases. However, it is improbable that either of these acted as a common pathogenic mechanism for the diversion colitis and ulcerative colitis occurring in our patients, since the luminal flora and short chain fatty acid content are likely to have been very different in the diverted and in-stream segments of bowel.

It is more probable that leucocytes, sensitised and activated in the vasculature of the inflamed diverted colon, circulated and were recruited to the mucosa through the phenotypically similar vascular endothelium of the in-stream large intestine. There they, in turn, may have caused an inflammatory process, which developed into ulcerative colitis in our genetically or otherwise predisposed patients. Anticolonic autoantibodies may also conceivably have been generated as a result of epithelial damage in the inflamed diverted colorectum. These could then also have targeted and contributed to inflammation in the in-stream colon. It is more difficult to see how systemic and inflammatory mediators produced in excess in the diverted colon could have initiated colitis elsewhere, as their distant actions would not have been organ specific.

A cellular mechanism has been proposed for the possible triggering effect of appendiceal inflammation in ulcerative colitis.^{2,3} In this setting, primed T helper lymphocytes from the

inflamed appendix¹⁴ may home in on more distal colonic mucosa, initiating inflammation there. This concept is supported by experiments in which the inflammatory bowel disease of T cell receptor α mutant mice could be prevented by appendectomy.¹⁵

The proposal that diversion colitis triggers ulcerative colitis in the in-stream colon in occasional predisposed individuals could have been tested in our two patients by total removal of the diverted large bowel. It is possible that, unless a self-perpetuating inflammatory process had already been established in the in-stream colon, this procedure could have led to remission of their ulcerative colitis. However, in patient 1, her other medical problems precluded elective abdominal surgery, and in patient 2, his initial desire to retain the possibility of anal evacuation in the long term prevented total excision of the rectosigmoid segment.

In conclusion, we have described two patients in whom diversion colitis appears to have precipitated ulcerative colitis in previously normal in-stream colon. Diversion colitis may be a risk factor, albeit rare, for ulcerative colitis in genetically or otherwise predisposed people: indeed, perhaps diversion surgery should be avoided for example, in patients who are pANCA positive. Lastly, the cases described here suggest that ulcerative colitis may be initiated by inflammation of other cause at anatomically discontinuous sites in the large bowel.

Note added in proof

Since the acceptance of this paper for publication, we have encountered a third patient in whom diversion colitis seemed to trigger in-stream ulcerative colitis about a year later. This non-smoking, strongly cANCA positive, 45 year old woman had a left end colostomy for severe diarrhoea after resection of 90 cm of small bowel for a volvulus in 1990. In 1997,

overt diversion colitis was diagnosed in her rectosigmoid stump. In 1998, recurrent diarrhoea through the stoma prompted colonoscopy with biopsy in March and early September: both examinations were normal. After frankly bloody diarrhoea in October 1998, further endoscopy of the in-stream colon showed gross macroscopic and microscopic ulcerative colitis to the caecum, with normal terminal ileum. The patient opted for an ileostomy with excision of the in-stream colon and rectal stump.

We would like to thank Professor NS Williams and Mr J Rogers for allowing us to report on their patients.

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