Case report

Crohn’s disease and ulcerative colitis in the same patient

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SUMMARY A well documented case of a patient with both Crohn’s disease and ulcerative colitis is presented. A 29 year old woman underwent resection of her terminal ileum and ascending colon for typical Crohn’s disease with ileocolitis. Eleven years later, an ileoproctocolectomy was performed for typical ulcerative colitis involving the left colon. The resection specimen also showed evidence of colonic Crohn’s disease near the anastomotic site. This unusual case shows that Crohn’s disease and ulcerative colitis can occur in the same patient. The rarity of such cases supports the concept that Crohn’s disease and ulcerative colitis are separate entities, rather than different manifestations of the same disease process.

Crohn’s disease and ulcerative colitis are the two well recognised forms of idiopathic inflammatory bowel disease. As the aetiologies (or aetiology) of idiopathic inflammatory bowel disease are unknown, these entities are distinguished on the basis of their pathologic and resulting clinical, and radiographic features. Some authors have suggested that these two forms of idiopathic inflammatory bowel disease are merely different manifestations of the same disease and represent the ends of a histopathologic spectrum.1 2 Over the last two decades, however, reliable pathologic criteria have evolved to separate the manifestations of Crohn’s disease and ulcerative colitis in the small and large bowel.3–6 Credible reports of patients with both Crohn’s disease and ulcerative colitis are rare,7–9 although many such cases were described before differential diagnostic criteria were established.10–12 We present a patient with well documented pathologic evidence of Crohn’s disease and ulcerative colitis. The implications for aetiology and differential diagnosis of idiopathic inflammatory bowel disease are discussed.

Case report

A 29 year old white woman presented to The Johns Hopkins Hospital in 1968 with a fissure in ano which healed with conservative measures. Four months later she developed rectal bleeding. Proctoscopy showed slightly inflamed rectal mucosa, but no biopsy was performed. Barium enema showed a stricture in the ascending colon; the caecum and colon distal to the hepatic flexure were normal. An ileocolotomy was performed with primary ileocolonic anastomosis in the transverse colon.

The resection specimen from 1969 consisted of 30 cm of ileum and 25 cm of colon. The gross and histopathologic findings of Crohn’s disease were present in the ileum and ascending colon. Strictures with overlying ulcers were found 6 cm proximal to and several centimetres distal to the ileocaecal valve (Figs. 1a, 1b). The mucosa of the terminal ileum showed loss of plicae and small ulcers. Histopathologic sections from the strictures showed fissuring ulceration with transmural inflammation and fibrosis (Figs. 1c, 1d). In addition, non-caseating epithelioid cell granulomas were present in the pericolic soft tissue (Fig. 1d) and regional lymph nodes. The colonic mucosa between the caecum and the stricture was normal.

Postoperative barium enema showed mild oedema in the left colon, but a repeat study one year later was normal. Thirteen months after the right ileocolectomy, the patient again developed rectal bleeding. Sigmoidoscopy revealed diffusely friable, granular rectal mucosa suggesting active ulcerative colitis, as did the biopsy findings. Over the next two years, the patient was treated with oral steroids and had periods of remission.

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Exacerbations characterised by diarrhoea, rectal discomfort, and stool blood and mucus occurred every few months. Rectal biopsies during exacerbations repeatedly showed low grade active inflammatory bowel disease with features suggesting ulcerative colitis. Nine years after the first resection, small bowel contrast studies and barium enema showed narrowing and mucosal irregularity in the sigmoid colon and rectum with normal proximal colon, interpreted as ulcerative colitis. Repeat barium enema 22 months later showed development of shortening of the colon. Because of repeated

