The Pathogenesis of Inflammatory Polyps

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Eighty-six consecutive colonic resection specimens for inflammatory bowel disease were studied to determine the modes of inflammatory polyp formation. The two major groups of inflammatory polyps were (1) polypoid mucosal tags due to undermining ulceration and (2) mature inflammatory polyps composed of mucosa, muscularis mucosae, and a submucosal core. Mature inflammatory polyps were derived from polypoid mucosal tags after regeneration and the adjacent mucosa showed regenerative changes and submucosal scarring. The study confirms that ulceration which undermines the muscularis mucosae is the major precursor of inflammatory polyps. [Key words: Inflammatory polyps, pseudopolyps; Inflammatory bowel disease; Crohn's disease; Ulcerative colitis, ulceration, undermining, muscularis mucosae]

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THE TERM PSEUDOPOLYPS, once used to include ragged mucosal remnants, granulation tissue polyps, mixed mucosal-granulation tissue polyps, and adenomatous polyps,[1] has now been replaced by the term inflammatory polyps.[2-4] Adenomatous or dysplastic polyps are recognized as separate entities. In clinical series, inflammatory polyps are found in 12.5 to 19 percent of patients with ulcerative colitis.[5-7] They are said to be less common in Crohn's colitis. Inflammatory polyposis is strongly associated with a previous episode of severe colitis, usually necessitating hospital admission and sometimes causing toxic dilatation.[7] This study is an investigation of the hypothesis that undermining ulceration is the main event in the pathogenesis of inflammatory polyps.

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Material and Methods

Eighty-six consecutive specimens of large bowel excised for inflammatory bowel disease were studied. Forty-nine were diagnosed by the usual criteria as ulcerative colitis, 35 as Crohn's disease, and two as colitis indeterminate.[8] The specimens were examined in the fresh state, opened along the anterior tenia coli and pinned flat on styrofoam before fixation in phosphate buffered formalin. After fixation each specimen was photographed, a line diagram was drawn, polyps were counted, and the range of height of polyps was measured. Blocks for histology were numbered and marked on the drawing. The depth of ulceration or regeneration was assessed histologically, with particular reference to penetration through the muscularis mucosae. Hematoxylin and eosin and trichrome stains were used for this assessment and step sections were cut as required. A polyp was defined as a portion of tissue projecting into the lumen from the internal surface of the gut. Anal tags, cobblestoned mucosa, and polyps which proved to be dysplastic or metaplastic were not included. The presence of mucosa, muscularis mucosae, submucosa, and granulation tissue within polyps was tabulated.

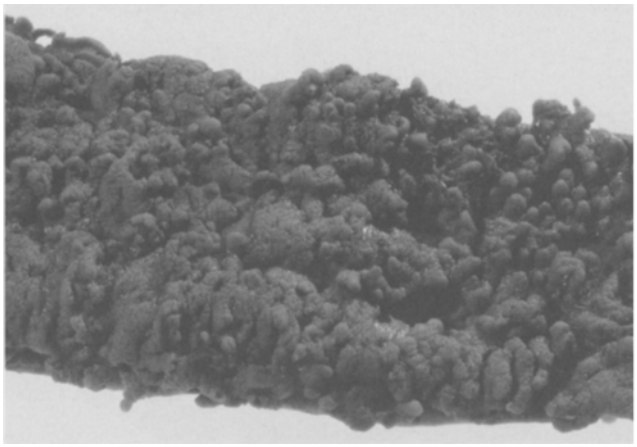

FIG. 1. Polypoid ragged mucosal remnants in ulcerative colitis. The mucosa is uniformly inflamed, congested, and granular, and there are many polypoid mucosal projections due to undermining ulceration.

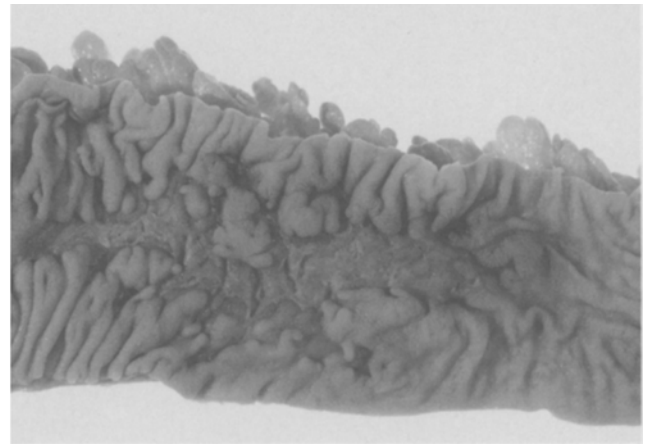

FIG. 2. Small polypoid mucosal tags in Crohn's disease are forming by undermining at the margins of a large discrete ulcer. Note the partial preservation of mucosal folds on the left.

