The gross pathology of inflammatory bowel disease

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Abstract

Inflammatory bowel disease is a broad term that describes conditions with chronic or recurring immune response, and inflammation of the gastrointestinal tract. The two major types are Crohn's disease and ulcerative colitis. Considering the evaluation of inflammatory bowel disease requires a multidisciplinary approach, gross pathologic examination represents an integral component in its diagnosis and classification. The purpose of this review is to address the following: (1) describe the main gross findings of inflammatory bowel disease that facilitate discrimination between Crohn's disease and ulcerative colitis; (2) discuss atypical/non-classical presentations of inflammatory bowel disease; (3) highlight the importance of gross inspection in detecting and sampling suspicious areas for dysplasia and/or malignancy in the setting of inflammatory bowel disease; and (4) offer practical guidelines for grossing inflammatory bowel disease specimens.

Keywords colorectal carcinoma; Crohn's disease; DALM; dysplasia; dysplasia-associated lesion or mass; gross examination; indeterminate colitis; inflammatory bowel disease; pouchitis; ulcerative colitis

Introduction

Inflammatory bowel disease (IBD) is a broad term that describes conditions with chronic or recurring immune response and inflammation of the gastrointestinal tract. The two major types are Crohn's disease (CD) and ulcerative colitis (UC). Crohn's disease is characterized by recurrent episodes of inflammation involving any part of the alimentary canal, from the mouth to the anus. The inflammation is transmural and can result in strictures, fistulas and perforations. In addition, the inflammation may be discontinuous in distribution resulting in skip lesions throughout the gastrointestinal tract. Similarly, ulcerative colitis is characterized by recurrent episodes of inflammation, but confined to the mucosal layer of the large intestines and within a continuous distribution.

While the exact etiopathogenesis of IBD is unclear, it is hypothesized to be due to a combination of factors that include a genetic predisposition, environmental involvement (e.g. smoking, dietary intake, etc.), and alterations or dysregulation of the immune response. Considerable variation in the epidemiology of IBD has been observed throughout the world. There is a wide

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range of estimates both within and between geographic regions.¹ However, IBD is believed to be associated with industrialized nations with the highest incidence rates and prevalence in North America and Europe. In North America, the incidence of CD and UC ranges between 3.1–20.2 cases and 2.2–19.2 cases per 100,000 person-years, respectively.^{1,2} Similarly, the prevalence of IBD is among the highest in North America.² The prevalence of CD and UC ranges between 26–319 and 37–249 per 100,000 individuals, respectively.^{1,2} Interestingly, within the United States, the prevalence is lower in the South, compared with the Northeast, Midwest, and West.³

Presently, there is no single laboratory test or clinical feature that establishes a diagnosis IBD and/or reliably distinguishes between CD and UC. Gross examination of surgical resection specimens is an integral component in the process of diagnosing and classifying IBD, as well as documenting the extent and severity of disease and to confirm or identify the presence of dysplasia and/or neoplasia. The purpose of this review is to address the following: (1) describe the main gross findings that facilitate discrimination between CD and UC; (2) discuss atypical/non-classical presentations of IBD; (3) highlight the importance of gross inspection in detecting and sampling suspicious areas for dysplasia and/or malignancy; and (4) offer practical guidelines for grossing IBD specimens.

Crohn's disease

Crohn's disease can involve any part of the digestive tract, from the esophagus to the anus. Approximately 30-40% of cases have small bowel involvement only; another 30-40% have ileocolonic disease, and 10-20% of cases have exclusive involvement of the colon. Within the colon, preferential rightsided involvement (including the terminal ileum) with rectal sparing and skip lesions are commonly identified. The mucosa in CD is often characterized by aphthous lesions that coalesce into long, serpentine linear ulcers to form the classic "cobblestone" appearance (Figure 1a). The transmural nature of the inflammation often causes strictures, fissures, fistulas, interloop adhesions, sinus tracts and abscesses (Figure 1b and c). In addition, mesenteric fat wrapping, so-called "creeping fat," may be present, and consists of fat encroachment and enveloping of the antimesenteric surface of the bowel with obliteration of the bowel-mesentery angle (Figure 1d). On cross section, the bowel wall appears thick and rubbery due to edema, inflammation, fibrosis and hypertrophy of the muscularis propria.

