Ulcerative colitis of the appendix (‘ulcerative appendicitis’) mimicking acute appendicitis

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RL Barclay, WT Depew, KK Taguchi, DJ Hurlbut. Ulcerative colitis of the appendix (‘ulcerative appendicitis’) mimicking acute appendicitis. *Can J Gastroenterol* 2001;15(3):201-204. Appendiceal involvement in ulcerative colitis may occur in the setting of either diffuse or distal disease, and is usually diagnosed incidentally at the time of proctocolectomy. The present patient had a rare case of ‘ulcerative appendicitis’ occurring on a background of clinically quiescent ulcerative colitis, and presented with the signs and symptoms of acute appendicitis.

Key Words: *Appendicitis; Ulcerative colitis*

Colite ulcéreuse de l'appendice (« appendicite ulcéreuse ») imitant l'appendicite aiguë

RÉSUMÉ : Dans certains cas de colites ulcéreuses, une atteinte de l'appendice peut survenir dans le contexte de maladies diffuses ou distales, et habituellement ce problème est constaté et diagnostiqué au cours de la proctocolectomie. Ce patient souffrait d'un cas rare d'« appendicite ulcéreuse », survenue dans un contexte de colite ulcéreuse cliniquement inactive, et il se plaignait des signes et symptômes d'une appendicite aiguë.

Ulcerative colitis is a chronic, relapsing inflammatory disorder of the large bowel. Its cardinal clinicopathological features are rectal bleeding, anemia and contiguous mucosal involvement beginning in the rectum and extending proximally to varying extents. Appendiceal involvement in ulcerative colitis may occur either in the setting of continuous disease of the entire colon (pancolitis) (1) or as discontinuous (‘skip’) appendiceal lesions, isolated from distal disease (2). A rare case of active ulcerative disease of the appendix is presented, in which the clinical presentation simulated acute appendicitis.

CASE PRESENTATION

In 1985, a 67-year-old man presented with rectal bleeding. Colonoscopy initially revealed only diverticulosis, and random biopsies showed nonspecific inflammation. His symp-

toms resolved spontaneously until one year later, when he developed intermittent, small volume rectal bleeding. Stool cultures were negative, and sigmoidoscopy showed proctitis limited to the distal rectum. The bleeding responded to a short course of topical steroid therapy, but 16 months later, he developed persistent, bloody diarrhea associated with a weight loss of 11.2 kg over a three-month period. His symptoms resolved after a course of empirical prednisone, and repeat sigmoidoscopy three months later showed no active disease. Biopsies were compatible with chronic, inactive ulcerative colitis. The patient was maintained on oral sulfasalazine (Salazopyrin, Pharmacia & Upjohn) and entered a long (seven-year) period of clinical remission.

In 1992, colon cancer in the patient's sister prompted a screening colonoscopy in the authors' patient, which surprisingly revealed diffuse, mucosal pseudopolyposis (repre-

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Figure 1 **A** Appendix shows inflammation confined to the mucosa (20× magnification), without ulceration or deeper mural involvement. **B** The active inflammation is characterized by crypt epithelial infiltration with neutrophils (cryptitis) and numerous crypt abscesses (**C** 200× magnification; **D** 400× magnification).

senting the sequelae of prior severe colitis) extending from the sigmoid to the ascending colon; however, there was no macroscopically active inflammation. Extensive biopsies from all segments showed chronic inflammatory changes. A single tubular adenoma was also identified and removed.

The patient remained in clinical remission and underwent yearly surveillance colonoscopy. There was no change in the disease pattern until 1995, when he had a reactivation of pancolitis, which settled after a short course of oral prednisone. Surveillance colonoscopy in December 1997 showed the aforementioned pseudopolyposis and no grossly active colitis. Multiple biopsies, including several specimens obtained from the cecum, showed neither chronic nor acute inflammation. There was no evidence of gland branching, chronic changes or dysplasia.

Five months later, while still free of the typical symptoms of active colitis, he experienced acute onset of rapidly progressive right lower quadrant pain lasting 12 h, which was associated with diaphoresis. Physical examination revealed pyrexia and focal peritoneal irritation in the right lower quadrant. There was leukocytosis with a predominance of granulocytes, and a clinical diagnosis of acute

appendicitis was made. At laparotomy, the appendix had a normal gross appearance, and no other intra-abdominal pathology was identified. The appendix was removed.

Pathology showed acute inflammation confined to the mucosa, with neutrophilic crypt epithelial infiltration (cryptitis) and crypt abscesses consistent with appendiceal involvement by ulcerative colitis (Figure 1). The inflammation did not extend beyond the mucosa, and no fecalith was identified. Following appendectomy, the patient made a rapid and uneventful recovery; he was asymptomatic one day after the operation and was discharged home on day 2. Six months later, the colitis remained in complete clinical remission, and there has been no recurrence of right lower quadrant symptoms.