Results

Inflammatory polyps were found in 46 specimens (31 ulcerative colitis and 15 Crohn's disease) but only 18 specimens contained more than 20 polyps. The greatest depth of ulceration or repair, deeper than the muscularis mucosae, occured in 42 of the 46 cases with polyps and in 22 of the 40 cases without polyps ($P < 0.01$). Descriptively, inflammatory polyps were of two main types—polypoid mucosal tags and mature inflammatory polyps.

Polypoid mucosal tags were due to active undermining ulceration and were present in 11 specimens (Figs. 1 and 2). They measured from 0.3 to 1.5 cm in height. In all cases active ulceration undermined the muscularis mucosae and the polypoid remnants were composed of mucosa and muscularis mucosae. In Crohn's disease, polyps arise at the margins of large discrete ulcers (Fig. 2) but in ulcerative colitis they result from confluence of mucosal ulcerations which arise in the heavily inflamed mucosa (Fig. 1).

Mature inflammatory polyps were surrounded by regenerative mucosa and appeared to derive from mucosal tags after repair and regeneration (Figs. 3 and 4). They varied in size from 0.3 to 5.0 cm and were present in 30 specimens. Four specimens had giant polyps greater than 2.0 cm in height and have been reported elsewhere.[4] The shapes included thin, filiform polyps, branching or bridging polyps, and short, squat polyps. Most mature polyps were of uniform thickness but some giant polyps had enlarged ulcerated heads (Fig. 4). Microscopically mature polyps were covered by mucosa and had a core of muscularis mucosae and submucosa including dilated blood vessels (Fig. 4A). Immediately adjacent to the polyp there was submucosal scarring with either absence or fibromuscular hypertrophy of the muscularis mucosae (Fig. 4B). Granulation tissue was sometimes present at the free ends of polyps and appeared to be due to secondary ulceration. Hemosiderin deposition was infrequent in the cores of the polyps. Rare mature polyps contained not only submucosa but also muscularis propria (Fig. 5). No inflammatory polyps displayed dyplastic elements.

Pure granulation tissue polyps and polyps which were devoid of a connective tissue or submucosal core were

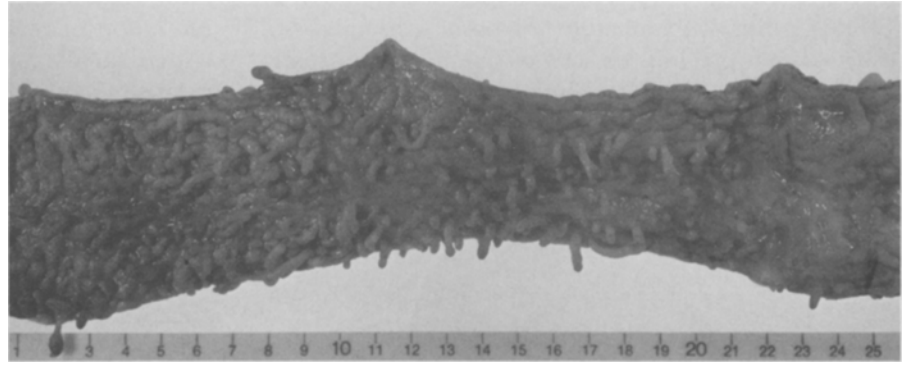

FIG. 3. Multiple, small, mature, inflammatory polyps against a background of flat regenerated mucosa.

