Role of Histologic Inflammation in the Natural History of Ulcerative Colitis

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KEYWORDS

• Ulcerative colitis • Histology • Prognosis • Severity

KEY POINTS

- Several histologic grading systems exist to document the severity of ulcerative colitis (UC).
- These systems have not been validated for universal use in evaluating changes in histologic findings in response to therapy.
- Histologic features have been associated with clinical outcomes in patients with UC.

INTRODUCTION

Ulcerative colitis (UC) is a chronic, episodic inflammatory disorder of the colon that classically affects the rectum, with variable, but continuous, involvement of the proximal colon. The clinical management of UC primarily includes aminosalicylates, corticosteroids, purine antimetabolites, and tumor necrosis factor antagonists, either used sequentially or in combination.[1] The goal of medical therapy is to achieve clinical remission. In current clinical practice, disease activity is monitored by assessing patients' clinical symptoms and severity of colonic inflammation by colonoscopy. Consensus guidelines for clinical practice and trial end points recommend striving beyond resolution of clinical symptoms to achieve endoscopic mucosal healing. Endoscopic mucosal healing in inflammatory bowel disease (IBD) is defined by resolution of visible mucosal inflammation and ulceration. Several studies have shown that mucosal healing, as assessed by endoscopic examination, is associated with better long-term clinical outcomes compared with evaluation of clinical symptoms alone.[2–5]

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However, there is evidence to suggest that endoscopic findings do not necessarily correlate with histologic disease, especially after treatment.[6,7] Numerous scoring systems have been developed to measure the histologic features of UC and predict clinical outcome. The goal of this article is to (1) review the general pathologic features of UC, (2) review effects of medications on histology of UC, (3) discuss the pattern of histology in patients in clinical remission, and (4) address key histologic features predictive of relapse of disease or development of neoplasia.

PATHOLOGIC FEATURES OF ULCERATIVE COLITIS

Depending on the phase of disease and the degree of inflammatory activity, UC is categorized as *normal* (no histologic abnormalities) (**Fig. 1**), *chronic inactive* (**Fig. 2**), or *chronic active* (**Figs. 3** and **4**). Some patients may show activity but without features of chronicity (**Box 1**). Chronic colitis (regardless of presence or absence of activity) is defined by the presence of histologic features indicating chronic repeated tissue injury, such as crypt architectural distortion, crypt atrophy, diffuse mixed lamina propria inflammation, basal plasmacytosis, basal lymphoid aggregates, lamina propria fibrosis, pyloric gland metaplasia, and Paneth cell metaplasia, among others. Histologically, untreated UC involves the colon in a diffuse and continuous manner. It always involves the distal most portion of rectum (except in children in rare cases). UC characteristically involves the mucosa and occasionally the superficial submucosa in severe cases. The inflammatory infiltrate is typically composed of lymphocytes, plasma cells, and a variable amount of eosinophils and neutrophils depending on the severity of activity. The density of plasma cells is usually greatest in the basal region of the lamina propria (termed *basal plasmacytosis*). Basal lymphoid aggregates are also commonly present. A characteristic morphologic feature of UC is crypt architectural distortion. When distorted, crypts usually appear irregular, distended, branched, dilated, and/or foreshortened. It is considered a histologic hallmark of

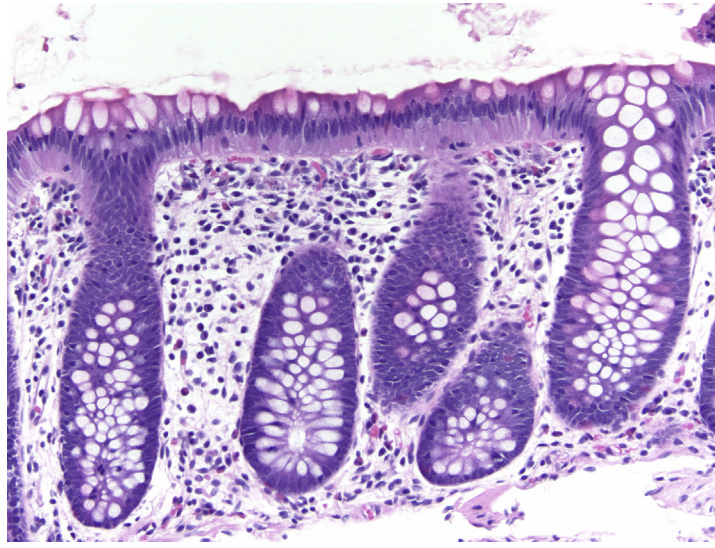

Fig. 1. Normal colon. The biopsy shows crypts that are arranged in a regular, test tube–like configuration. The lamina propria is composed of lymphocytes, plasma cells, and rare eosinophils. Hematoxylin-eosin, original magnification ×200.