Occasionally inflammation in CD is limited to the mucosa and, thus, mimics UC. The key to the diagnosis lies in identifying classic features of CD elsewhere within the GI tract. For example, patients with colonic mucosal changes suggestive of UC but concomitant severe anal/perianal disease or upper gastrointestinal manifestations should be suspected of having CD. In addition, appropriate sampling can be very helpful in these cases; often, undersampling of CD cases can result in a "superficial CD" appearance on microscopic examination.

Pediatric cases

When the classic features of CD are present (e.g., skip lesion, perianal disease, cobblestone mucosa, fissures, strictures, etc.) a



Figure 1 Representative gross findings in Crohn's disease include longitudinal ulceration and cobblestoning of the intestinal mucosa (a), thickening of the bowel wall resulting in strictures (b), fistula formation (c, black arrow indicates an enteroenteric fistula), and a firm and contracted subserosal fat, so-called "creeping fat" (d).

diagnosis is relatively easy to establish. Pediatric cases of CD also have a high frequency of upper gastrointestinal tract involvement, which can be useful to distinguish from UC. However, the diagnosis becomes difficult when disease involvement is confined to the colon and prior mucosal biopsies have failed to identify other features often associated with CD (e.g., granulomata). In these cases, systematic and thorough gross examination with tissue sampling can aid in arriving at a more definitive diagnosis.

Ulcerative colitis

Classically, untreated UC demonstrates a continuous involvement of the colonic mucosa. The disease is usually limited to the colon and tends to be most severe distally. The mucosal changes consist of ulceration, hemorrhage, granularity and friability (Figure 2a—c). These abnormalities can be diffuse throughout the rectum and colon (pancolitis) or isolated to the rectum (proctitis). Anal lesions can sometimes be seen, consisting of fissures, fistulas, skin excoriation and abscesses. Features typically associated with Crohn's disease, such as deep fissuring ulceration, strictures, sinus tract formation, small intestinal involvement, serositis, bowel wall thickening and creeping fat, should be absent.

Some cases displaying classic features of ulcerative colitis also show inflammation of the terminal ileum. This phenomenon, referred to as "backwash ileitis," is seen in approximately 20 –25% of patients with severe pancolitis, presumably related to reflux of colonic contents. Grossly, backwash ileitis can be differentiated from CD involvement of the terminal ileum as it

involves a shorter segment of small bowel. This is usually within 10 cm of the ileocecal valve and lacks transmural involvement. Interestingly, the presence of backwash ileitis is a risk factor for colorectal carcinoma (CRC) in UC patients. Heuschen et al. showed a strong association between backwash ileitis and CRC in patients with UC who undergo proctocolectomy. The authors found CRC in 29% of UC patients with pancolitis and backwash ileitis. In comparison, 9% of UC patients with pancolitis without backwash ileitis and 1.8% of patients with limited left-sided colitis developed CRC.

In some cases, a small area of inflammation surrounding or near the appendiceal orifice can be identified in patients with left-sided UC (Figure 2d). This discontinuous involvement of the cecum is known as a "cecal patch" and should not be confused as a skip lesion of CD.^{6,7} The cecal patch is most common in younger patients and males. In addition, backwash ileitis is more common in UC patients with cecal patch.

Post-treatment UC

After administration of oral or topical therapy, intestinal inflammation in UC patients can become patchy in distribution and show rectal sparing. Kim et al. identified patients with wellestablished UC, who underwent sequential colonoscopy or flexible sigmoidoscopy with biopsies, and found 59% of patients had patchy involvement and/or rectal sparing during the course of their treatment. The discontinuous disease distribution upon initiation of treatment can certainly be mistaken for CD. Further, this can prove challenging when a specific diagnosis of UC or CD has not been established and must be correlated with other clinicopathologic findings.

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