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**Fig. 1** Specimen from right ileocolectomy for Crohn's disease in 1969. (a) Ileocaecal region of gross specimen. Ulceration and loss of plicae are seen in portion of terminal ileum (TI) immediately proximal to ileocaecal valve (ICV). (b) Ascending colon of gross specimen. Segmental ulceration with stricture formation (arrow) is present. Colon between the caecum (*) and stricture is grossly uninvolved. (c) Histopathologic section of abnormal terminal ileum shown in (a). Active fissuring ulcer (U) is present. Underlying submucosa shows scarring (*) and aggregates of lymphocytes (arrow) extending to muscularis propria (MP). (H & E, ×8). (d) Histopathologic section of ascending colon stricture shown in (b). Active fissuring ulcer (U) is present with underlying transmural inflammation extending into muscularis propria (MP). Non-caseating epithelioid cell granuloma (arrow) with multinucleated giant cell (see inset) is present in the pericolonic soft tissue. (H & E, ×8; inset ×230).
Fig. 2  Specimen from ileoproctocolectomy for ulcerative colitis in 1980. (a) Gross specimen. Haustra are lost and mucosa is featureless throughout entire left colon, including rectum. Ileocolonic anastomotic site (ICA) is in transverse colon. (b) Histopathologic section of rectosigmoid region. Mucosa shows marked generalised atrophy. Chronic inflammation is limited to mucosa, rarely extending deeper than muscularis mucosae (MM). Muscularis propria (MP) and pericolonic tissue is normal. (H & E, ×21) (c) Histopathologic section of rectosigmoid region shown in (b). Marked crypt loss is evident. Remaining crypts show prominent distortion and epithelial mucin depletion. Muscularis mucosae (MM) contains scattered chronic inflammatory cells (H & E, ×130). (d) Histopathologic section of ileocolonic anastomotic site (ICA) represented by scar through muscularis propria and transition from small intestinal to colonic mucosa. Focal active inflammation (arrow) is present in colonic mucosa. (H & E, ×21). (e) Histopathologic section of colonic mucosa near region indicated by arrow in (d). Granulomatous inflammation characterised by epithelioid histiocytes (short arrow) and a multinucleated giant cell (long arrow) is present near an erosion. Epithelial mucin is maintained. Although located near the anastomosis site, these features suggest clinically inapparent Crohn's disease involving this area of the colon. (H & E, ×310).
exacerbations of her inflammatory bowel disease, 11 years after her first resection she underwent ileo-proctocolectomy at age 41.

The resection specimen (Fig. 2a) showed continuous, uniform loss of hastra and mucosal atrophy involving the entire left colon including the rectum. These features and their distribution are those of ulcerative colitis. Histopathologic examination confirmed the mucosal atrophy characterised by marked crypt loss with distortion of those crypts remaining, distributed uniformly throughout the left colon. In addition, acute and chronic inflammation was present in the mucosa without involvement of the submucosa or deeper layers (Fig. 2b). The acute inflammation was confined largely to the rectum and was accompanied by generalised mucin depletion (Fig. 2c). The distal predominance of the active inflammation, destruction of crypt architecture, and mucin depletion are histopathologic features of ulcerative colitis. No anal or perirectal inflammation was present. Granulomas, which were easily identified in the previous resection, were not found in the left colon despite examination of histologic sections from 16 areas. The colon in the mid-portion of the specimen was normal in three tissue blocks. In the colonic mucosa near the anastomotic site (Fig. 2d), however, focal non-specific inflammation and granulomatous inflammation with epithelioid histiocytes and multinucleated giant cells (Fig. 2e) were present, suggesting clinically apparent recur- descent Crohn's disease. The ileum was uninvolved in two tissue blocks.

Discussion

Crohn's disease and ulcerative colitis are the two well recognised forms of idiopathic inflammatory bowel disease. The accepted pathologic criteria for the differentiation of these two patterns of idiopathic inflammatory bowel disease in the colon were emphasised by Warren and Sommers in 1954 and Lockhart-Mummery and Morson in 1960. The criteria were expanded subsequently by others. Briefly, ulcerative colitis is characterised by continuous loss of hastra and mucosal atrophy on gross examination. The findings consistently involve the left colon, including the rectum. The histopathologic features of ulcerative colitis include diffuse acute and chronic inflammation generally limited to the mucosa, mucosal atrophy with crypt loss and distortion, and epithelial mucin depletion. The gross pathologic features of colonic Crohn's disease, on the other hand, include discontinuous gross involvement with intervening normal areas ('skip lesions'), a more frequent right sided distribution and relative rectal sparing. The ileum is involved also in a majority of the cases with colonic involvement. The histopathologic features of Crohn's disease include fissuring ulceration; transmural extension of aggregates of lymphocytes into the deep layers of the bowel wall and pericolonic soft tissue; and discontinuous or focal mucosal inflammation. The most characteristic feature, of course, is the non-caseating epithelioid cell granuloma, which has been reported in up to 63% of Crohn's disease cases.