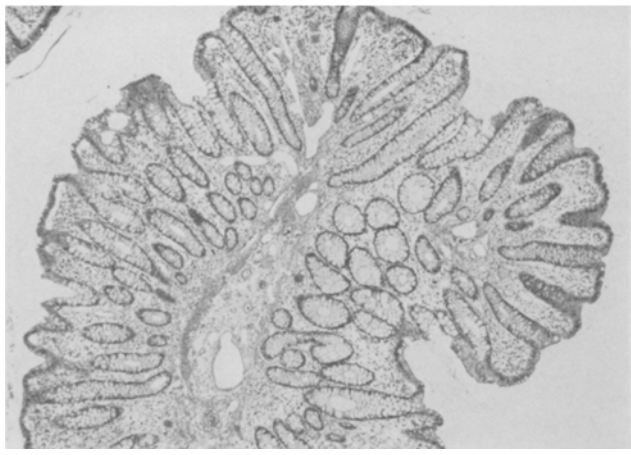

FIG. 4A. A mature inflammatory polyp contains a core of muscularis mucosae and submucosa and is covered by intact colonic mucosa.

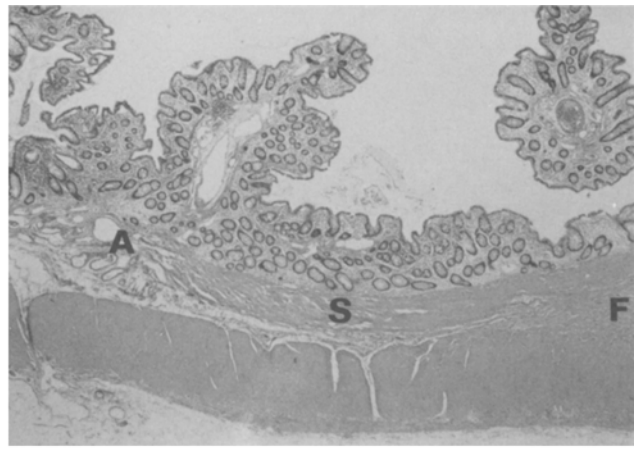

FIG. 4B. The mucosa between inflammatory polyps displays regenerative changes. The underlying muscularis mucosae displays fusion with the circular muscle coat (F), hypertrophy and scarring (S) and is focally absent (A), signs of former ulceration.

found in five specimens. They were usually less than 0.8 cm in height, often solitary, and displayed no firm evidence of undermining ulceration. Pure granulation tissue polyps appeared to arise from lamina propria in which the epithelial components were destroyed and the capillaries proliferated.

Flat mucosal islands in a sea of ulceration were not regarded as polyps and were found in eight specimens of ulcerative colitis and in two specimens of colitis indeterminate which did not contain polyps (Fig. 6). These are the only lesions which might appropriately be called pseudopolyps and were sometimes present in specimens of ulcerative colitis containing polypoid mucosal tags.

Other polyps encountered included solitary pedunculated adenomas in two specimens, sessile areas of dyplasia in three specimens of ulcerative colitis, solitary metaplastic polyps in three specimens, and nodular mucosal elevations due to misplaced glands in the submucosa in one case.

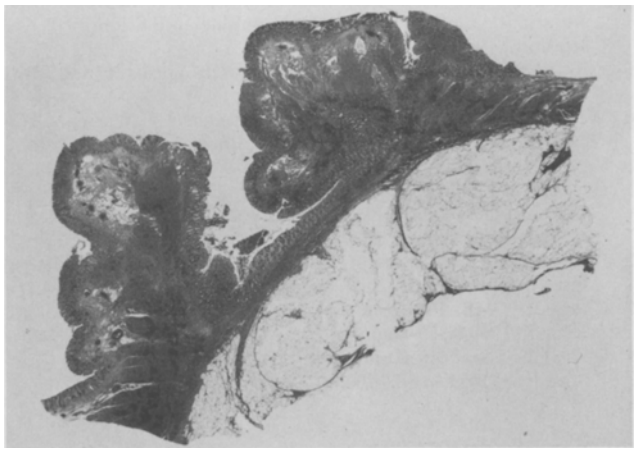

FIG. 5. A healed deep ulcer has resulted in polyps which contain muscularis propria. Grossly this lesion was an irregular sessile mass in a case of Crohn's colitis.