DISCUSSION

This was the first reported case of active ulcerative appendicitis in which the clinical presentation simulated acute appendicitis. The most convincing evidence implicating the appendix as the source of this patient's sudden illness was his rapid and complete return to normal health almost immediately following appendectomy. It is possible that the

pathological finding of ulcerative appendicitis was an incidentally detected marker of chronically active, diffuse colitis, rather than a localized, inflammatory process. However, the patient had no symptoms of active luminal disease at the time of presentation; also, random biopsies (including several from the cecum) obtained shortly before presentation showed no evidence of inflammation. Furthermore, no active cecal disease was evident on numerous previous surveillance colonoscopies. These features thus support active ulcerative appendicitis, in the setting of remote and currently inactive pancolitis, as the cause of his acute illness.

The appendix is affected in at least half of all cases of ulcerative colitis requiring surgery (3). Appendiceal skip lesions – namely, discontinuous involvement of the appendix in which the remainder of the cecum is spared – was once thought to be rare in ulcerative colitis (4). Davison and Dixon (5) questioned this perception by demonstrating isolated ulcerative appendicitis in 21% of 62 proctocolectomy specimens from ulcerative colitis patients. Our patient is another case of discontinuous ulcerative appendicitis and is, to our knowledge, the first case detected at appendectomy, rather than incidentally at colectomy.

Acute appendicitis is relatively uncommon in patients with ulcerative colitis (6-8). While some authors (6) believe that appendectomy may confer protection against ulcerative colitis, others (8) speculate that this lower frequency of acute appendicitis may stem from a downregulated immune response associated with chronic ulcerative colitis, which may be less susceptible to stimulation by an etiological, perhaps viral, pathogen of acute appendicitis (9). Despite our patient's clinical presentation of 'appendicitis', the absence of transmural inflammation in the resected appendix suggests an unusual pathophysiological mechanism for his presenting symptoms and signs. Traditional teaching has always held that the acute abdominal pain of appendicitis arises due to peritoneal irritation from the adjacent inflamed serosa of the appendix. However, a certain proportion of appendiceal specimens removed from patients with clinically suspected appendicitis contain only mucosal inflammation (10,11). For example, of 942 emergency appendectomy specimens examined by Pieper and colleagues (10), 77 (8%) contained inflammation limited to the mucosa. Likewise, in our patient, appendiceal inflammation was confined to the mucosa; there was no histological evidence of serosal or peritoneal inflammation. We are not aware of any other reported cases of 'acute ulcerative appendicitis', and no study of appendiceal histopathology has specifically examined the incidence of acute appendicitis-like pain in patients with ulcerative colitis involving the appendix. Okawa and colleagues (12) noted skip lesions at the mouth of the appendix in 10 of 56 (18%) of their patients with ulcerative colitis, but none of these patients were noted to have acute abdominal pain.

Although speculative, we suggest that our patient's acute appendiceal pain syndrome derived from a complex interplay of mucosal immune, vascular and neurogenic factors

(13), driven by a localized, active focus of ulcerative colitis. In contrast to the remainder of the colon, inflammation in the vermiform appendix was incompletely suppressed, perhaps due, in part, to suboptimal delivery of 5-aminosalicylate therapy to the appendiceal lumen. The appendix is a highly vascular organ with a rich lymphoid complement of B cells and CD4 T-helper cells, making it an important component of the gut-associated mucosal immune system (14,15). These immune cells participate in the mucosal inflammation of ulcerative colitis through various mechanisms, including the elaboration of cytokines and vasoactive mediators (13). Both mucosal and systemic concentrations of such substances are increased in active ulcerative colitis (16,17). In our patient, the markedly increased numbers of neutrophils in the appendiceal mucosa could have reflected a response to local release of neutrophil chemotactic agents, such as leukotriene B₄ (17). In addition, there is a close association between subepithelial neuroendocrine cells and nerve fibres of the mucous plexus in the appendix (18). The mucosal release of serotonin, a potent vasoactive and neurogenic mediator, has been implicated in the pathogenesis of acute appendiceal pain, even without significant inflammation (19,20).

Thus, it seems plausible that with the degree of acute mucosal inflammation observed in our patient, the combination of cytokine release (17), localized ischemia mediated by alterations in endothelial integrity (21) and activation of neurogenic inflammation could result in sufficiently increased tension and spasm within the inflamed bowel wall (22) to cause acute appendicitis-like pain. The observation of clinical appendicitis in the setting of mucosally limited inflammation has been reported in patients with appendiceal *Campylobacter* infection (23) and with appendiceal sarcoidosis (24), suggesting that diverse etiologies may similarly activate these neurohumoral pathways in susceptible individuals.

In summary, the present report describes a patient with discontinuous, ulcerative appendicitis, whose clinical presentation mimicked acute appendicitis. Appendectomy provided both the diagnosis and the cure of this acute illness. Although rare (and perhaps under-recognized), acute right lower quadrant pain in the setting of clinically quiescent ulcerative colitis may herald active ulcerative appendicitis, rather than typical suppurative appendicitis.

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