Despite the development of reliable differential criteria, difficulty still arises in the clinical, radiographic, and occasionally the pathologic distinction between ulcerative colitis and Crohn's disease. Such difficulties continue to raise questions regarding the nosology and ultimately the aetiology of these diseases. Historically, as pathologic criteria began to evolve for the separation of colonic Crohn's disease from ulcerative colitis, series of cases were reported describing coexistence of the two entities in individual patients. These early reports, however, greatly overestimated the proportion (up to 12.8%) of cases which showed such coexistence. The confusion in terminology which existed in the older literature contributed to this overestimation. Counsell, for example, pointed out the term 'ileocolitis' was used variously by different authors to mean involvement of terminal ileum and colon by Crohn's disease, retrograde (or 'backwash') ileitis in ulcerative colitis, or the actual coexistence of Crohn's disease and ulcerative colitis in an individual patient. Secondly, many of the older reports were published before the establishment of differential criteria. For example, French and Vander, and Counsell described the presence of granulomas in the colonic wall of specimens said to show ulcerative colitis, but almost certainly representing Crohn's disease of the colon.
Aside from problems of terminology, overlap in the pathologic features of Crohn's disease and ulcerative colitis can occur in the occasional patient. Mucosal changes like those in ulcerative colitis are sometimes present in some areas of a colectomy specimen showing otherwise typical Crohn's disease. The greatest overlap, however, is observed in specimens from patients who undergo urgent surgery for fulminant colitis ("toxic megacolon"). Specifically, deep ulceration with transmural inflammation is common in fulminant ulcerative colitis, and may be interpreted as evidence of Crohn's disease. Price and Morson referred to such difficult cases as 'colitis indeterminate', indicating that final classification cannot be determined in the specimen under consideration. Review of sequential pathologic material from such patients, including pre- and post-operative biopsies, will allow a large proportion of these cases to be classified as either ulcerative colitis or Crohn's disease. Furthermore, difficulty in the pathologic distinction between ulcerative colitis and Crohn's disease in a particular specimen does not imply an overlapping form of inflammatory bowel disease in the patient. Rather, it signifies a lack of findings strongly favouring either ulcerative colitis or Crohn's disease in the particular biopsy or resection specimen under consideration.

In contrast with apparent overlap between Crohn's disease and ulcerative colitis based upon insufficient distinguishing features, some authors have reported that overlap exists because Crohn's disease and ulcerative colitis may actually represent the same disease. Also, Shorter et al suggested that, while ulcerative colitis and Crohn's disease are not necessarily the same nosologic entity, they may merely represent separate responses to different antigenic challenges, or individualised responses to similar antigenic stimuli.

As knowledge of the pathologic manifestations of ulcerative colitis and Crohn's disease has evolved, recent case reports of coexistent ulcerative colitis and Crohn's disease have provided acceptable pathologic documentation. As a report of synchronous ulcerative colitis and Crohn's disease by Voitk et al illustrates, however, emergency colectomy performed for fulminant colitis complicates interpretation. By contrast, we present a patient with Crohn's disease and ulcerative colitis whose course is well documented pathologically in two resection specimens and serial biopsies. Furthermore, our case was not complicated by fulminant colitis and was evaluated with strictly applied pathologic criteria in numerous histopathologic sections. This case, therefore, provides strong evidence that Crohn's disease and ulcerative colitis can occur in the same patient.

The frequent overlap of ulcerative colitis and Crohn's disease in earlier series of cases was cited as evidence that these two forms of idiopathic inflammatory bowel disease merely represented the ends of a spectrum, as various manifestations of a disease could occur together frequently in a particular patient with that disease. Most of such cases with 'overlap', however, were based on loosely applied criteria and therefore spurious. The actual rarity of patients with both ulcerative colitis and Crohn's disease supports the alternative concept that these two types of idiopathic inflammatory bowel disease are separate entities, as the chances of a given patient having two uncommon and unrelated diseases are small. Indeed, Eyer has pointed out that the calculated rate of coincidence of ulcerative colitis and Crohn's disease based on prevalence data for each entity would predict between 15 and 60 patients in the United States with both diseases. The number of reported bona fide cases of Crohn's disease and ulcerative colitis is far fewer than these data would suggest. Although such cases of ulcerative colitis and Crohn's disease in the same patient are, therefore, of considerable interest, the final answer to the question of the relationship between these two forms of idiopathic inflammatory bowel disease depends on the answer to the question of aetiology.

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