Discussion

This study confirms the long-held view that inflammatory polyps result principally from ulceration which penetrates through and undermines the barrier of muscularis mucosae. The muscularis mucosae appears to have a crucial defensive role in limiting both the depth and the area of ulcers by contracting and thickening when the overlying mucosa is lost. By contrast the submucosa is a loose connective tissue which provides little mechanical barrier to the extension of inflammation and permits mucosal undermining. Nevertheless, deep ulceration is not always accompanied by undermining and other factors such as intraluminal pressure may play a part in undermining.

Large mature inflammatory polyps appear to derive from large mucosal tags and such polyps are drawn out by the propulsive action of the gut, as adenomatous polyps are, and become secondarily traumatized and ulcerated.[4] When granulation tissue is a component of mature inflammatory polyps, it is most often seen at the free end, suggesting secondary traumatization. The cores of mature inflammatory polyps may contain hemosiderin, indicating former hemorrhage due to torsion. Inflammation without full thickness mucosal ulceration appears to produce only small polyps composed of mucosa and exuberant granulation tissue[9] and may be responsible for the inflammatory polyps reported in an ileal blind loop.[10]

The incidence of inflammatory polyps in this series is much greater than in clinical series but is comparable to the 65 percent incidence noted by Goldgraber *et al.*[11] in a surgically resected series and probably reflects the fact that resection is a treatment of last resort where the end stage of recurrent cycles of ulceration and repair are seen. The greater frequency of inflammatory polyps in ulcerative

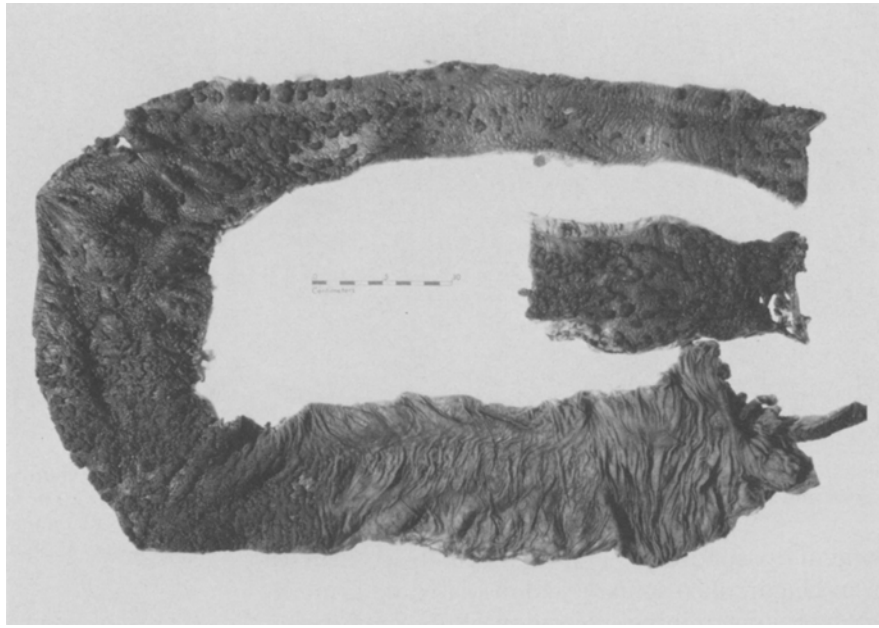

FIG. 6. Flat mucosal islands remain amidst denuded submucosa and do not project as polyps in this case of ulcerative colitis. The ascending colon is spared.

colitis than in Crohn's disease colitis is confirmed although the disparity is not great.

In the present study no dysplastic areas were found in inflammatory polyps. The dysplastic lesions encountered were either pedunculated adenomas or sessile areas of mucosal dysplasia. This is further evidence against the suggestion that inflammatory polyps undergo dysplastic and neoplastic change[12,13] and is in agreement with most authors.[2,3,14]

The terminology applied to polypoid and related lesions is confusing. It is suggested that the term "pseudopolyps" be restricted to flat mucosal islands in a sea of ulceration. The term "polypoid mucosal tags" is suggested for the inflammatory polyps caused by undermining ulceration. The term "mature inflammatory polyps" is suggested for the inflammatory polyps remaining after repair and regeneration have reconstituted the mucosa. The term "inflammatory polyps" is the best one to embrace the whole spectrum of polyps since it has now attained widespread acceptance. However, it is stressed that even though inflammation is the initial underlying pathology, ulceration undermining the muscularis mucosae is more important in generating polyps than inflammation alone.

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